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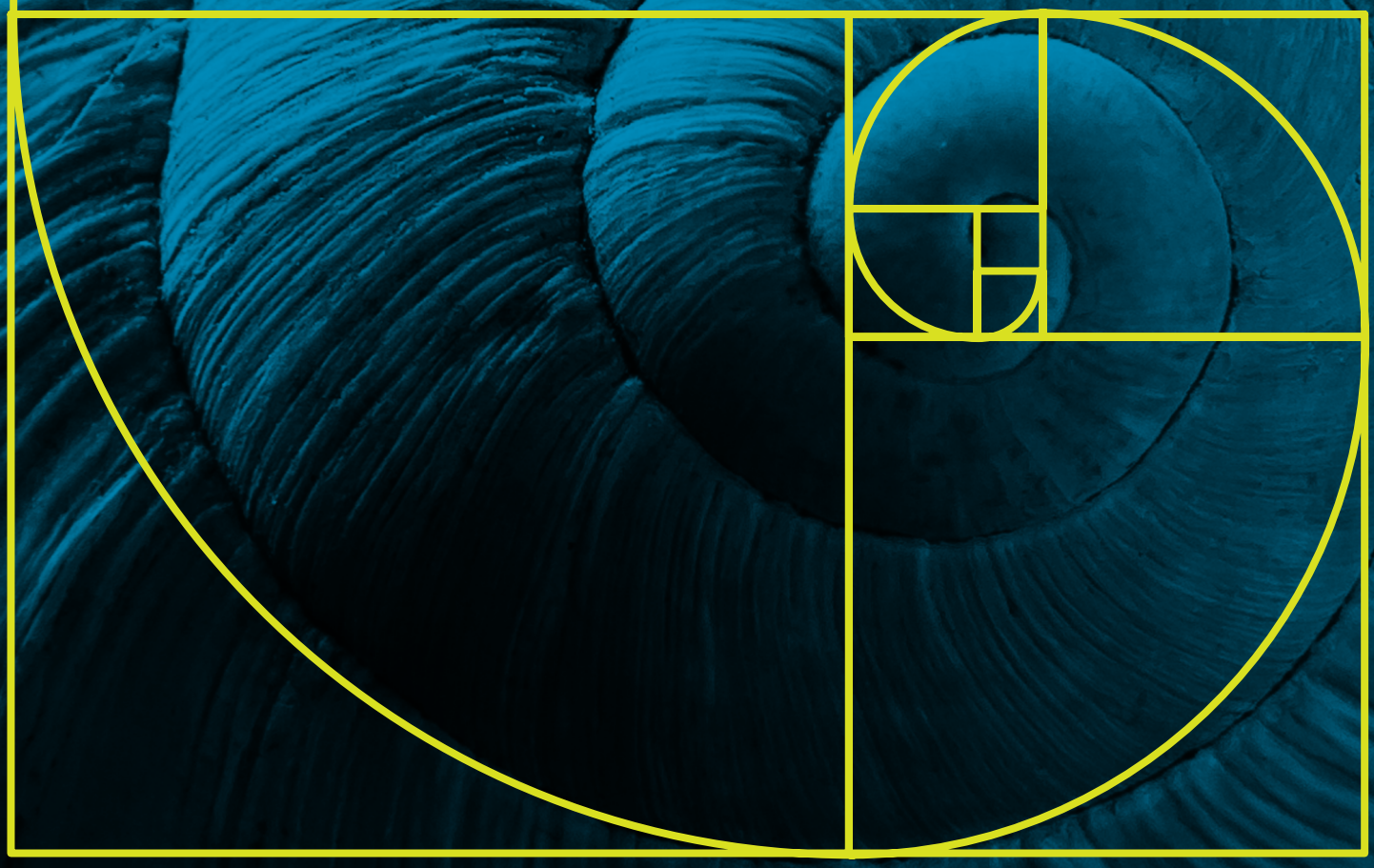
Grupo MatBio-UTEM
Departamento de Matemática
Facultad de Ciencias Naturales, Matemática y Medio Ambiente



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[A partir del presente Vól. la revista MMSB pasa a modalidad de publicación continúa].

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Grupo MatBio-UTEM
Departamento de Matemáticas Facultad de Ciencias Naturales, Matemática y Medio Ambiente

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Editorial

¿MODELOS MATEMÁTICOS?, ¿PARA QUÉ?

Dr. Fernando Momo
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Provincia de Buenos Aires, Argentina

El modelamiento matemático de procesos biológicos es una actividad de larga tradición científica, así como lo es el modelamiento matemático en todas las ciencias, desde las ciencias naturales canónicas, como la Física, hasta las ciencias sociales y humanidades. Es más, hasta podríamos pensar que esta actividad aplicada a problemas biológicos ya puede considerarse una disciplina en sí, e incluso una ciencia independiente (tiene bien definidos sus objetos de estudio, sus metodologías, su vocabulario mínimo).

Pero claro, en toda actividad científica es saludable tomar conciencia y reflexionar de manera sistemática y habitual acerca del sentido de nuestra tarea, de su porqué y su para qué. En este caso, nos proponemos explorar algunas cuestiones metodológicas y epistemológicas que parecieran estar todavía en un terreno de discusión o, al menos, en un terreno de diversidad de interpretaciones.

Veamos; este es un texto editorial que se publica en una Revista de Modelamiento Matemático de Sistemas Biológicos. Entonces, ¿tiene sentido interrogarse acerca de los objetivos del modelamiento? ¿Qué queremos lograr cuando modelamos matemáticamente? ¿Porqué nos interesa particularmente modelar estos sistemas y qué de nuevo, especial o importante pueden aportar los modelos en este terreno?

Si hacemos un breve recorrido en alguna bibliografía fundamental del tema, veremos que las interpretaciones y respuestas no son uniformes y tienen enfoques sutilmente variados.

Por ejemplo, Teresa González Manteiga[1], en su excelente libro, coloca a las matemáticas en un lugar privilegiado, como ciencia central. Apoyada en abundantes citas, que incluyen físicos como Galileo o Newton, filósofos como Kant o Manero, y hasta poetas como Paul Valéry, esta autora coloca al modelado matemático en el lugar del descubrimiento y la abstracción de los principios últimos de la naturaleza. Como vemos, una posición que va mucho más allá de la usual idea instrumental del modelado. En el otro extremo tenemos definiciones que apuntan a la matemática como herramienta. Hastings[2], en su libro de dinámica de poblaciones, dice escuetamente que el objetivo de la biología de poblaciones es comprender y predecir la dinámica de las poblaciones y que el entendimiento, explicación y predicción de esa dinámica requiere de modelos matemáticos. Como vemos, lo que se subraya es un papel auxiliar en el cual el énfasis está puesto en el problema biológico en sí y la matemática toma un papel subsidiario pero útil, porque permite un formalismo que facilita la comprensión y también la predicción cuantitativa. Este enfoque ha sido dominante, sobre todo, en el modelamiento matemático dentro de la ecología de poblaciones, olvidando de hecho que muchos de los conceptos puramente ecológicos que se enseñan como leyes tienen su origen en el análisis de los modelos; por ejemplo, el principio de exclusión competitiva en la formulación de Gause[3].

En una zona intermedia se ubican algunos otros autores; por ejemplo, Gillman y Hails[4] sostienen que un modelo ecológico debe ser capaz de describir los cambios en las variables de interés (por ejemplo, densidad poblacional) con algún grado de exactitud, y también que dichos modelos deben expresarse matemáticamente en razón de la brevedad y formalismo de la descripción, la posibilidad de manipulación del modelo y la posibilidad de descubrir propiedades emergentes que no son aparentes ante el razonamiento no matemático. Como vemos, aquí aparece una novedad fundamental que tiene que ver con el carácter iluminador de los modelos matemáticos en tanto capaces de mostrar lo que no se veía. Esa idea subyace en otros textos, como el delicioso libro de Hernández y Velasco Hernández[5], en el cual los autores nos advierten los peligros de limitar el uso de los modelos matemáticos a la mera predicción y abogan, por el contrario, por un manejo más ambicioso donde el uso de los modelos puede incluso poner a prueba hipótesis o profundizar nuestra comprensión de sistemas muy complejos. De hecho presentan una analogía muy bonita, según la cuál los modelos matemáticos pueden

considerarse también como instrumentos de observación: para observar lo muy lejano podemos usar un telescopio; para observar lo muy pequeño, un microscopio; para observar lo muy complejo, los modelos matemáticos. Es una idea provocadora y estimulante.

En su trabajo clásico acerca de los modelos en ecología, Pielou[6] clasifica los mismos según su uso y los verbos y expresiones que utiliza para designar las funciones de los modelos son: explicar, predecir, generar hipótesis testeables, servir como patrones ideales contra los que contrastar los procesos reales. Tenemos aquí unas funciones adicionales a las que venimos comentando. ¿Podemos pedirles más cosas a los modelos? Pues parece que sí, porque cuando abrimos el espectro más allá de lo ecológico y los llevamos a todos los fenómenos que estudia la biología no encontramos con otros tópicos que es necesario tener en cuenta para definir mejor el alcance del modelado matemático. Por ejemplo, en el excelente libro de Esteva y Falconi[7] se afirma que "La modelación matemática ofrece una herramienta de investigación que permite al biólogo estudiar la esencia de un fenómeno y dejar de lado detalles que no son relevantes para su comprensión", una visión que se relaciona íntimamente con la metáfora que ya mencionamos del instrumento de observación y con el espíritu mostrado en el libro de Manteiga abogando por la matemática como el camino privilegiado para la abstracción y la elaboración de principios generales a partir de casos particulares. Otro punto muy delicado y relevante que plantea en su introducción el libro de Esteva y Falconi es el del carácter profundamente interdisciplinario de la biología matemática y recalca que "[...] sin un conocimiento profundo de la biología es imposible fundamentar un modelo matemático y saber si es interesante o irrelevante".

Esto nos lleva a los dos últimos tópicos que me gustaría plantear antes de intentar una síntesis del asunto. En primer lugar, el problema de la naturaleza particular de los sistemas biológicos y cómo dicha naturaleza influye en lo que podemos o no hacer a partir de los modelos matemáticos; esto está brillantemente desarrollado en un artículo de Germinal Cocho Gil[8], publicado como capítulo de un libro coordinado por Sánchez Garduño; Miramontes y Gutiérrez Sánchez. Allí el autor nos presenta dos ejercicios de hermenéutica diatópica planteando las oposiciones entre dos escuelas de la biología evolucionista y también la clásica contradicción Evo-Devo. Lejos de agotarse en una simple descripción histórica, Cocho nos muestra cuestiones que se anclan en algunas características esenciales del mundo biológico, en particular el hecho de que los sistemas biológicos son históricos, dinámicos y mutables y, por lo tanto, difíciles de encasillar con definiciones estáticas por un lado; y, por otro, la existencia de una jerarquización de niveles de complejidad (lo cual implica también una jerarquización de controles y retroalimentaciones) en cualquier estructura biológica funcionando. Aquí pasa a jugar un papel importante la cuestión termodinámica (otra vez lo interdisciplinario) y el autor asocia estas cuestiones con lo que sucede en el plano de la discusión epistemológica de la propia disciplina.

El otro punto que es clave para lo que queremos plantear está puesto en primer plano en el libro de Torres Curthi[9] y es sumamente inquietante: el problema de la verdad de los modelos. Allí la autora nos llama la atención sobre la diferente cualidad de las verdades de las ciencias fácticas, que dependen de hechos pero son necesariamente provisorias y tienen detrás un proceso inductivo, con hipótesis que se ponen a prueba y admiten ser refutadas; y las verdades de las ciencias formales que son absolutas (ya sean axiomas o teoremas); es decir, ya sea porque se aceptan como verdades para el sistema formal del que forman parte o porque han sido demostradas a partir de aquellas, las verdades de los sistemas axiomáticos lo son para siempre y no admiten refutación. ¿Podemos entonces representar adecuadamente sistemas y problemas de las ciencias naturales (que son fácticas) mediante los objetos y leyes de las ciencias formales (como las matemáticas) y lograr una buena representación? Algunos aspectos de ese problema y sus posibles respuestas han sido explorados por el distinguido colega y amigo Fernando Córdova-Lepe en esta misma sección en el número anterior. Allí, nuestro colega hace énfasis en la problemática que implica el trabajo interdisciplinario que le es propio al modelador matemático que aplica sus conocimientos a los sistemas biológicos.

INTENTANDO DESENREDAR EL HILO

Habiendo hecho este repaso obligadamente breve, podemos ver que el lugar del modelado matemático en las ciencias biológicas es múltiple y que los temas de meditación que acompañan la tarea son muchos.

¿Actúa la matemática como una herramienta cuando modelamos sistemas biológicos? Podríamos decir que sí, pero que no siempre es el mismo tipo de herramienta; depende del objetivo que tengamos. Está claro que esta herramienta no se agota en la búsqueda de predicciones solamente; que las predicciones no son solamente tendencias o valores que se podrían ajustar mejor o peor a los datos empíricos; que el desarrollo de modelos mecanísticos de los procesos biológicos no sólo implica la comprensión profunda de los procesos, sino que también ayuda a esa comprensión, ilumina aspectos, sugiere simplificaciones y generalizaciones que no se tenían en cuenta.

Pero hay más aún, y esto no sólo es válido para las ciencias biológicas sino que puede pensarse de manera análoga para otras ciencias: de alguna manera, la habilidad de modelar matemáticamente lo biológico nos abre una puerta hacia otros mundos biológicos posibles. De alguna manera, el modelado matemático no necesita ser ulterior al fenómeno biológico observable; podría plantearse preguntas acerca de fenómenos aún no observados; por ejemplo, ¿porqué no existen organismos que obtengan energía biológica rodando cuesta abajo y transformando la energía cinética en química? Y si existiesen, ¿cómo podrían funcionar biológicamente; qué mecanismos deberían tener, cómo se reproducirían, qué organelas tendrían sus células, cómo los afectaría la selección natural? El modelado también nos permite imaginar organismos y ecologías que podrían existir en ambientes de otros planetas (Carl Sagan fue pionero en esta clase de hipótesis).

Por otra parte, es bastante habitual que los problemas biológicos más conocidos, al intentar ser modelados planteen también problemas matemáticos particulares que a veces nos llevan al desarrollo de técnicas o al rescate de áreas de las matemáticas un tanto olvidadas. Un ejemplo posible de temas que están requiriendo del desarrollo de técnicas matemáticas nuevas o, incluso, del desarrollo de nuevos conceptos, es el amplio desarrollo que está experimentando el estudio de redes biológicas, desde redes de interacciones entre especies (redes tróficas, redes de competencia, redes mutualistas) hasta redes metabólicas, de regulación genética, de relaciones sociales entre animales, etc. Uno de los temas difíciles de resolver en el estudio de estas estructuras dinámicas es determinar su estabilidad ante perturbaciones externas; otro es el terreno de la predicción de la dinámica de esas redes. Actualmente las herramientas matemáticas con que contamos han demostrado ser insuficientes o poco sutiles para captar estas dinámicas complejas. Las métricas de estabilidad se multiplican y se apoyan en una multiplicidad de hipótesis auxiliares no siempre plausibles, o bien se obtienen de simulaciones reduccionistas (que subestiman las interacciones no lineales). Seguramente hay propiedades de las matrices que pueden asociarse con variables análogas a la energía libre[10] y que valdría la pena explorar en equipos multidisciplinarios.

En síntesis: nuestra área de trabajo, que tiene en esta revista un vehículo académico, es cada vez más amplia, desafiante y provocativa. Y un territorio fértil para otra de las capacidades humanas que está en la base de toda ciencia: la imaginación.

Notas al final

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Editorial

MATHEMATICAL MODELS, WHAT FOR?

Dr. Fernando Momo
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Making mathematical models of biological processes is an old scientific activity with a long tradition. In fact, mathematical modeling is a common activity in all sciences, from the "canonical" natural sciences, such as Physics, to the social sciences and humanities. Moreover, we could think that model biological systems can already be considered as a discipline itself, and even an independent science (it has objects of study, methodologies, and a minimal well-defined vocabulary).

But of course, in all scientific activity, it is healthy to become aware and think systematically (and regularly) about the meaning of our task, its why and what for. In this case, we intend to explore some methodological and epistemological issues that seem to still be in discussion or, at least, present diverse interpretations.

Let's see, this is an editorial text that is published in a Journal of Mathematical Modeling of Biological Systems. So, does it make sense to ask about the objectives of modeling? what do we want to achieve when we model mathematically? Why are we particularly interested in modeling these systems and what new, special or important can models contribute in this field?

If we take a brief tour of some fundamental bibliography on the subject, we will see that the interpretations and answers are not uniform and have subtly varied approaches.

For example, Teresa González Manteiga, in her excellent book, places mathematics in a privileged place as a central science. Supported by abundant citations, which include physicists like Galileo or Newton, philosophers like Kant or Manero, and even poets like Paul Valéry, this author places mathematical modeling in the place of discovery and abstraction of the ultimate principles of nature. As we can see, it is a position that goes far beyond the usual instrumental idea of modeling. At the other extreme, we have definitions that point to mathematics as a tool. Hastings, in his book on population dynamics, says succinctly that the goal of population biology is to understand and predict population dynamics and that understanding, explaining, and predicting these dynamics requires mathematical models. As we can see, what is underlined here is an auxiliary role in which the emphasis is placed on the biological problem itself and mathematics takes a subsidiary but useful role because it allows a formalism that facilitates understanding and also quantitative prediction. This approach has been dominant especially in mathematical modeling within population ecology, forgetting in fact that many of the "purely" ecological concepts that are taught as laws have their origin in model analysis, for example, the principle of competitive exclusion in Gause's formulation.

Some other authors are located in an intermediate zone; For example, Gillman and Hails argue that an ecological model must be able to describe the changes in the variables of interest (for example, population density) with some degree of accuracy, and also that such models must be expressed mathematically due to the brevity and formality of the description, the possibility of manipulation of the model, and the possibility of discovering emergent properties that are not apparent to non-mathematical reasoning. As we can see, a fundamental novelty appears here that has to do with the illuminating nature of mathematical models as they are capable of showing what is not seen. This idea underlies other texts, such as the wonderful book by Hernández and Velasco Hernández in which the authors warn us of the dangers of limiting the use of mathematical models to mere prediction and advocate, on the contrary, for more ambitious management where the use of models can even test hypotheses or deepen our understanding of very complex systems. In fact, they present a very nice analogy according to which mathematical models can also be considered an observation instrument: to observe the very distant we can use a telescope; to observe the very small, a microscope; to observe the very complex, mathematical models. It is a provocative and stimulating idea.

In his classic work on models in ecology, Pielou classifies them according to their use. The verbs and expressions used to designate the functions of the models are explain, predict, generate testable hypotheses, serve as ideal patterns against which to contrast real processes. We have here some additional functions to those that we have been commenting on. Can we ask the models for more things? Well, it seems so, because when we open the spectrum beyond the ecological and we take them to all the phenomena that biology studies, we find other topics that must be taken into account to better define the scope of mathematical modeling. For example, in the book by Esteva and Falconi it is stated that "Mathematical modeling offers a research tool that allows the biologist to study the essence of a phenomenon and leave aside details that are not relevant to its understanding", a vision that is closely related to the metaphor that we already mentioned of the observation instrument and with the spirit shown in Manteiga's book advocating mathematics as the privileged path for abstraction and the elaboration of general principles from particular cases. Another very delicate and relevant point that Esteva and Falconi's book raises in its introduction is the deeply interdisciplinary nature of mathematical biology which stresses that "...without a deep knowledge of biology it is impossible to establish a mathematical model and know if it is interesting or irrelevant...".

This brings us to the last two topics that I would like to raise before attempting a synthesis of the matter. First, the problem of the particular nature of biological systems and how this nature influences what we can or cannot do from mathematical models; this is brilliantly developed in an article by Germinal Cocho Gil, published as a chapter of a book coordinated by Sánchez Garduño, Miramontes and Gutiérrez Sánchez. There, the author presents us with two exercises in diatopical hermeneutics posing the oppositions between two schools of evolutionary biology and also the classic Evo-Devo contradiction. Far from exhausting himself in a simple historical description, Cocho shows us issues that are anchored in some essential characteristics of the biological world, in particular the fact that biological systems are historical, dynamic and mutable, and therefore, difficult to classify with static definitions; on the other, the existence of a hierarchy of levels of complexity (which also implies a hierarchy of controls and feedback) in any functioning biological structure. Here the thermodynamic question (once again the interdisciplinary) comes to play an important role and the author associates these questions with what happens at the level of the epistemological discussion of the discipline itself.

The other point that is key to what we want to raise is brought to the fore in Torres Curth's book and is extremely disturbing: the problem of the "truth" of the models. There the author draws our attention to the different qualities of the "truths" of the factual sciences, which depend on facts but are necessarily provisional and have an inductive process behind them, with hypotheses that are put to the test and admit to being refuted; and the truths of the formal sciences that are absolute (either axioms or theorems); that is to say, either because they are accepted as truths for the formal system of which they are part, or because they have been demonstrated from those, the "truths" of the axiomatic systems are forever and do not admit refutation. Can we then adequately represent systems and problems of the natural sciences (which are factual) by means of the objects and laws of the formal sciences (such as mathematics) and achieve a good representation? Some aspects of this problem and its possible answers have been explored by the distinguished colleague and friend Fernando Córdova-Lepe in this same section in the previous issue. There, our colleague emphasizes the problems involved in the interdisciplinary work that is proper to the mathematical modeler who applies his knowledge to biological systems.

TRYING TO UNTANGLE THE THREAD

Having made this necessarily brief review, we can see that the place of mathematical modeling in the biological sciences is manifold and that the themes for meditation that accompany the task are many.
Does mathematics act as a tool when we model biological systems? We could say yes, but it is not always the same type of tool; It depends on the goal we have. It is clear that this tool does not end with the search for predictions only; that the predictions are not only trends or values that could fit better or worse to the empirical data; that the development of mechanistic models of biological processes not only implies a deep understanding of the processes; but also helps that understanding, illuminates aspects, suggests simplifications and generalizations that were not taken into account.

But there is even more, and this is not only valid for the biological sciences but can be thought of in a similar way for other sciences: in a way, the ability to model the biological mathematically opens a door to other possible biological worlds. Somehow, mathematical modeling need not be ulterior to observable biological phenomena; could ask questions about phenomena not yet observed; For example, why aren't there organisms that obtain biological energy by rolling downhill and transforming kinetic energy into chemical energy? And if they did exist, how could they function biologically; What mechanisms should they have, how would they reproduce, what organelles would their cells have, and how would natural selection affect them? Modeling also allows us to imagine organisms and ecologies that could exist in environments on other planets (Carl Sagan pioneered this kind of hypothesis).

On the other hand, it is quite common that the best-known biological problems, when trying to be modeled, also pose particular mathematical problems that sometimes lead us to the development of techniques or to the rescue of somewhat forgotten areas of mathematics. A possible example of topics that are requiring the development of new mathematical techniques or, even, the development of new concepts, is the broad development that the study of biological networks is undergoing, from interaction networks between species (trophic webs, competition networks , mutualistic networks) to metabolic networks, genetic regulation, social relations between animals, etc. One of the difficult issues to resolve in the study of these dynamic structures is to determine their stability in the face of external disturbances; another is the field of predicting the dynamics of these networks. Currently, the mathematical tools we have have proven to be insufficient or not very subtle to capture these complex dynamics. Stability metrics are multiplied and are supported by a multiplicity of auxiliary hypotheses that are not always plausible, or are obtained from reductionist simulations (which underestimate non-linear interactions). Surely there are properties of matrices that can be associated with variables analogous to free energyi and that would be worth exploring in multidisciplinary teams.

In summary: our area of work, which has an academic guideline in this journal, is increasingly broad, challenging and provocative. And a fertile territory for another of the human capacities that is at the base of all science: imagination.

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Chemotactically induced search and defense strategies in a tritrophic system

Estrategias de búsqueda y defensa inducidas por quimiotaxis en un sistema tritrófico

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ABSTRACT

In this paper, we define an intraguild predation model of one-resource and two-predator, in which the mesopredator catched by a top predator, feeds on a resource that grows according to a logistic growth law; for both the meso and the top predator, Holling type II functional responses are considered. Predators and prey diffuse into a connected bounded region in $\mathbb{R}^2$. Two scenarios are considered: 1. As a defense mechanism, the resource attracts the top predator that feeds on the mesopredator; 2. The top predator in search of food moves towards areas where the mesopredator population is increasing. Some general properties of the solutions of the model are proved. In addition, the results of the numerical simulations carried out to analyze the effect on the spatial distribution of the populations of the indirect defense mechanism of the first scenario are shown. This is contrasted with the results of the model simulations corresponding to the second scenario, in which the diffusion of the top predator is regulated by a tendency to move towards the mesopredator gradient.

Keywords:

Competing species; Intraguild predation; Chemotaxis, Active-search hunting

RESUMEN

En este trabajo se define un modelo de depredación intragremial de un recurso y dos depredadores, en el cual el recurso crece de acuerdo a una ley de crecimiento logístico y es el alimento de un mesodepredador que es capturado por el depredador principal; para ambas clases de depredadores se considera una respuesta funcional Holling tipo II. Depredadores y presas se difunden en una región conexa y acotada de $\mathbb{R}^2$. Se estudian dos escenarios: 1) El recurso atrae, como un mecanismo de defensa, al depredador principal que se alimenta del mesodepredador; 2) En la búsqueda de alimento, el depredador principal se mueve hacia las áreas donde es creciente la población del mesodepredador. Se demuestran algunas propiedades generales de las soluciones del modelo. Además, se realizan simulaciones numéricas para analizar los efectos sobre la distribución espacial de las poblaciones, del mecanismo de defensa indirecta del primer escenario. Esto es confrontado con los resultados de la simulaciones del modelo correspondiente al segundo escenario, en el que la difusión del depredador principal está regulada por su tendencia a moverse hacia el gradiente del mesodepredador.

Palabras Claves:

Competencia de especies; Depredación intragremial; Quimiotaxis; Cazador de búsqueda activa

2020 AMS Mathematics Subject Classification: Primary: 92B05; Secondary:

1 INTRODUCTION

Individual movement regulated by concentrations of chemical substances is a very frequent natural phenomenon; known as *Chemotaxis* is an important mechanism, for instance, of bacterial populations in search of nutrients or to establish symbiotic relationships (see (Raina *et al.*, 2019)). Chemical components has been observed as a defense strategy of several species. In (Pereira *et al.*, 2000), the authors review some recent studies focused on characterizing the so-called plant volatiles induced by herbivores and the olfactory mechanisms present in some tritrophic interactions. The way in which organisms respond to chemotaxis has been discussed in (Iino and Yoshida, 2009). In particular, it describes the movements that *C. elegans* makes when the NaCl concentration decreases. In this paper it is mentioned that *C. elegans* rapidly changes the direction of locomotion through the use of a set of stereotyped behaviors, in response to a decrease in the concentration of the chemical substance. To get some insight of the impact of chemotactic processes on the population dynamics of some species, (Pereira *et al.*, 2000) studied the chemical defense of two species of brown alga *Dictyota menstrualis* and *Dictyota mertensii* used against herbivores with limited mobility, the amphipod *Parhyale hawaiensis* and the crab *Pachygrapsus transversus*. In fact, natural defense against predation is very well documented and it is present in both invertebrate and vertebrate species, see (Dumbacher and Pruett-Jones, 1996), (Eisner *et al.*, 2000), (Fattorini *et al.*, 2010), (Matz *et al.*, 2008), (Buonomo *et al.*, 2019). On the other hand, the study about the relationship of organism dispersal and community structure of interacting species has a long history. Since the works of Kolmogorov (Kolmogorov, 1937) and Skellam (Skellam, 1951), mathematical modeling of diffusion and random walk has been widely applied in the study of the effect of individual movement on the dynamic properties of different kinds of species interaction. Among the recent works on this topic it is (Yang and Fu, 2008) where the authors consider a tritrophic food chain with predators and one resource; the existence and boundedness of solutions and stability of equilibrium solutions are analyzed. Stability and Turing patterns of a diffusive predator-prey model have been analyzed in (Song *et al.*, 2020). Diffusion and delay effect has been incorporated in an intraguild predation model in (Han and Dai, 2017), where the authors studied how the delay on the conversion rate of mesopredator induces spatiotemporal patterns. About diffusion in predator-prey context see (Venturino and Petrovskii, 2013) and (Ai *et al.*, 2017). In this work we analyzed how the emission of chemical substances which attract predators of consumers of a resource impacts the spatial distribution of species. A laboratory study on this topic is (Kessler and Baldwin, 2001) where Kessler and Baldwin have found that volatile emissions from *Nicotiana attenuata* could reduce the number of herbivores up to 90%.

In this work, we consider an intraguild predation model of one resource and two predators; the importance of this interaction for population ecology has been explained by Polis and Holt in (Polis and Holt, 1992). We consider that mesopredator feed on a resource which grows acoording to a logistic growth law and it is consumed by a top predator; functional responses of meso and top predators are of Holling type II. Predators and prey difusse in a connected bounded region $\Omega \subset \mathbb{R}^2$ of the plane whose boundary $\partial\Omega$ is a regular curve. We consider two cases: in the first case, the model is

$$\begin{aligned} \frac{\partial u}{\partial t} &= d_0\Delta u + \alpha u\left(1-\frac{u}{K}\right) - \frac{buv}{u+a}, \\ \frac{\partial v}{\partial t} &= d_1\Delta v + \gamma\frac{buv}{u+a} - \frac{cvw}{v+d} - \mu v, \\ \frac{\partial w}{\partial t} &= d_2\Delta w + \beta\frac{cvw}{v+d} - \rho w - \nabla\cdot\left(\chi_1(v,w)\nabla v\right), \end{aligned} \tag{1}$$

the random dispersal of top predators is tempered by a certain tendency to move up the gradient of mesopredators. Pheronomes have been reported (see (Yoshimizu *et al.*, 2018)) to affect foraging behavior in such a way that the individual chemotactic response is modulated by interactions with other organisms in the population. For this reason, the chemotactic sensitivity $\chi_1(v,w)$ depends on w.

In the second case, as a chemotactic defense mechanism of the prey is considered, the resource population attracts top predators which feeds on mesopredator; this kind of indirect defense against predators has been reported in (Aljbory and Chen, 2018), see also (Buonomo *et al.*, 2019); 2) top predator in search of food moves towards areas where the mesopredator population is increasing The model is given by

$$\begin{aligned} \frac{\partial u}{\partial t} &= d_0\Delta u + \alpha u(1-\frac{u}{K}) - \frac{buv}{u+a}, \\ \frac{\partial v}{\partial t} &= d_1\Delta v + \gamma\frac{buv}{u+a} - \frac{cvw}{v+d} - \mu v, \\ \frac{\partial w}{\partial t} &= d_2\Delta w + \beta\frac{cvw}{v+d} - \rho w - \nabla\cdot(\chi_2(u,w)\nabla u), \end{aligned} \tag{2}$$

in this model the random movement is regulated by the gradient of population density of the resource. In the above models, the carrying capacity $K = K(x,y)$ is a non-negative function defined in Ω and describes the diverse suitability of the niche of the resource. Niche suitability and size population has been addressed in (Osorio-Olvera and Falconi, 2019). It is assumed that the flux vanishes in the boundary of Ω,

$$\frac{\partial u}{\partial \eta}(x,t) = \frac{\partial v}{\partial \eta}(x,t) = \frac{\partial w}{\partial \eta}(x,t) = 0, x \in \partial\Omega, t > 0 \tag{3}$$

where $\partial/\partial\eta = \eta\cdot\nabla$, and η is the normal vector to $\partial\Omega$.
The intrinsic growth of the resource u is denoted by α; b and c are the mortality rate by predation on u and v, respectively. The conversion rate of biomass captured by v and w are γ and β, respectively. The parameters μ and ρ stand for the mortality rate of meso and top predators, respectively. The half saturation constant a estimates the handling time of prey by predators. In Model (1) it is assumed that the regulating mechanism against of random dispersal of w depends

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on a volatile substance generated by v; in Model (2), it is generated by u. Two predators which feed on a common resource subject to a Lotka-Volterra interaction was considered in (Wang *et al.*, 2017), where it was assumed that diffusive movement of predators is controlled by the prey density gradient. In (Tello and Wrzosek, 2016) was analyzed a predator-prey model where predator moves toward the gradient of a chemical released by prey.
The underlying ordinary differential system corresponding to Models (1) and (2) is given by

$$\begin{aligned} u' &= \alpha u\left(1-\frac{u}{K}\right)-\frac{buv}{u+a}, \\ v' &= \gamma\frac{buv}{u+a}-\frac{cvw}{v+d}-\mu v, \\ w' &= \beta\frac{cvw}{v+d}-\rho w. \end{aligned} \tag{4}$$

The system (4) has the following equilibrium points

i) $P_1=(0,0,0)$

ii) $P_2=(K,0,0)$

iii) $P_3=\left(\frac{a\mu}{b\gamma-\mu},\frac{a\alpha\gamma(b\gamma K-\mu(a+K))}{K(b\gamma-\mu)^2},0\right)$.

Under appropriate conditions, this system posses one equilibrium point $P_4=(u_1,v_1,w_1)$ with positive coordinates given by

$$\begin{aligned} u_1 &= \tfrac{1}{2}\left(-a+K+\sqrt{\frac{c\alpha\beta(a+K)^2-\left(4bdK+(a+K)^2\alpha\right)\rho}{(c\beta-\rho)\alpha}}\right) \\ v_1 &= \frac{d\rho}{c\beta-\rho} \\ w_1 &= \frac{(d+v_1)\left(b\gamma u_1-(a+u_1)v_1\mu\right)}{c\left(a+u_1\right)} \end{aligned}$$

Point P_1 is always unstable; P_2 is locally asymptotically stable if $bK\gamma-a\mu-K\mu<0$ and unstable if $bK\gamma-a\mu-K\mu>0$; P_3 is stable if $bK\gamma-a\mu-K\mu>0$ and $b\gamma a>bK\gamma-a\mu-K\mu$ and unstable if $bK\gamma-a\mu-K\mu>0$ and $b\gamma a<bK\gamma-a\mu-K\mu$.

2 EXISTENCE OF POSITIVE SOLUTION

In this section we provide conditions for the existence of positive solutions of systems (1) and (2) for the initial conditions

$$t=0\text{: } u=u_0(x),\ v=v_0(x),\ w=w_0(x),\ x\in\Omega \tag{5}$$

and the boundary conditions given by (3). Let $p>n\geq 1$; then $W^{1,p}(\Omega,\mathbb{R}^n)$ is continuously embedded in the continuous function space $C(\Omega;\mathbb{R}^n)$. Let

$$X:=\{y\in W^{1,p}(\Omega,\mathbb{R}^3)\,|\,\eta\cdot\nabla y_{|_{\partial\Omega}}=0\}.$$

It is assumed that there exist $0<\varepsilon_m$, ε_M, such that

$$\varepsilon_m<K(x,y)<\varepsilon_M,\ \text{for all}(x,y)\in\Omega \tag{6}$$

Theorem 1 *If $(u_0,v_0,w_0)\in X$, then*

(i) There exists $T=T_{\max}\in[0,\infty)$, which depends on the initial conditions (5) such that the problem (1),(3)and (5) has a unique maximal solution $(u,\ v,\ w)$ on $\Omega\times[0,T_{\max})$ and $(u(\cdot,t),\ v(\cdot,t),\ w(\cdot,t))\in C((0,\ T_{\max}),\Omega)$, $(u,v,w)\in C^{2,1}\left((0,T_{\max})\times\overline{\Omega},\mathbb{R}^3\right)$;

(ii) If $u_0,\ v_0,\ w_0\geq 0$ on $\overline{\Omega}$, then $u,\ v,\ w\geq 0$ on $\Omega\times[0,T_{\max})$;

(iii) If $\|(u,w,w)(\cdot,t)\|_{L^\infty(\Omega)}$ is bounded for all $t\in[0,T_{\max})$, then $T_{\max}=+\infty$; equivalently, (u,v,w) is a global solution.

Proof Let $z=(u,v,w)\in\mathbb{R}^3$. Then, (1),(3) and (5) can be written as

$$\begin{aligned} z_t &= \nabla\cdot(A(z)\nabla z)+F(z)\ \text{on}\ \Omega\times[0,\infty) \\ B_z &= \frac{\partial}{\partial\eta}z=0\ \text{on}\ \partial\Omega\times[0,\infty) \\ z(\cdot,0) &= (u_0,v_0,w_0)\ \text{en}\ \Omega, \end{aligned} \tag{7}$$

where

$$A[z]=\begin{bmatrix} d_0 & 0 & 0 \\ 0 & d_1 & 0 \\ 0 & -\chi_1 & d_2 \end{bmatrix}$$

and

$$F(z)=\begin{bmatrix} u\left(\alpha\left(1-\frac{u}{K}\right)-\frac{bv}{u+a}\right) \\ v\left(\gamma\frac{bu}{u+a}-\frac{cw}{v+d}-\mu\right) \\ w\left(\beta\frac{cv}{v+d}-\rho\right) \end{bmatrix}$$

Matrix $A[z]$ is triangular, then the eigenvalues are the diagonal entries d_0, d_1 and d_2, which are assumed to be positive, then the systen (7) is normally elliptic, see pages 15-16 of (Amann, 1990). The result follows from (Haskell and Bell, 2020). □

According to the above theorem, to prove the existence of global solutions it is necessary to show that u, v and w are uniformly bounded in $L^\infty(\Omega)$.

Theorem 2 *If $(u_0,v_0,w_0)\in X$, then the solutions of the System (1), with boundary conditions (3) and initial conditions (5) are bounded.*

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Proof Let $W(x,t) = u + \frac{1}{\gamma}v + \frac{1}{\gamma\beta}w$, so

$$\begin{aligned}
\frac{d}{dt}\int_\Omega (W(x,t)) &= \int_\Omega \left(d_0\Delta u + \alpha u\left(1-\frac{u}{K}\right) - \frac{buv}{u+a}\right)dx \\
&+ \int_\Omega \left(\frac{1}{\gamma}\left(d_1\Delta v\right)\right)dx \\
&+ \int_\Omega \left(\frac{1}{\gamma}\left(\gamma\frac{buv}{u+a} - \frac{cvw}{v+d} - \mu v\right)\right)dx \\
&+ \int_\Omega \left(\frac{1}{\gamma\beta}\left(d_2\Delta w + \beta\frac{cvw}{v+d} - \rho w\right)\right)dx \\
&- \int_\Omega \left(\frac{1}{\gamma\beta}\left(\nabla\cdot\left(\chi_1(v,w)\nabla v\right)\right)\right)dx \\
&= \int_\Omega \left(d_0\Delta u + \frac{1}{\gamma}d_1\Delta v + \frac{1}{\gamma\beta}d_2\Delta w\right)dx \\
&+ \int_\Omega \left(\alpha u\left(1-\frac{u}{K}\right)\right)dx \\
&+ \int_\Omega \left(-\frac{buv}{u+a} + \frac{buv}{u+a} - \frac{c}{\gamma}\frac{vw}{v+d}\right)dx \\
&+ \int_\Omega \left(-\frac{\mu}{\gamma}v + \frac{c}{\gamma}\frac{cvw}{v+d} - \frac{\rho}{\gamma\beta}w\right)dx \\
&\leq \int_\Omega \left(\alpha u\left(1-\frac{u}{K}\right) - \frac{\mu}{\gamma}v - \frac{\rho}{\gamma\beta}\right)dx
\end{aligned}$$

It follows that

$$\frac{d}{dt}\int_\Omega W dx + \int_\Omega \left(\frac{\mu}{\gamma}v + \frac{\rho}{\gamma\beta}w\right)dx \leq \int_\Omega \alpha u\left(1-\frac{u}{K}\right)dx. \tag{8}$$

On the other hand, let $\mu_0 = \min\{\mu,\rho\}$ that implies

$$\frac{d}{dt}\int_\Omega W dx + \mu_0\int_\Omega \left(\frac{1}{\gamma}v + \frac{1}{\gamma\beta}w\right)dx \leq \frac{d}{dt}\int_\Omega W dx + \int_\Omega \left(\frac{\mu}{\gamma}v + \frac{\rho}{\gamma\beta}w\right)dx. \tag{9}$$

From (8) and (9), we obtain that

$$\frac{d}{dt}\int_\Omega W dx + \mu_0\int_\Omega \left(u + \frac{1}{\gamma}v + \frac{1}{\gamma\beta}w\right)dx \leq \int_\Omega \left(\alpha u\left(1-\frac{u}{K}\right)\right)dx + \int_\Omega \mu_0 u dx \tag{10}$$

Note that

$$\begin{aligned}
\int_\Omega \left((\alpha+\mu_0)u - \frac{\alpha u^2}{K}\right)dx &\leq \\
\int_\Omega \frac{1}{4}\frac{K(\alpha+\mu_0)^2}{\alpha}dx &\leq \\
\frac{1}{4}\frac{\varepsilon_M(\alpha+\mu_0)^2}{\alpha}|\Omega| &
\end{aligned} \tag{11}$$

Now, let $K_0 = \frac{1}{4}\frac{\varepsilon_M(\alpha+\mu_0)^2}{\alpha}|\Omega|$, then from (10) and (12) we have that

$$\frac{d}{dt}\int_\Omega W dx + \mu_0\int_\Omega \left(u + \frac{1}{\gamma}v + \frac{1}{\gamma\beta}w\right)dx \leq K_0$$

from this, is clearly evident that

$$\int_\Omega \left(u + \frac{1}{\gamma}v + \frac{1}{\gamma\beta}w\right)dx \leq K_0 + ce^{-t}$$

It follows that solutions are bounded, since according to Theorem 1.(ii), u,v,w are nonegative. □

The proof of the following theorem is similar to those of Theorem 1.

Theorem 3 *Let* $(u_0,v_0,w_0) \in X$.

- *There exists* $T = T_{\max} \in [0,\infty)$, *which depends on the initial conditions (5) such that the problem (2),(3) and (5) has a unique maximal solution* $(u,\ v,\ w)$ *on* $\Omega \times [0,T_{\max})$ *and* $(u(\cdot,t),\ v(\cdot,t),\ w(\cdot,t)) \in C((0,\ T_{\max}),\Omega)$, $(u,v,w) \in C^{2,1}\left((0,T_{\max})\times\overline{\Omega},\mathbb{R}^3\right)$;
- *If* $u_0,\ v_0,\ w_0 \geq 0$ *on* $\overline{\Omega}$, *then* $u,\ v,\ w \geq 0$ *on* $\Omega\times[0,T_{\max})$;
- *If* $\|(u,w,w)(\cdot,t)\|_{L^\infty(\Omega)}$ *is bounded for all* $t \in [0,T_{\max})$, *then* $T_{\max} = +\infty$; *i.e.,* (u,v,w) *is a globally bounded solution.*

Note that v and w vanish if $\gamma b \leq \mu$ and $\beta c \leq \rho$, respectively. From now on, we assume that $\gamma b > \mu$ and $\beta c > \rho$.

Let $Y = \left\{U = (u,v,w) \in \left[C^1\left(\overline{\Omega}\right)\right]^3 | \partial_\rho u(x) = 0,\ x \in \partial\Omega\right\}$, and μ_i be the eigenvalues of the operator $-\Delta$ on Ω with the homogeneous Neumann boundary condition. We denote by $E(\mu_i)$, the eigenspace corresponding to μ_i in $C^1\left(\overline{\Omega}\right)$. let

$$\left\{\phi_{i,j},\ j = 1,2,...,\dim(E(\mu_i))\right\}$$

be a orthonormal basis of $E(\mu_i)$ and $Y_{ij} = \left\{C\cdot\phi_{ij} | C \in \mathbb{R}^3\right\}$. Then,

$$Y_i = \oplus_{j=1}^{\dim(E(\mu_i))} Y_{ij}, Y = \oplus_{i=1}^{\infty} Y_i.$$

Theorem 4 *Let* $0 < K \in \mathbb{R}$. *If* $bK\gamma - a\mu - K\mu < 0$ *then the equilibrium point* P_2 *of system (1) is asymptotically stable.*

Proof Let $A[z] = \begin{pmatrix} d_0 & 0 & 0 \\ 0 & d_1 & 0 \\ 0 & -\chi_1 & d_2 \end{pmatrix}$ as in theorem 1 and $L = A[z]\Delta + J_1$ where J_1 is the Jacobian matrix of the system without diffusion evaluated at P_2; i.e.

$$J_1 = \begin{pmatrix} -\alpha & -\frac{bK}{a+K} & 0 \\ 0 & \frac{bK\gamma}{a+K} - \mu & 0 \\ 0 & 0 & -\rho \end{pmatrix}.$$

The linearization of the system at P_2 is $U_t = LU$. Y_i is invariant with respect to operator L for all $i \geq 1$; λ is an eigenvalue of L restricted to Y_i if and only if is an eigenvalue of matrix $-\mu_i A[z]\Delta + J_1$.

The characteristic polynomial of $\mu_i A[z]\Delta + J_1$ is

$$\varphi_i(\lambda) = (\lambda + \mu_i d_1 + \alpha)\left(\lambda + \mu_i d_2 - \frac{bK\gamma}{a+K} + \mu\right)(\lambda + \mu_i d_2 + \rho)$$

whose roots are $-\mu_i d_1-\alpha$, $-\mu_i d_2+\frac{bK\gamma}{a+K}-\mu$ and $-\mu_i d_2-\rho$. Therefore, the point-spectrum of L consists of eigenvalues that satisfy $\{\mathrm{Re}\,\lambda \leq -(1/2)\max\{\alpha, -\frac{bK\gamma}{a+K}+\mu, \rho\}\}$ whenever $bK\gamma - a\mu - K\mu < 0$; from which stability around P_2 follows, [(Henry, 2006),Th. 5.1.1]. □

The spatial discretization that we apply to perform some numerical simulations of the previous models are describes in the Appendix. In the following computations we apply the finite element method with a time step $\Delta t = 0.001$ and the mesh is conformed by 17385 vertices, 34288 triangles and $h_{\min} = 0.0117835$. $h_{\max} = 0.028418$.

3 NUMERICAL SIMULATIONS

In this section, some numerical simulations are carried out in order to obtain some knowledge about the effect on the population density of the indirect defense mechanism of the resource against the meso–predator, which consists on the attraction of the main predator towards the resource. This will be contrasted with the results of the corresponding simulations of Model (1), in which the random diffusion of the main predator is regulated by a tendency to move towards the gradient of the meso-predator; this is the case of predators actively searching for prey, see (Ioannou and Krause, 2008), (Ross and Winterhalder, 2015) and the references cited there.

MODEL 1: ACTIVE-SEARCH HUNTING.

In the following we consider Model (1) where the top predator is an active-search hunter. We take

$$\chi_1(v,w) = e_1 w - e_2 v.$$

Therefore the top predator move towards the gradient of mesopredator only if its population density is large enough compared to that of the mesopredator. The ratio $\frac{e_2}{e_1}$ measures the defensive capacity of the mesopredator in terms of its population size; the larger this ratio, the greater the density of the predator required to advance towards the prey. The parameter values are given by $\alpha = 5, a = 2.0, b = 5.0, c = 0.1, d = 2.0, \beta = 1.0, \gamma = 1.0, \mu = 0.05, \rho = 0.05, d_0 = 0.1, d_1 = 1, d_2 = 1$.

For this parameter values, the equilibrium points of system (4) are $P_1 = (0,0,0)$, $P_2 = (K,0,0)$, $P_3 = (\frac{2}{99}, \frac{200(99K-2)}{9801K}, 0)$. Existence and stablity properties of these equilibrium points are described in Table 1. Notice that there is no CEP point for the above parameter values. For the numerical computations we assume that $\Omega = [-1,1]\times[-1,1]$ and we have used the `FreeFem++` software (Hecht, 2012). Initial conditions for the spatial distribution of the resource, the meso-predator and top predator are considered as

$$\begin{aligned} u_0(x,y) &= 2\exp(-10(x^2+(y-.9)^2))(1-x^2)^2(1-y^2)^2; \\ v_0(x,y) &= 2\exp(-(x+.9)^2-(y+.9)^2)(1-x^2)^2(1-y^2)^2; \\ w_0(x,y) &= 1.5 \end{aligned}$$

for all $x, y \in \Omega$. In contrast with the meso predator and the resource, the top predator is initially uniformly distributed, (see Figure 1).

Table 1

Point	Existence Interval	Stable	Unstable
P_1	$K>0$		$K>0$
P_2	$K>0$	$K<\frac{2}{99}$	$K>\frac{2}{99}$
P_3	$K>\frac{2}{99}$	$\frac{2}{99}<K<\frac{202}{99}$	$K>\frac{202}{99}$
P_4	$K>\frac{200}{99}$		$K>\frac{200}{99}$

Defensive capacity and species distribution

We consider five different defensive capacities of the prey. The suitability of the habitat of the resource is given by

$$\begin{aligned} K(x,y) &= 2\exp(-5((x+.75)^2+(y-.75)^2)) \\ &\quad +2\exp(-5((x-.75)^2+(y+.75)^2)) \\ &\quad +2\exp(-5((x+.75)^2+(y+.75)^2)) \\ &\quad +2\exp(-5((x-.75)^2+(y-.75)^2)). \end{aligned}$$

Notice that the range of K in Ω is contained in the interval $(\frac{2}{99}, \frac{200}{99})$. Therefore, according to Table 1 system 4 without diffusion does not have the coexistence point P_4 and also the point P_3 is asymptotically stable. Thus, without diffusion the top predator w would become extinct.

First, let $e_1 = 1.0, e_2 = 1.0$. In this case, the defensive capacity of the prey is neutral. Top predator move towards mesopredator whenever its density be greater than the one of the mesopredator

Second, let $e_1 = 1.0, e_2 = 0.5$ In this case, the mesopredator defense against of top predator is lesser than the above case. Thus, we observe that predators are closer to the mesopredators than in the first case (see Figures 2 and 6).

Third, let $e_1 = 1.0, e_2 = 2.0$. Prey presents a strong defense capacity. Notice that predators tends to move towards the lower density areas of the prey population, (see Figures 2 and 3).

Fourth case, let $e_1 = 1.0, e_2 = 10.0$. Prey presents still a defense capacity stronger than the previous case.

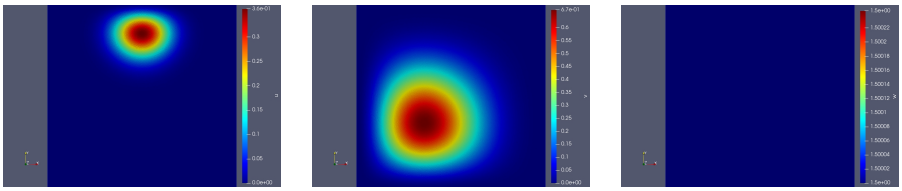
Fifth case, Let $e_1 = 10.0, e_2 = 1.0$ This is the smallest defensive capacity considered in this section.

From the comparison of Figures 6-5, we conclude that defensive capacity has a negligible effect on the prey population, if the predation rate is not large enough. Indeed, the main impact is over the spatial distribution of both the meso predator and the top predator.

Habitat suitability and species distribution

To understand how the ecological landscape impact species distribution, we consider two different characterization of the carrying capacity. In either case, the values of parameters of χ_1 are $e_1 = 1.0, e_2 = 10.0$, and the initial condition of u is

$$u_0(x,y) = 2\exp(-10(x^2+y^2))(1-x^2)^2(1-y^2)^2$$



$(a_1)\ u, \quad t=0$ $(b_1)\ v, \quad t=0$ $(c_1)\ w, \quad t=0$

Figure 1: *Contour plots* of time evolution of the resource u, mesopredador v and top predador w at different times.

The initial conditions $v_0(x,y)$ and $w_0(x,y)$ are the same as above.
First, we consider a carrying capacity given by

$$\begin{aligned} K(x,y) &= 2\exp(-5((x+.75)^2+(y-.75)^2)) \\ &\quad +2\exp(-5((x-.75)^2+(y+.75)^2)) \\ &\quad +2\exp(-5((x+.75)^2+(y+.75)^2)) \\ &\quad +2\exp(-5((x-.75)^2+(y-.75)^2)). \end{aligned}$$

The highest suitability is reached at four symmetrical points respect to the origin.

In Figure 7 are shown plots of the numerical solutions of u, v and w at different times. Note that as time passes, the resource tends to occupy the most suitable sites. The mesopredator moves towards the sites with the higher resource density and its defensive capacity (e_2/e_1) is large enough to keep the top predator away.

In this second case, the habitat of the resource is richer since its suitability is given by

$$\begin{aligned} K(x,y) &= 2\exp(-5((x+.75)^2+(y-.75)^2)) \\ &\quad +2\exp(-5((x-.75)^2+(y+.75)^2)) \\ &\quad +2\exp(-5((x+.75)^2+(y+.75)^2)) \\ &\quad +2\exp(-5((x-.75)^2+(y-.75)^2)) \\ &\quad +2\exp(-5(x^2+y^2)) \end{aligned}$$

The highest suitability is reached at four symmetrical points respect to the origin and at the origin. The spatial distribution of the three species is shown in Figure 8.
As in the first case, the mesopredators move towards the sites of higher density of the resource and the top predator is located far enough away from its prey because e_2/e_1 is relatively high. It seems that the richness of the habitat does not induce any change in the distribution patterns. Top predator tends to occupy the areas less densely populated by mesopredators, if e_2/e_1 is high enough.

Resource defense and species distribution

Some species defend themselves by attracting predators from their natural enemies. This is very frequent for instance in plant species, see (Price *et al.*, 1980) and the bibliography cited there. In (Aljbory and Chen, 2018) it has been described 24 species of predators which are attracted by volatiles generated by plants damaged by herbivores. In this paper, the authors raise the question about the effectiveness of predator species in controlling specific insect pests. In the following we analyze numerically the impact on the mesopredator distribution of an increasing predation rate of the top predator when this is attracted by the resource species. To analyze the relationship between the distribution of the mesopredator and the predation rate of a top predator that is attracted to the resource, we use Model (2) which is shown below.

$$\begin{aligned} \frac{\partial u}{\partial t} &= d_0\Delta u+\alpha u(1-\frac{u}{K(x,y)})-\frac{buv}{u+a}, \\ \frac{\partial v}{\partial t} &= d_1\Delta v+\gamma\frac{buv}{u+a}-\frac{cvw}{v+d}-\mu v, \\ \frac{\partial w}{\partial t} &= d_2\Delta w+\beta\frac{cvw}{v+d}-\rho w-\nabla\cdot(\chi_2(u,w)\nabla u). \end{aligned} \tag{12}$$

The sensitivity function is $\chi_2(u,w)=quw$. Thus, the movement of top predators towards the gradient of u is faster the higher its own density or that of the resource.
Initial conditions for the spatial distribution of the resource, the meso-predator and top predator are considered as

$$\begin{aligned} u_0(x,y) &= 2\exp(-(x^2+(y-.9)^2)(1-x^2)^2(1-y^2)^2; \\ v_0(x,y) &= 2\exp(-(x+.9)^2-(y+.9)^2)(1-x^2)^2(1-y^2)^2; \\ w_0(x,y) &= 1.5 \end{aligned}$$

for all $x,y\in\Omega$. The suitability of the habitat of the resource is given by

$$\begin{aligned} K(x,y) &= 2\exp(-5((x+.75)^2+(y-.75)^2)) \\ &\quad +2\exp(-5((x-.75)^2+(y+.75)^2)) \\ &\quad +2\exp(-5((x+.75)^2+(y+.75)^2)) \\ &\quad +2\exp(-5((x-.75)^2+(y-.75)^2)). \end{aligned}$$

Let the parameter values be given by $\alpha=5, a=2.0, b=5.0, d=2.0, \beta=1.0, \gamma=1.0, \mu=0.05, \rho=0.05, d_0=0.1, d_1=1, d_2=1$.
The sensitivity function is $\chi_2(u,w)=quw$. The below simulations are executed for different values of q and c.

It is worth to note that an increment of the predation rate c not necessarily induces an increment on the predator population. In Figure 10 the predation rate is c=1.5, and the predator population is lesser than the population showed in Figure 9 where the predaton rate is $c=1.0$. This is due, in

part, to the weak attraction of the resource on the individual predators, as this allows predators to remain randomly dispersed throughout space preventing the mesopredator population from reaching a level high enough to support a large population of predators. On the other hand, By comparing Figure 10 with Figure 11 we observe that the main effect on the increment of the attraction paremeter q is on the spatial distribution of meso and top predators. For $q = 1.0$ (Figure 11), top predators tend to occupy the places most densely populated by the resource; in contrast, mesopredators occupy the places least densely populated by top predators. However, if the predation rate is large enough, the mesopredator population is depleted and spatial complementarity is lost (see Figure 12). This effect vanishes if he resource's attraction to top predators grows; in fact, for $q = 10$, the separation of top and mesopredators habitats is strengthened for $c = 1$ and all three species reach relatively large populations levels compared to $c = .1$ (see Figure (13-15). The coexistence of the three species requires a proper balance between the rate of predation and the attraction of predators to the resource population. In Figure 14, we observe very low mesopredator population levels and a sharp concentration of top predators around the areas most populated by mesopredators.

4 CONCLUSIONS

With the aim to analyze the rol of migration and defensive mechanisms of the prey, in this work two variations of a tritrophic model have been considered. According to Table (1), if the three species remain in the same location (Model 4 without diffusion), top predator would become extinct since only the equliibrium point P_3 is stable. In the first case, where a top predator is an active-search hunter it is assumed that as prey density increases, searching intensity decreases (Model (1) with $\chi_1(v,w) = e_1 w - e_2 v$). Numerical simulations show that all three species coexist and both resource and prey tend to be concentrated around sites $(x^*, y^*) \in \Omega$ where resource suitability is greatest; that is, sites (x^*, y^*) where the carrying capacity $K(x^*, y^*)$ is the maximum. The spatial distribution of predator depends on the defensive capacity of the prey; for e_2/e_1 low enough, predators and prey have a similar distribution (see Figures 6, 5). However, if e_2/e_1 reaches a large enough level, the resource and prey populations share the same space, but the predator occupies the locations less populated by prey(see Figures 2, 3, 4). Hence, our numerical simulations provide evidence that migration favors coexistence and behavioral characteristics, such as a defense mechanism, can impact the spatial distribution of species. Furthermore, we find that the distribution of prey follows a pattern similar to that of the resource, which tends to be distributed near the places of greatest suitability. The spatial distribution is topic which has been analyzed from a diverse points of interest. For instance, the cost of a defense mechanism has been considered in (Wang *et al.*, 2017) where the authors analyze how this cost impact on pattern distribution of predators and preys. The role of predators on the spatial distribution has been studied from a experimental point of view in (Livingston *et al.*, 2017), where preys do not present a defense against predators. They found that was not the patch type but the distribution of predators that most strongly predicted the composition of the prey community. The effect of diffussion on the spatial distribution has beeen analyzed in (Kumari, 2013) .

A second point of interest in this work is how the attraction of enemies of my enemies influences the dynamics of a community. In some cases, the attraction activity is caused by volatiles emitted by the resource organisms. We have analyzed this question with the Model (2) where the predator moves toward the resource gradient according to the sensivity function $\chi_2(u,w) = quw$; that is, the higher the population density of the resource or the predator, the greater the tendency of the predator to move towards the resource. From Figures 9 and 15, we observe that a high attraction favors a greater concentration of both the top predators and the resource around the patches with the highest carrying capacity of the resource; as the predation pressure decreases in the other patches, they are occupied by the mesopredator. This phenomenon becomes more acute if predation increases (see Figure 14). It is also apparent that the larger q the greater the concentration of the populations. A fact that seems counterintuitive is that an increase in the predation rate does not necessarily lead to lower mesopredator densities; this is shown in Figures 9 and 10, where even we observe a similar pattern of the spatial distribution of the three species, the population levels of the mesopredator are higher in 10 with $c = 1.5$ than in 9, ($c = 1.0$); Possibly, this is a consequence of the fact that the greater the predation, the lower the population of mesopredators that arrive in the areas of greatest productivity of the resource. The general findings shown in this paper could be useful to the study of the biological factors that impact the spatial distribution of species.

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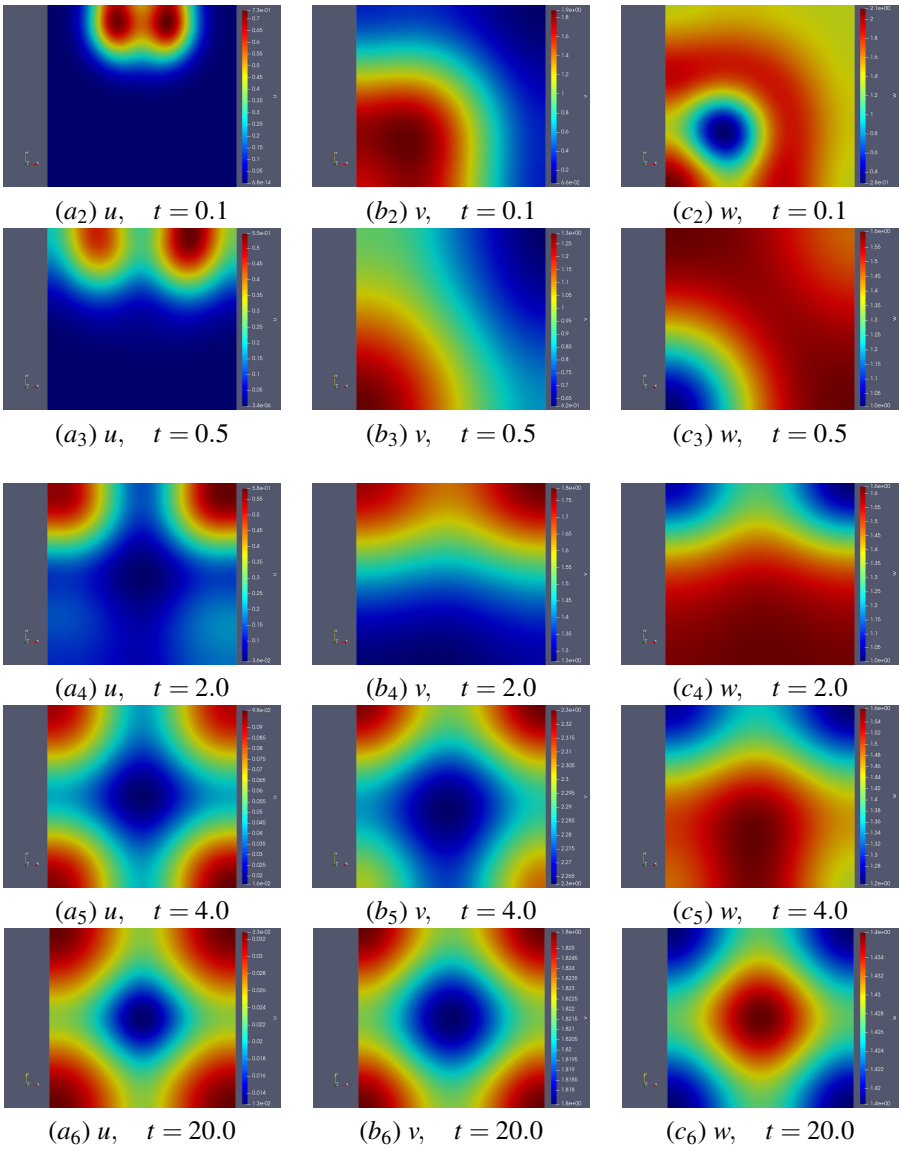

$(a_2)\ u, \quad t = 0.1$ $(b_2)\ v, \quad t = 0.1$ $(c_2)\ w, \quad t = 0.1$

$(a_3)\ u, \quad t = 0.5$ $(b_3)\ v, \quad t = 0.5$ $(c_3)\ w, \quad t = 0.5$

$(a_4)\ u, \quad t = 2.0$ $(b_4)\ v, \quad t = 2.0$ $(c_4)\ w, \quad t = 2.0$

$(a_5)\ u, \quad t = 4.0$ $(b_5)\ v, \quad t = 4.0$ $(c_5)\ w, \quad t = 4.0$

$(a_6)\ u, \quad t = 20.0$ $(b_6)\ v, \quad t = 20.0$ $(c_6)\ w, \quad t = 20.0$

Figure 2: Evolution of the spatial distribution of the three species. $e_1 = 1.0, e_2 = 1.0$

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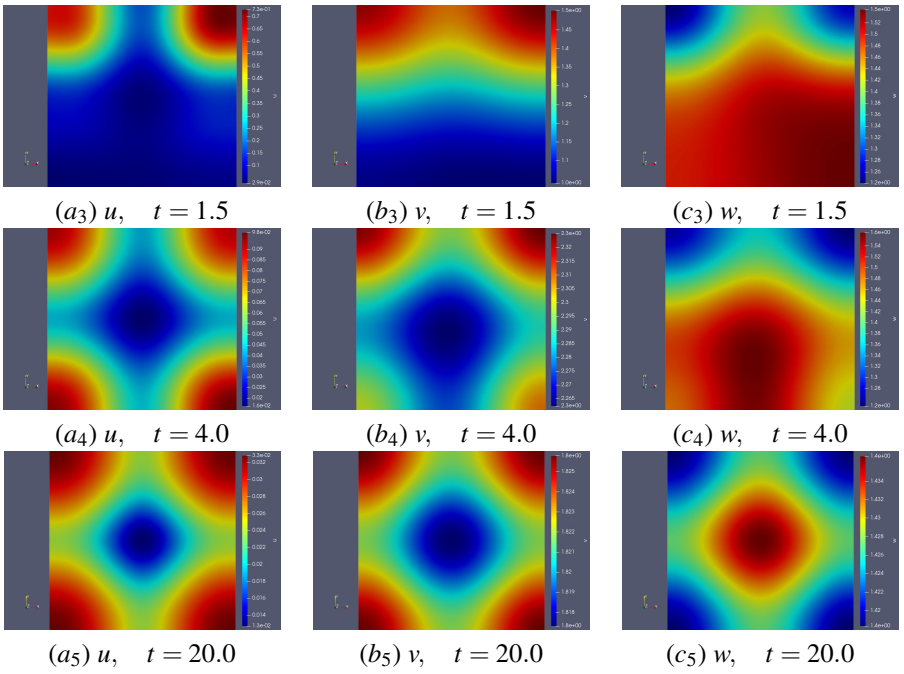
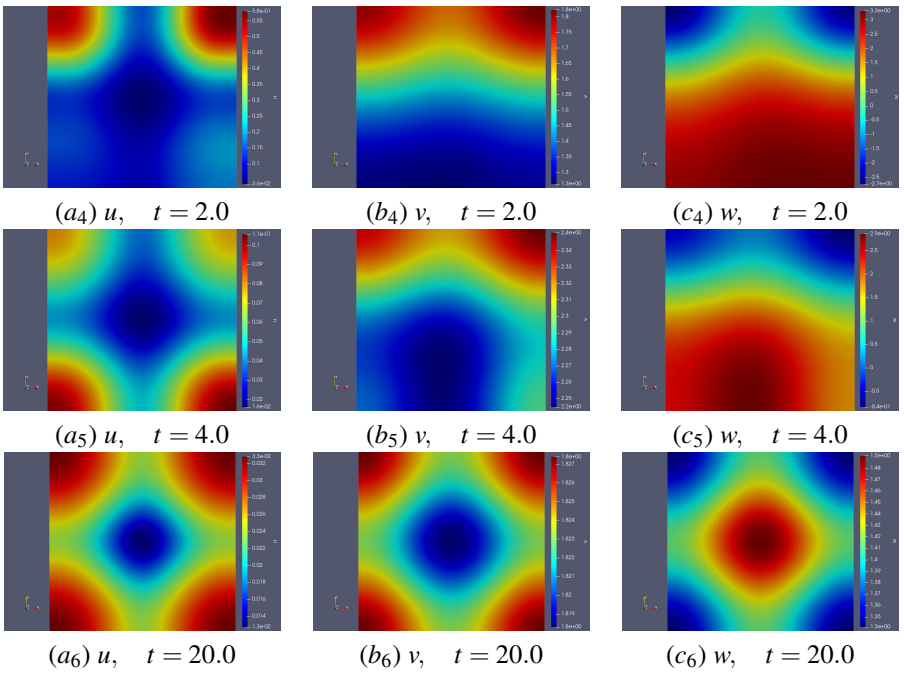


$(a_3)\ u, \quad t = 1.5$ $(b_3)\ v, \quad t = 1.5$ $(c_3)\ w, \quad t = 1.5$

$(a_4)\ u, \quad t = 4.0$ $(b_4)\ v, \quad t = 4.0$ $(c_4)\ w, \quad t = 4.0$

$(a_5)\ u, \quad t = 20.0$ $(b_5)\ v, \quad t = 20.0$ $(c_5)\ w, \quad t = 20.0$

Figure 3: Evolution of the spatial distribution of the three species. $e_1 = 1.0, e_2 = 2.0$



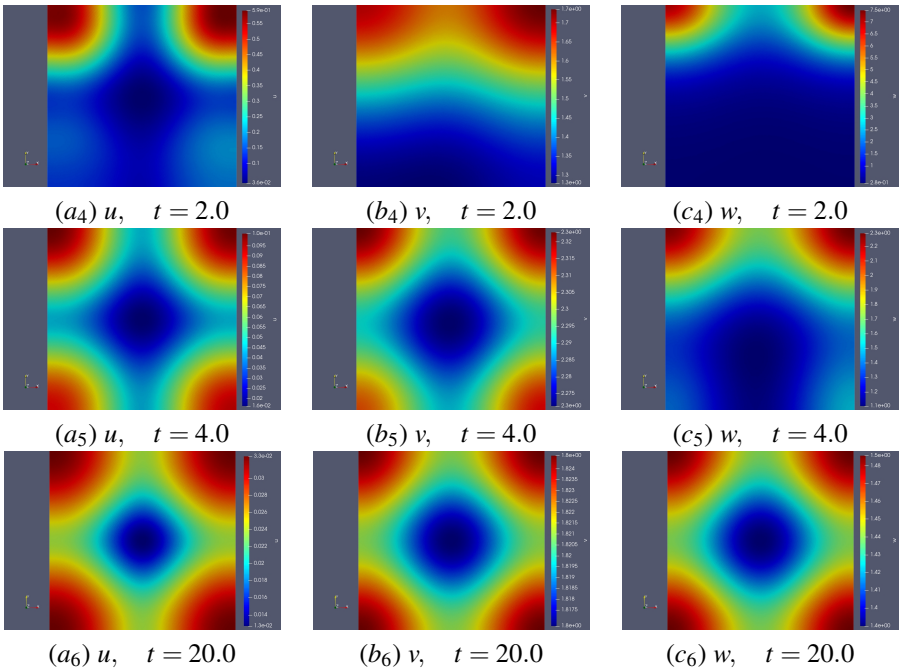
$(a_4)\ u, \quad t = 2.0$ $(b_4)\ v, \quad t = 2.0$ $(c_4)\ w, \quad t = 2.0$

$(a_5)\ u, \quad t = 4.0$ $(b_5)\ v, \quad t = 4.0$ $(c_5)\ w, \quad t = 4.0$

$(a_6)\ u, \quad t = 20.0$ $(b_6)\ v, \quad t = 20.0$ $(c_6)\ w, \quad t = 20.0$

Figure 4: Evolution of the spatial distribution of the three species. $e_1 = 1.0, e_2 = 10.0$

doi: 10.58560/rmmsb.v03.n02.023.08

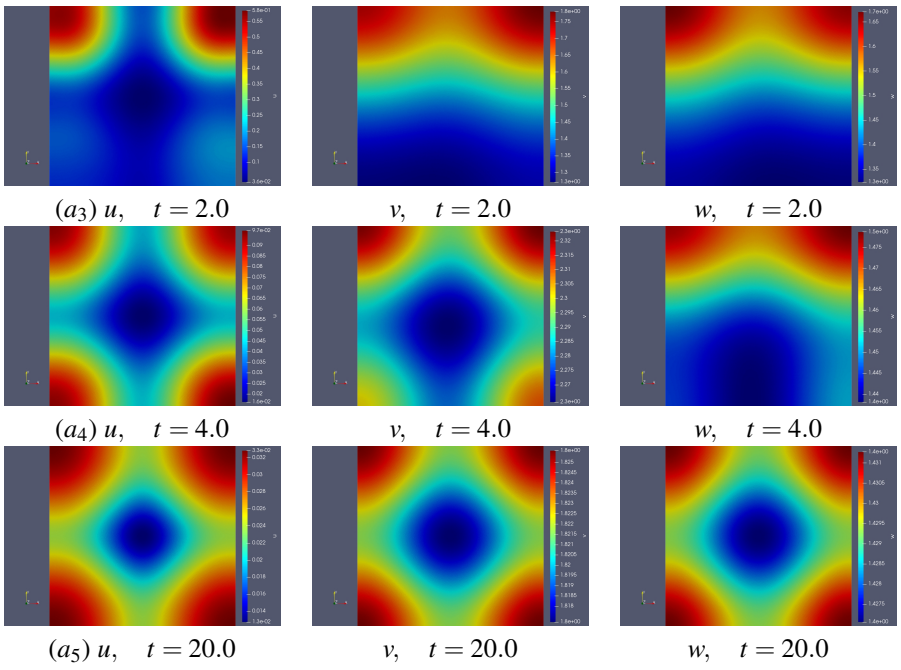


$(a_4)\ u, \quad t = 2.0$ $(b_4)\ v, \quad t = 2.0$ $(c_4)\ w, \quad t = 2.0$

$(a_5)\ u, \quad t = 4.0$ $(b_5)\ v, \quad t = 4.0$ $(c_5)\ w, \quad t = 4.0$

$(a_6)\ u, \quad t = 20.0$ $(b_6)\ v, \quad t = 20.0$ $(c_6)\ w, \quad t = 20.0$

Figure 5: Evolution of the spatial distribution of the three species. $e_1 = 10.0, e_2 = 1.0$



$(a_3)\ u, \quad t = 2.0$ $v, \quad t = 2.0$ $w, \quad t = 2.0$

$(a_4)\ u, \quad t = 4.0$ $v, \quad t = 4.0$ $w, \quad t = 4.0$

$(a_5)\ u, \quad t = 20.0$ $v, \quad t = 20.0$ $w, \quad t = 20.0$

Figure 6: Evolution of the spatial distribution of the three species. $e_1 = 1.0, e_2 = 0.5$

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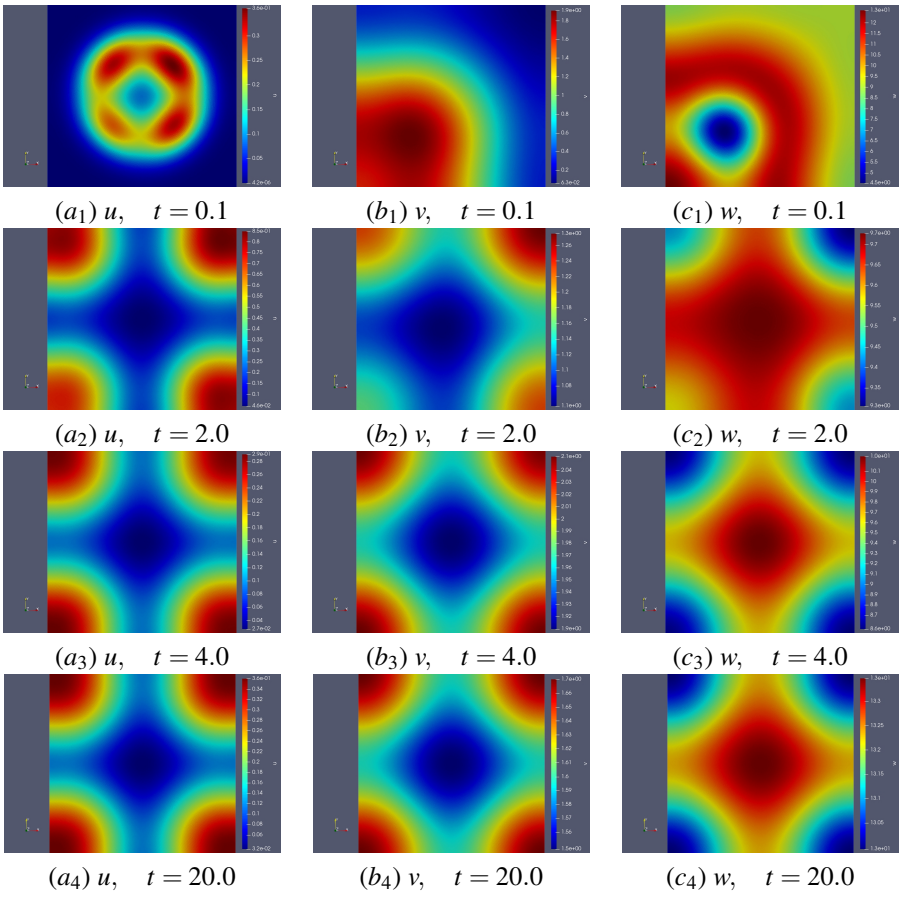

Figure 7: Evolution of the spatial distribution of the three species.

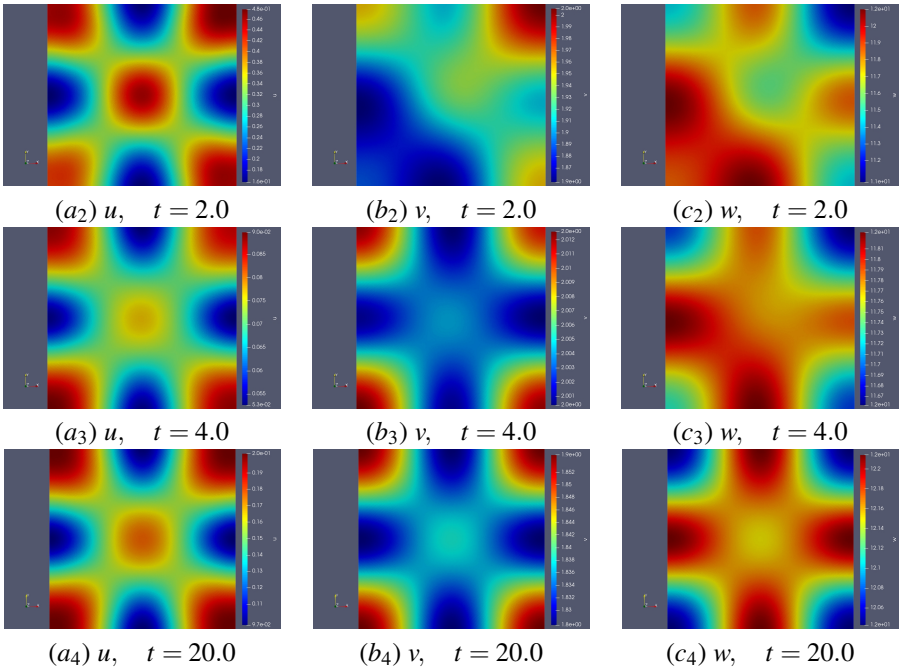

Figure 8: Evolution of the spatial distribution of the three species. The suitability of resource habitat is given by (12)

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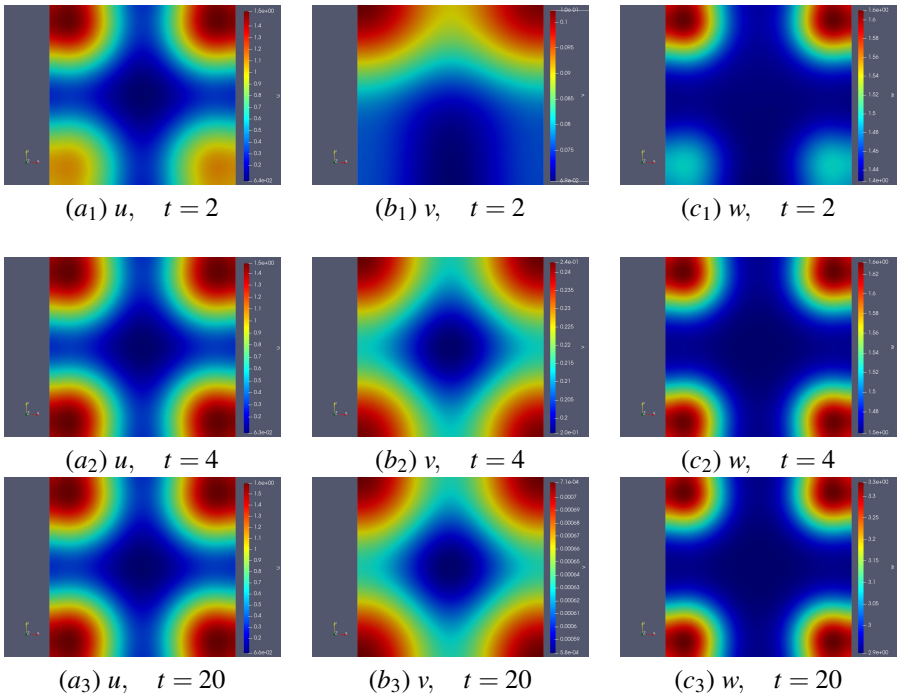
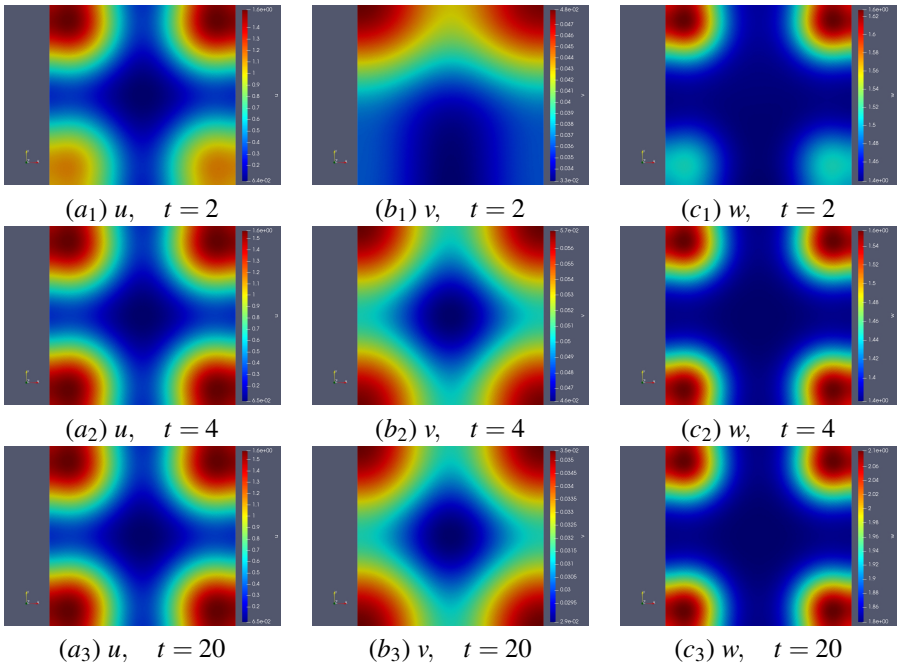


$(a_1)\ u, \quad t = 2$ $(b_1)\ v, \quad t = 2$ $(c_1)\ w, \quad t = 2$

$(a_2)\ u, \quad t = 4$ $(b_2)\ v, \quad t = 4$ $(c_2)\ w, \quad t = 4$

$(a_3)\ u, \quad t = 20$ $(b_3)\ v, \quad t = 20$ $(c_3)\ w, \quad t = 20$

Figure 9: *Contour plots* of time evolution of the resource u, mesopredador v and top predador w at different times. $q = 0.1$, $c = 1.0$



$(a_1)\ u, \quad t = 2$ $(b_1)\ v, \quad t = 2$ $(c_1)\ w, \quad t = 2$

$(a_2)\ u, \quad t = 4$ $(b_2)\ v, \quad t = 4$ $(c_2)\ w, \quad t = 4$

$(a_3)\ u, \quad t = 20$ $(b_3)\ v, \quad t = 20$ $(c_3)\ w, \quad t = 20$

Figure 10: *Contour plots* of time evolution of the resource u, mesopredador v and top predador w at different times. $q = 0.1$, $c = 1.5$

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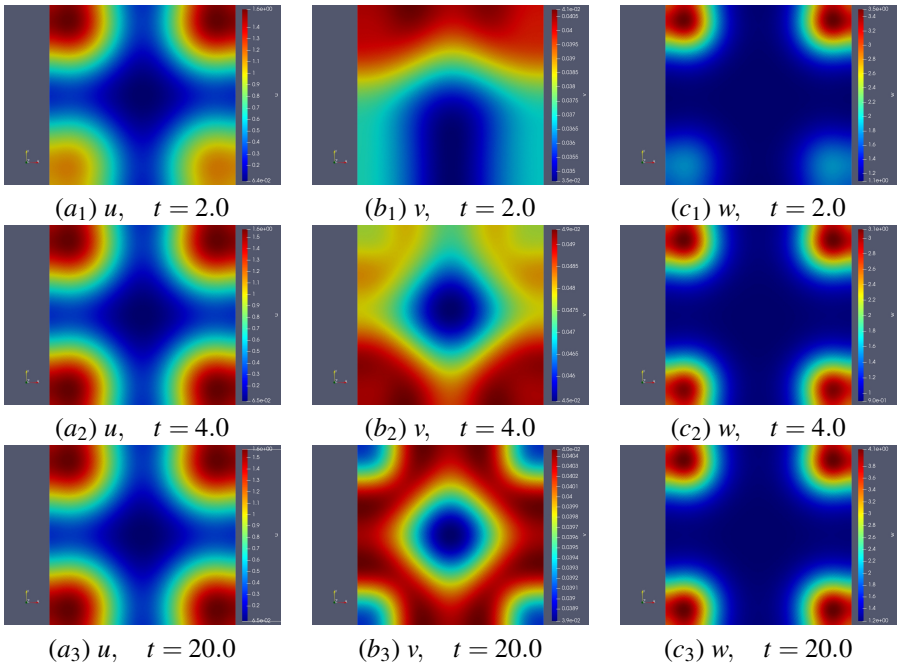

Figure 11: *Contour plots* of time evolution of the resource u, mesopredador v and top predador w at different times. $q = 1.0$, $c = 1.5$

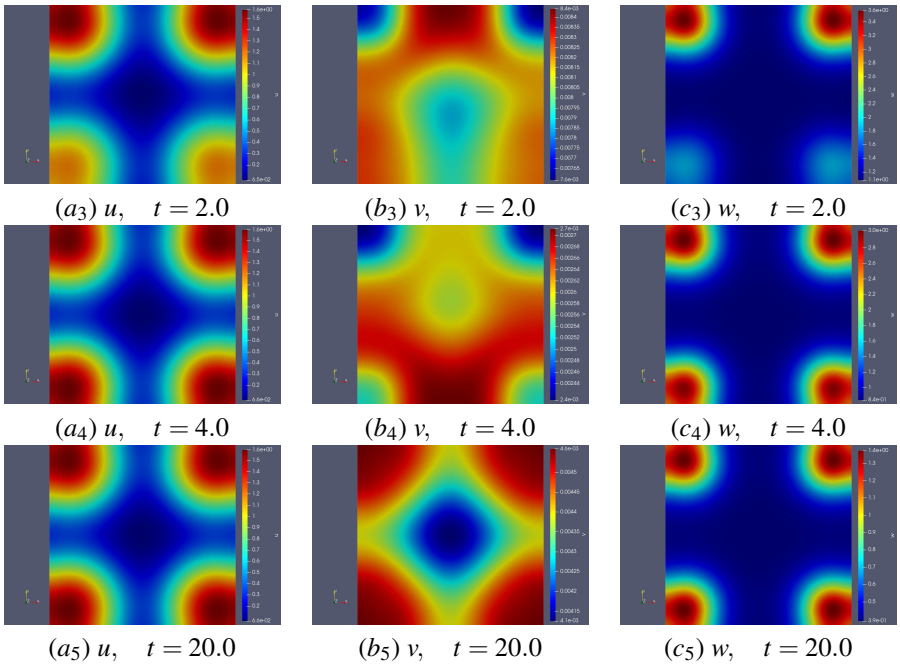

Figure 12: *Contour plots* of time evolution of the resource u, mesopredador v and top predador w at different times. $q = 1.0$, $c = 2.5$

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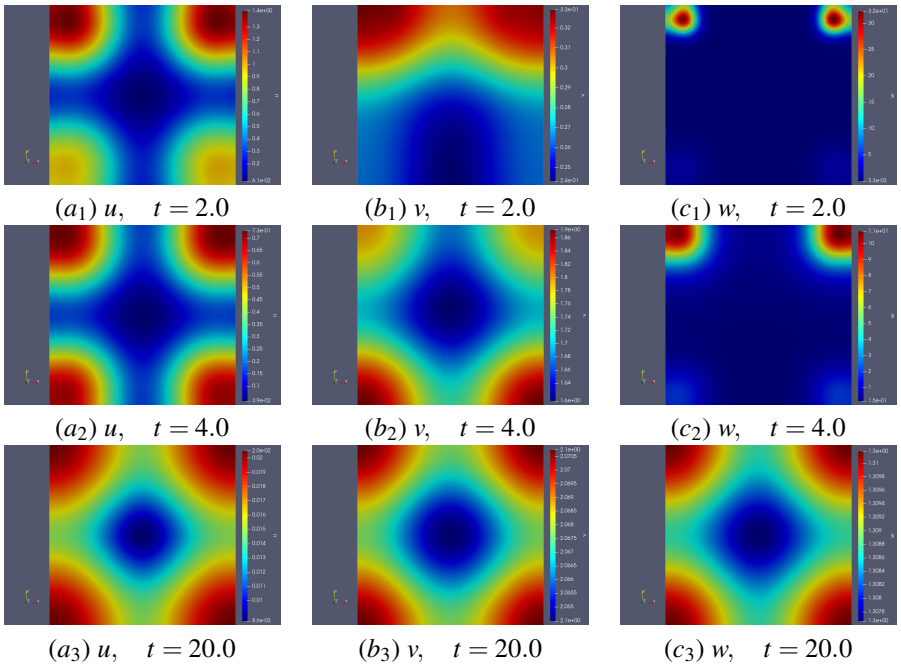

Figure 13: *Contour plots* of time evolution of the resource u, mesopredador v and top predador w at different times. $q = 10.0$, $c = .1$

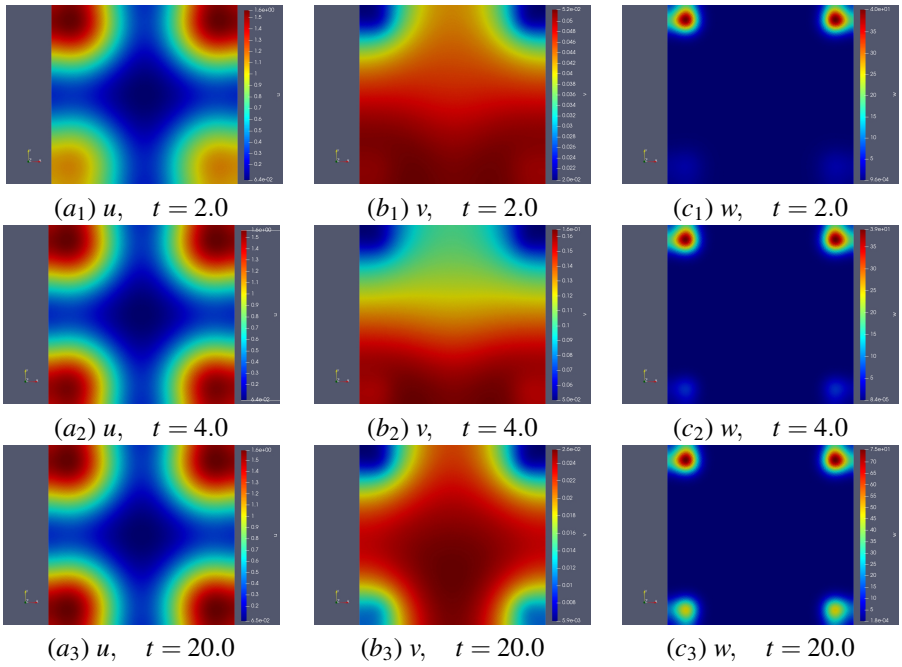

Figure 14: *Contour plots* of time evolution of the resource u, mesopredador v and top predador w at different times. $q = 10.0$, $c = 1.5$

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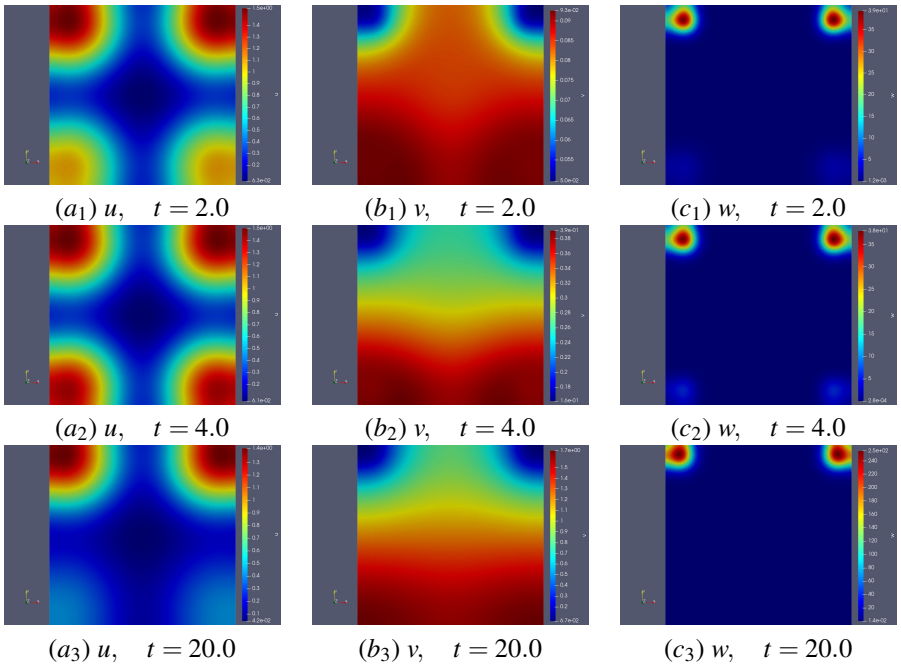

$(a_1)\ u, \quad t = 2.0$ $(b_1)\ v, \quad t = 2.0$ $(c_1)\ w, \quad t = 2.0$

$(a_2)\ u, \quad t = 4.0$ $(b_2)\ v, \quad t = 4.0$ $(c_2)\ w, \quad t = 4.0$

$(a_3)\ u, \quad t = 20.0$ $(b_3)\ v, \quad t = 20.0$ $(c_3)\ w, \quad t = 20.0$

Figure 15: *Contour plots* of time evolution of the resource u, mesopredador v and top predador w at different times. $q = 10.0$, $c = 1.0$

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CONTRIBUTION OF THE AUTHORS (CREDIT)

The three authors contributed equally in

- Conceptualization
- Formal Analysis
- Investigation
- Writing – original draft

A APPENDIX

SPATIAL DISCRETIZATION

Variational formulation

We consider a general reaction-diffusion problem with Neumann boundary conditions

$$\begin{aligned} -\Delta u + \mu u &= f \quad \text{en } \Omega && (13)\\ u(x,0) &= u_0(x) \quad \text{en } \Omega && (14)\\ \partial_n u(x,t) &= 0 \quad \text{en } \partial\Omega && (15) \end{aligned}$$

where function $f \in C^0(\Omega)$ is regular, $\mu \in \mathbb{R}$. As it is usual $\partial_n u = \nabla u \cdot \mathbf{n}$, where $\mathbf{n}$ is the exterior normal vector to $\partial\Omega$.

A classic solution of the above problem (13)–(15) is a function $u : \bar{\Omega} \mapsto \mathbb{R}$, $u \in C^2(\bar{\Omega})$ which satisfies (13)–(15). In order to facilitate the search of u we reformulate the problem to find a equivalent solution.

Let $v \in C^2(\bar{\Omega})$. Multiplying (13) by v it is obtained

$$-v\Delta u + \mu uv = fv$$

Integrating on Ω

$$-\int_\Omega v\Delta u \, d\Omega + \mu \int_\Omega uv \, d\Omega = \int_\Omega fv \, d\Omega \qquad (16)$$

Applying the Green Theorem

$$\int_\Omega \nabla u \cdot \nabla v \, d\Omega - \int_{\partial\Omega} (\nabla u \cdot \mathbf{n}) v \, dS + \mu \int_\Omega uv \, d\Omega = \int_\Omega fv \, d\Omega. \qquad (17)$$

Since $\partial_n u = 0$ for $x \in \partial\Omega$, we have

$$\int_\Omega \nabla u \cdot \nabla v \, d\Omega + \mu \int_\Omega uv \, d\Omega = \int_\Omega fv \, d\Omega. \qquad (18)$$

This expression is known as variational formulation of the problem (13)–(15), see (Vidar, 2007). Notice that in (18) it is only required that $u, v \in C^1(\bar{\Omega})$. Furthermore, they can even be just continuous.

Discretization Finite Element Method

Let $H^k(\Omega)$ a Sobolev space and $C^1(0,T,C^2(\bar{\Omega}))$ is the space of continuously differentiable functions from $[0,T]$ on $C^2(\bar{\Omega})$. Ω_h is a polygonal approximation of Ω. We consider a mesh T_h of Ω_h consisting of convex elements $E_i \in T_h$, $i \in I$, $I \subset \mathbb{N}$.

Let $\{\varphi_j(x,y)\}_{1\le j\le N}$ be a base of V_h

$$\begin{aligned} u_h(x,y,t) &= \sum_{j=1}^{N} u_i(t)\varphi_j(x,y)\\ v_h(x,y,t) &= \sum_{j=1}^{N} v_i(t)\varphi_j(x,y)\\ w_h(x,y,t) &= \sum_{j=1}^{N} w_j(t)\varphi_j(x,y) \end{aligned}$$

$x, y \in \Omega$, $0 \le t \le T$. The basis $\varphi_j(x,y)$ are compact support functions and we use the usual linear elements $P1$ defined on triangles.

Parameter h represents the size of element E_i of mesh T_h and is defined as

$$h = \max_{E_i \in T_h} \operatorname{diam}(E_i),$$

as $h \mapsto 0$, space V_h is closer to $H^k(\Omega)$.

SEMI-DISCRETIZATION OF TIME

Let

$$0 = t_0 < t_1 < \cdots t_N = T,$$

a partition of the interval $[0,T]$ with constant step $dt = t_{m+1} - t_m$ for all $m \in \{0,\ldots,N-1\}$. The derivative with respect to time is approximated using forward finite differences

$$u_t = \frac{u^{m+1}-u^m}{dt}, \quad v_t = \frac{v^{m+1}-v^m}{dt}, \quad w_t = \frac{w^{m+1}-w^m}{dt}$$

where $u^m = u(x,t_m), v^m = v(x,t_m), w^m = w(x,t_m)$.

By substituting the above approximation in Model (1) we obtain that

$$\begin{aligned} u^{m+1} &= u^m + dt\cdot d_0\Delta u^{m+1} + dt\cdot \alpha u^{m+1}(1-\frac{u^{m+1}}{K(x,y)})\\ &\quad -dt\cdot\frac{bu^{m+1}v^{m+1}}{u^{m+1}+a},\\ v^{m+1} &= v^m + dt\cdot d_1\Delta v^{m+1} + dt\cdot\gamma\frac{bu^{m+1}v^{m+1}}{u^{m+1}+a}\\ &\quad -dt\cdot\frac{cv^{m+1}w^{m+1}}{v^{m+1}+d} - \mu v^{m+1} \qquad (19)\\ w^{m+1} &= w^m + dt\cdot d_2\Delta w^{m+1} + dt\cdot\beta\frac{cv^{m+1}w^{m+1}}{v^{m+1}+d}\\ &\quad -dt\cdot\rho w^{m+1} - dt\cdot\nabla\cdot(\chi_2(v^{m+1},w^{m+1})\nabla v^{m+1}). \end{aligned}$$

This is the Implicit Euler Method which depends on both $(x,y) \in \Omega$ for each element E_i and the boundary conditions

$$\nabla u^{m+1}\cdot\mathbf{n}=0,\ \nabla v^{m+1}\cdot\mathbf{n}=0,\ \nabla w^{m+1}\cdot\mathbf{n}=0,\quad m\geq 0. \quad (20)$$

From the initial values u_0, v_0, and w_0, we compute the next iterations $(u_1,v_1,w_1),\ \ldots,(u_N,v_N,w_N)$. The system (19) is solved by FEM, assuming that $u_0,v_0,w_0\in C^2(\bar{\Omega})$, see (Douglas and Dupont, 1970). To avoid some complications which arise from the nonlinearity involved in (19), the terms corresponding to temporal variation are solved using a semi-implicit Runge-Kutta method of second order. The two steps of this computational process are depicted in the following. First, the right side of equations (1) are rewritten as

$$\begin{aligned} F(u,v,w) &= d_0\Delta u+\alpha u(1-\frac{u}{K(x,y)})-\frac{buv}{u+a},\\ G(u,v,w) &= d_1\Delta v+\gamma\frac{buv}{u+a}-\frac{cvw}{v+d}-\mu v, \qquad (21)\\ H(u,v,w) &= d_2\Delta w+\beta\frac{cvw}{v+d}-\rho w-\nabla\cdot(\chi_2(v,w)\nabla v). \end{aligned}$$

The first step of the RK–method of second order consists in an one Euler step computed at central point of each time interval.

$$u^{m+1/2} = u^m+\frac{dt}{2}\cdot F(u^m,v^m,w^m) \quad (22)$$

$$v^{m+1/2} = v^m+\frac{dt}{2}\cdot G(u^m,v^m,w^m) \quad (23)$$

$$w^{m+1/2} = w^m+\frac{dt}{2}\cdot H(u^m,v^m,w^m) \quad (24)$$

In the second step, computations are made at time $m+1$ like

$$u^{m+1} = u^m+dt\cdot F(u^{m+1/2},v^{m+1/2},w^{m+1/2}) \quad (25)$$

$$v^{m+1} = v^m+dt\cdot G(u^{m+1/2},v^{m+1/2},w^{m+1/2}) \quad (26)$$

$$w^{m+1} = w^m+dt\cdot H(u^{m+1/2},v^{m+1/2},w^{m+1/2}) \quad (27)$$

Now we considered the diffusion in an implicit form, then the schema becomes a semi-implicit one. For each step, the equations are solved by applying the FEM Galerkin-Ritz method described above.The same scheme of discretization is applied to Model (2).

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Pathogenesis throughout the systems: a reaction networks model of the infection process of *Salmonella enterica*

Patogénesis a través de los sistemas: un modelo de redes de reacción del proceso de infección de *Salmonella enterica*

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ABSTRACT

Salmonella enterica is a gut-associated bacterial pathogen that can invade host cells and disseminate through the body using complex molecular machinery. The interplay between the host immune response and the bacteria is filled with many interactions at different complexity levels and molecular scales. This host-pathogen interaction can be modelled through reaction networks (RNs). RNs are mathematical models that represent interactions and dynamics of its components to provide a quantitative framework for studying complex biological processes. Even though RNs has been used to model biological processes, the multilevel dynamics of host-pathogen interaction is hard to model with current modelling approaches that limit the insights of the system. Here we show that the infection process of *Salmonella enterica* and its interplay with the host immune system can be modelled through RNs to form a host-pathogen model and gain insight into key processes of infection.

Keywords:

Mathematical Modelling, Pathogenesis, Host-Pathogen Interaction, Salmonella enterica

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RESUMEN

Salmonella enterica es un patógeno bacteriano asociado al intestino que puede invadir las células del huésped y diseminarse a través del cuerpo usando maquinaria molecular compleja. La interacción entre la respuesta inmune del huésped y la bacteria está llena de muchas interacciones en diferentes niveles de complejidad y escalas moleculares. Esta interacción huésped-patógeno se puede modelar a través de redes de reacción. Las redes de reacción son modelos matemáticos que representan interacciones y dinámicas de sus componentes para proporcionar un marco cuantitativo para el estudio de procesos biológicos complejos. Aunque las redes de reacción se han utilizado para modelar procesos biológicos, la dinámica multinivel de la interacción huésped-patógeno es difícil de modelar con los enfoques de modelado actuales que limitan el entendimiento del sistema. Aquí mostramos que el proceso de infección de *Salmonella enterica* y su interacción con el sistema inmunologico del huésped se pueden modelar a través de redes de reacción para formar un modelo de patógeno-hospedero y obtener información sobre los procesos clave de infección.

Palabras Claves:

Modelamiento Matemático, Patogénesis, Interacción Patógeno-Hospedero, Salmonella enterica

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1 INTRODUCTION

Pathogenesis refers to the process by which a pathogen causes disease within a host organism. It involves a series of interactions between the pathogen and the host, leading to the development and progression of the disease. Understanding the pathogenic processes is crucial since it provides insights into how pathogens invade the host, evade immune responses, and cause tissue damage. By unraveling the mechanisms underlying pathogenesis, researchers can identify potential targets for intervention, develop effective treatments, and design preventive strategies such as vaccines (Karkey *et al.*, 2018).

Moreover, studying the pathogenesis of specific pathogens, such as *Salmonella enterica*, allows us to gain a deeper understanding of the factors that contribute to their virulence, transmission, and persistence within the host. Through this knowledge, we can develop more targeted approaches to combat and control infectious diseases.

There is a plethora of modelling technologies one can use, each one with their pros and cons (Veloz, 2019), but Reaction Networks (RNs) stand out for the modelling of complex host-pathogen interactions (Loskot *et al.*, 2019). In this article we rely on them since they shine where different components interact with each other using reactions. These reactions are specific to each process (e.g. cell growth, infection, cell death, etc.) and they are independent of each other in time scales (Loskot *et al.*, 2019; Lambusch *et al.*, 2018). The emergence of dangerous pathogens presents the need to research their infection process to develop better treatment strategies. The need to obtain information at different levels of complexity is more and more a necessity in biological research. Here we propose a RNs model to show that complex host-pathogen interactions can be modelled by using *S. enterica* as an example.

2 PATHOGENESIS OF *Salmonella enterica*

Salmonella enterica (*S. enterica*) is a pathogenic bacterium primarily associated with gastrointestinal infections. It is widely studied as a model organism for understanding the mechanisms of disease. Within the species, various serovars exist, with *S. enterica* sv. Typhimurium and *S. enterica* sv. Typhi being the most relevant (Jajere, 2019).

S. Typhimurium is known to infect a wide range of hosts, including humans and animals, while *S.* Typhi specifically targets humans. Even though there are notable differences in the severity and progression of the diseases caused by these two serovars, they share many common characteristics that contribute to their ability to infect their respective hosts (Jajere, 2019).

Both *S.* Typhimurium and *S.* Typhi possess a set of virulence factors and mechanisms that enable them to colonize and invade the host's intestinal tract. These factors include adhesins that facilitate the attachment of the bacteria to the intestinal epithelium, invasion proteins that promote the entry of *S. enterica* into host cells, and effector proteins

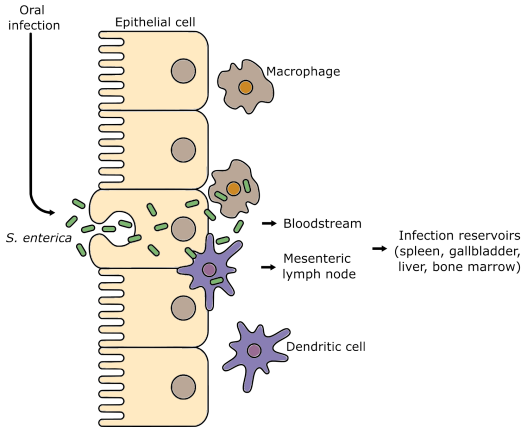

Figure 1: Process of *S. enterica* infection from oral infection, to invasion and persistence in organ reservoirs.

delivered via the type III secretion system (T3SS) that manipulate host cell processes and suppress the immune response (Hume *et al.*, 2017).

S. enterica is equipped with various survival mechanisms to evade the immune system and establish a persistent infection. These include the ability to survive and replicate within macrophages and other phagocytes, where it can evade immune clearance and disseminate to other tissues. Additionally, *S. enterica* can invade dendritic cells, which are crucial for initiating immune responses, allowing the bacterium to influence the host's immune defenses (Mastroeni *et al.*, 2009; Li, 2022; Kurtz *et al.*, 2017).

While *S.* Typhimurium causes a self-limiting gastroenteritis in humans, *S.* Typhi causes a more severe systemic infection known as typhoid fever. The latter is characterized by prolonged fever, gastrointestinal symptoms, and potential complications in various organs. However, despite the differences in disease severity, the underlying mechanisms of infection and pathogenesis are shared to a large extent between these two serovars (Jajere, 2019; Runkel *et al.*, 2013).

INTESTINAL INFECTION

First and foremost, *S. enterica* enters the host by ingestion of contaminated food or water (Figure 1). Various sources can contribute to the contamination, including raw or undercooked poultry, eggs, unpasteurized dairy products, and raw fruits and vegetables that have been exposed to fecal matter containing *S. enterica*. Upon ingestion, *S. enterica* passes through the harsh acidic environment of the stomach and eventually reaches the small intestine, which is its primary target for colonization (Hume *et al.*, 2017; Li, 2022; Runkel *et al.*, 2013).

Within the intestinal tract, *S. enterica* encounters a dynamic microenvironment characterized by changes in pH, temperature, and nutrient availability. These environmental cues act as signals that trigger specific adaptive responses in *S. enterica*, allowing the bacterium to adapt, survive, and establish

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infection within the intestinal environment (Runkel *et al.*, 2013; Spector and Kenyon, 2012; Mastroeni *et al.*, 2009; Li, 2022).

S. enterica exploits specialized epithelial cells called M cells, which are primarily located in the gut-associated lymphoid tissue (GALT), including the Peyer's patches (lymphoid follicles found in the small intestine) (Mastroeni *et al.*, 2009; Li, 2022; Jajere, 2019). M cells lack the protective mucus layer present in other intestinal epithelial cells, making them particularly vulnerable to bacterial invasion. *S. enterica* utilizes the molecular machinery of the T3SS to inject virulence factors directly into the M cells (Mastroeni *et al.*, 2009; Li, 2022). These injected virulence factors facilitate the breach of the epithelial barrier, enabling *S. enterica* to gain entry into the underlying tissues (Mastroeni *et al.*, 2009).

Once *S. enterica* has successfully invaded M cells, it subsequently gains access to the underlying epithelial cells. Within these cells, *S. enterica* triggers its own uptake through a process called "triggered phagocytosis". This process involves the manipulation of host cell signaling pathways by *S. enterica*, leading to the engulfment of the bacterium by the epithelial cells. Once inside, *S. enterica* harnesses the host cell's machinery to replicate, creating localized infection foci called "Salmonella-containing vacuoles" (SCVs). *S. enterica* manipulates the host cell's cytoskeleton and molecular processes to establish a protected replication niche favorable for its survival and proliferation (Mastroeni *et al.*, 2009; Li, 2022; Dandekar *et al.*, 2015; Ilyas *et al.*, 2017; Fang and Méresse, 2022).

Once epithelial cells from the intestinal tract have been infected, they act as a reservoir for further intestinal infections. *S. enterica* is able to induce cell death in these cells, making them burst open and releasing the bacteria (Mastroeni *et al.*, 2009).

SYSTEMIC INFECTION

S. enterica has the ability to invade various immune system cells, macrophages being a prominent target (Gogoi *et al.*, 2018) along with dendritic cells (Mastroeni *et al.*, 2009; Li, 2022).

Once inside the SCV, *S. enterica* actively manipulates host cell's machinery to create a replication niche. The bacterium secretes effector proteins through its T3SS into the cytoplasm of the host cell. These effectors modulate various cellular processes, including cytoskeletal rearrangements, vesicular trafficking, and signaling pathways, to promote SCV integrity and nutrient acquisition (Li, 2022; Mastroeni *et al.*, 2009).

During the course of infection, macrophages are recruited to the site of *S. enterica* invasion in an attempt to suppress the pathogen. However, *S. enterica* has developed several evasion strategies to survive and replicate within macrophages. These mechanisms include the production of efflux pumps to expel antimicrobial peptides, modification of lipopolysaccharide structure to avoid immune recognition, modification of macrophage polarization from a proinflammatory (M1 type) to an antiinflamatory (M2 type), and inhibition of phagosome-lysosome fusion to prevent bacterial degradation (by modifying the lipid composition of the SCV membrane and interfering with the recruitment of lysosomal components) (Li, 2022).

By surviving within macrophages, *S. enterica* can evade immune responses and establish a persistent infection (Mastroeni *et al.*, 2009; Li, 2022). The ability of *S. enterica* to persist within macrophages contributes to its evasion of the immune system and establishment of a systemic infection.

Another set of immune cells that *S. enterica* can invade are dendritic cells. These cells are found in the Peyer's patches. Along with macrophages, Salmonella can make its way inside dendritic cells by signalling phagocytosis using pathogen-associated molecular patterns (PAMPs) that are recognized by immune system cells. After invasion, Salmonella can use dendritic cells as vehicles to reach the mesentheric lymph node, facilitating migration and dissemination through the system (Li, 2022). Dendritic cells, when detecting a bacterial pathogen, can activate killer T cells to target and remove the pathogen from the infection site (Wick, 2007; Tam *et al.*, 2008).

Infection and inflammatory responses activate the recruitment of monocytes to the affected area. Monocytes are a special type of mononuclear phagocytes that leave the bone marrow to the site of infection, releasing antimicrobial components to control the spread of *S. enterica*. Monocytes once in the site of infection will differentiate into macrophages or dendritic cells, which can be infected by *S. enterica* (Li, 2022; Tam *et al.*, 2008). Along with monocytes, neutrophils also react to inflammatory responses in the site of infection. This type of immune cell is short-lived and similarly to monocytes, they will be the first line of immune defense against *S. enterica* infection (Cheminay *et al.*, 2004). They are considered a very effective control of intracellular pathogens. Their high numbers present in the body at all times make them a constant monitoring agent against infections, although they seem to have a lower effect against non-typhoidal *S. enterica* (Castanheira and García-del Portillo, 2017).

As the infection progresses, *S. enterica* can breach the intestinal epithelial barrier and disseminate to other tissues and organs. The bacteria can access the bloodstream by directly penetrating the intestinal epithelium or by crossing the gut-associated lymphoid tissue. Once in the bloodstream, *S. enterica* can travel to various organs throughout the body, including the liver, spleen, kidneys, and bone marrow. This systemic dissemination leads to the establishment of infection in these organs and contributes to the severity of the disease. The ability of *S. enterica* to survive and multiply within host cells, including epithelial cells and immune system cells, facilitates its dissemination and persistence within different body compartments (Runkel *et al.*, 2013; Jajere, 2019; Hume *et al.*, 2017).

The process of pathogenesis of *S. enterica* although well understood still impose challenges to the treatment of the bacteria, specially with the appearance of multidrug-

resistant strains and the increase of infection rates of dangerous serovars (e.g. *S.* Typhi) (Karkey *et al.*, 2018). This is why we developed a RNs model of the infection process of *S. enterica* to determine the main processes and stages that are required for the bacteria to develop the intestinal and systemic progression of disease.

3 Reaction Networks Modeling of Host-Pathogen Interactions

RNs are mathematical models that represent the interactions and dynamics of biochemical reactions within a biological system (Dittrich and di Fenizio, 2007). They provide a quantitative framework for studying complex biological processes and understanding the behavior of biochemical networks. RNs capture the connectivity between molecular species, the rates of biochemical reactions, and the dependencies between different reactions. By characterizing the network of interactions, RNs enable the simulation and prediction of how changes in molecular concentrations and reaction rates influence the overall behavior of the system (August and Papachristodoulou, 2009; Centler *et al.*, 2008; Styles *et al.*, 2021).

The usefulness of RNs in modeling biological processes lies in their ability to capture the intricate details of biochemical reactions and their dependencies. They provide a systematic approach to study the dynamics of cellular processes, signaling pathways, and metabolic networks. RNs allow researchers to test hypotheses, simulate different scenarios, and gain insights into the underlying mechanisms of complex biological phenomena. Moreover, they can be used to integrate experimental data, validate theoretical models, and make predictions about the behavior of the system under different conditions (Loskot *et al.*, 2019; Lambusch *et al.*, 2018; Zhang and Zhou, 2019; Duso and Zechner, 2020).

Since complex biological and chemical processes are hard to understand on their own, modelling techniques provide a great alternative to gain insight on complex systems (Wen *et al.*, 2023). RNs have been widely used for modelling complex networks and processes where computational approaches are needed. Anything from chemical processes and gene regulatory networks to population dynamics and symbiosis interaction can be benefited by them. From molecular biology to biotechnological applications, RNs are used to gain insight of processes with non-linear dynamics (Loskot *et al.*, 2019).

One of such applications is to understand the interaction of two organisms in the context of symbiosis, which in general terms could be mutualistic or parasitic. These interactions are highly regulated by genes, nutrient acquisition, immune suppression and molecular communication. Such complex systems can gain a lot of insight from RNs, recognizing that components are not limited to a on/off state or the same time scale (Centler *et al.*, 2008; August and Papachristodoulou, 2009).

In the context of host-pathogen interactions, RNs are valuable tools for modeling and understanding the dynamic interplay between the host and the pathogen. They can capture the molecular interactions involved in infection, immune responses, and pathogen evasion strategies. By constructing RNs that represent the interactions between host cells and pathogens, researchers can simulate the progression of infection of disease, investigate the effects of host immune responses, and identify potential targets for therapeutic intervention (Vlazaki *et al.*, 2019; Styles *et al.*, 2021). These models can provide valuable insights into the pathogenesis of specific pathogens, such as *S. enterica*, shedding light on the underlying molecular mechanisms driving the infection process.

It is of special interest the use of RNs to model the process of infection. Since *S. enterica* is a well known model of gastrointestinal infection, it comes as a great candidate to evaluate the systemic pathogenesis model. In this case we evaluate the process of pathogenesis from the intestinal survival and invasion, the internalization of *S. enterica* into epithelial cells and macrophages, and finally the systemic dissemination and infection.

4 Systemic Pathogenesis Model

The model uses *S. enterica* as its model organism. The components of the RNs model are shown in Table 1 and the network graph is shown in Figure 2. For the given components, 27 reactions ($r_1 - r_{27}$) are extracted from literature based on the main processes from *S. enterica* infection:

$r_1 : S_{en} \xrightarrow{I_{nvasion}} SM_c$: *S. enterica* senses the intestinal environment and nutrients that activate the molecular machinery of the T3SS, thus granting it the ability to invade specialized epithelial cells. These are called M cells and are a common way of infection of *S. enterica* since they lack a key protective mucus layer.

$r_2 : S_{en} + D_c \xrightarrow{I_{nvasion}} SD_c$: From the intestinal environment, *S. enterica* can also invade dendritic cells that are between the gap junctions of epithelial cells in the intestine, making

Table 1: Model components and their respective annotations

S_{en}	*S. enterica* in intestinal lumen
SM_c	*S. enterica* in M cells
M_p	Macrophages
SM_p	*S. enterica* in Macrophages
D_c	Dendritic cells
SD_c	*S. enterica* in Dendritic cells
SP_p	*S. enterica* in Peyer's Patches
M_{ln}	*S. enterica* in Mesenteric Lymph Node
SS_y	Systemic infection (bacteremia)
R_s	*S. enterica* in Organ Reservoirs
M_y	Monocytes
N_p	Neutrophils
$\varnothing$	Cell death

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it a good intermediary for later spreading systemically.

$r_3 : SM_c + M_p \xrightarrow{I_{nvasion}} SM_p$: *S. enterica* can also invade macrophages that are found roaming around the epithelial barrier. It survives inside them and can travel throughout the body via blood or the mesenteric lymph node. This becomes a hostile environment for *S. enterica*, where it needs to activate and deactivate host processes to avoid the normal immune response of the cell.

$r_4 : SM_c \xrightarrow{I_{nvasion}} SP_p + N_p + M_y$: From M cells, *S. enterica* can pierce through the epithelial barrier and reach a lymphoid tissue called Peyer's patches. This process of infection releases inflammatory responses that signal neutrophils and monocytes to fight bacteria at the site of infection.

$r_5 : SP_p + D_c \xrightarrow{I_{nvasion}} SD_c$: From the Peyer's patches, *S. enterica* can invade dendritic cells that are recruited to the site of infection.

$r_6 : SP_p + M_p \xrightarrow{I_{nvasion}} SM_p$: From the Peyer's patches, *S. enterica* can invade macrophages that are recruited to the site of infection.

$r_7 : M_{ln} + D_c \xrightarrow{I_{nvasion}} SD_c$: From the mesenteric lymph node, *S. enterica* can invade dendritic cells that are recruited to the site of infection.

$r_8 : M_{ln} + M_p \xrightarrow{I_{nvasion}} SM_p$: From the mesenteric lymph node, *S. enterica* can invade macrophages that are recruited to the site of infection.

$r_9 : R_s + M_p \xrightarrow{I_{nvasion}} SM_p$: From the organ reservoirs, *S. enterica* can invade macrophages that are recruited to the site of infection.

$r_{10} : R_s + D_c \xrightarrow{I_{nvasion}} SD_c$: From the organ reservoirs, *S. enterica* can invade dendritic cells that are recruited to the site of infection.

$r_{11} : SD_c \xrightarrow{D_{issemination}} SP_p + M_{ln} + SS_y + R_s + N_p + M_y$: After invading dendritic cells, *S. enterica* can travel to different sites to spread infection, such as the Peyer's patches, mesenteric lymph node, the bloodstream and organ reservoirs. This process of infection releases inflammatory responses that signal neutrophils and monocytes to fight bacteria at the site of infection.

$r_{12} : SP_p \xrightarrow{D_{issemination}} M_{ln} + N_p + M_y$: From the Peyer's patches, *S. enterica* can gain access to the mesenteric lymph node, and thus, disseminating from it to other sites. This process of infection releases inflammatory responses that signal neutrophils and monocytes to fight bacteria at the site of infection.

$r_{13} : M_{ln} \xrightarrow{D_{issemination}} SS_y$: From the mesenteric lymph node, *S. enterica* can disseminate through the blood stream.

$r_{14} : SM_p \xrightarrow{D_{issemination}} SS_y + R_s + N_p + M_y$: Infected macrophages can spread *S. enterica* through the bloodstream and organ reservoirs. This process of infection releases inflammatory responses that signal neutrophils and monocytes to fight bacteria at the site of infection.

$r_{15} : SS_y \xrightarrow{D_{issemination}} R_s + N_p + M_y$: From the bloodstream, *S. enterica* can reach organ reservoirs, promoting a persistent infection in them.

$r_{16} : R_s \xrightarrow{D_{issemination}} SS_y$: From the organ reservoirs, *S. enterica* can disseminate through the bloodstream, reaching different sites to infect and making it a persistent infection.

$r_{17} : N_p + SP_p \xrightarrow{I_{mmunity}} \varnothing$: Neutrophils recruited to the site of infection in the Peyer's patches, fight *S. enterica* by engulfing and later degrading it. Since neutrophils are short-lived, the result of this process becomes cell death for both parties.

$r_{18} : N_p + M_{ln} \xrightarrow{I_{mmunity}} \varnothing$: Neutrophils recruited to the site of infection in the mesenteric lymph node, fight *S. enterica* by engulfing and later degrading it. Since neutrophils are short-lived, the result of this process becomes cell death for both parties.

$r_{19} : N_p + R_s \xrightarrow{I_{mmunity}} \varnothing$: Neutrophils recruited to the site of infection in the organ reservoirs, fight *S. enterica* by engulfing and later degrading it. Since neutrophils are short-lived, the result of this process becomes cell death for both parties.

$r_{20} : M_y + SP_p \xrightarrow{I_{mmunity}} D_c$: Monocytes recruited to the site of infection in the Peyer's patches, differentiate into dendritic cells, which signal other immune cells to fight the infection of *S. enterica*.

$r_{21} : M_y + M_{ln} \xrightarrow{I_{mmunity}} D_c$: Monocytes recruited to the site of infection in the mesenteric lymph node, differentiate into dendritic cells, which signal other immune cells to fight the infection of *S. enterica*.

$r_{22} : M_y + SS_y \xrightarrow{I_{mmunity}} D_c$: Monocytes recruited to the site of infection in the bloodstream, differentiate into dendritic cells, which signal other immune cells to fight the infection of *S. enterica*.

$r_{23} : M_y + R_s \xrightarrow{I_{mmunity}} D_c$: Monocytes recruited to the site of infection in the organ reservoirs, differentiate into dendritic cells, which signal other immune cells to fight the infection of *S. enterica*.

$r_{24} : M_y + SP_p \xrightarrow{I_{mmunity}} M_p$: Monocytes recruited to the site of infection in the Peyer's patches, differentiate into macrophages, which fight the infection of *S. enterica* by engulfing and degrading it.

$r_{25} : M_y + M_{ln} \xrightarrow{I_{mmunity}} M_p$: Monocytes recruited to the site of infection in the mesenteric lymph node, differentiate into macrophages, which fight the infection of *S. enterica* by engulfing and degrading it.

$r_{26} : M_y + SS_y \xrightarrow{I_{mmunity}} M_p$: Monocytes recruited to the site of infection in the bloodstream, differentiate into macrophages, which fight the infection of *S. enterica* by engulfing and degrading it.

$r_{27} : M_y + R_s \xrightarrow{I_{mmunity}} M_p$: Monocytes recruited to the site of infection in the organ reservoirs, differentiate into macrophages, which fight the infection of *S. enterica* by engulfing and degrading it.

All these reactions are a simplification of the complex process of infection, immune response and host-pathogen interaction. With these key processes it's important to notice that there are main host cells that play a role as a target of

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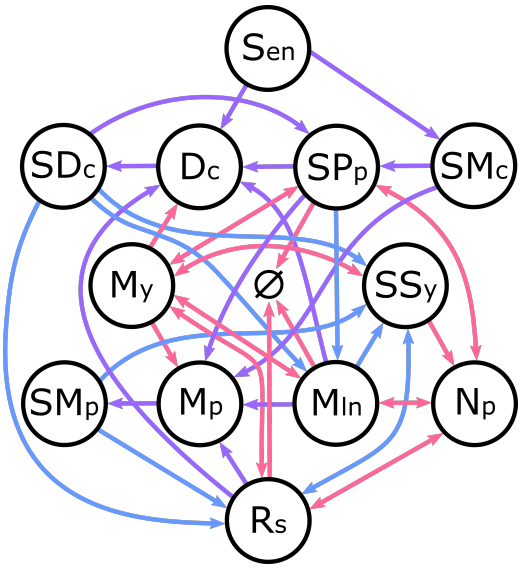

Figure 2: Network graph of the infection process of *Salmonella enterica*. Purple edges represent *S. enterica* invasion to host cells, blue edges represent dissemination of *S. enterica* (lymphoid tissue, bloodstream and organ reservoirs), red edges represent immune response to fight *S. enterica*.

S. enterica like M cells, macrophages and dendritic cells, or as specialized cells to fight the infection such as neutrophils and monocytes.

It is also important to mention that throughout the infection process of *S. enterica*, several environments are found and will affect bacteria in different ways. The high nutrient content of the intestine grants *S. enterica* the ability to grow and activate the molecular machinery to begin the infection process. In a different way, the nutrient starved and harsh environment found inside macrophages will delay bacterial growth and activate survival instead. These differences are key for further inspection of the model since they will affect the kinetics of the reactions and thus, will affect how fast certain processes will occur.

In a similar way, *S. enterica* must avoid being detected by the immune system and has to rely on specific genes to suppress the immune response of the host (such as PhoP/Q two-component system). The dynamics of these processes add another layer of complexity to the system since they will affect the kinetics of the interactions negatively. Finally, the fact that *S. enterica* uses reservoirs to maintain the infection and produce a subsequent reinfection is a key process to understanding the infection process of *S. enterica*. It not only affects the survival aspects of the bacteria in the whole process, but also how the system regulates itself.

For the identification of key processes, simulations are required to check if the model is robust, as well as to compare different scenarios of infection (e.g. typhoidal infection vs non-typhoidal infection, immunized host vs non-immunized host, etc.)

5 Simulation of the model

Here are shown the results of the simulations of the systemic pathogenesis model. In this case, the only initial conditions were in the S_{en}, M_y, N_p, M_p and D_c components, as they are both the infection of *S. enterica* and the immune cells present in the body at all times. From literature, the kinetic constants were determined regarding invasion Tahoun *et al.* (2012), infection (Tam *et al.*, 2008; Monack *et al.*, 1996; Bueno *et al.*, 2008) and immune response (Cheminay *et al.*, 2004; Castanheira and García-del Portillo, 2017; Tam *et al.*, 2008; Hurley *et al.*, 2014).

In Figure 3 it is possible to see that the infection of typhoidal *S. enterica* is quick and proceeds to generate infection sites throughout the body. In this case, *S. enterica* survives within the host due to the generation of reservoirs which both increases bacterial density and decreases immune response. This goes in hand with literature, where common ways to test for *S. enterica* infection is to check samples of bone marrow, blood and stool (Wain *et al.*, 2001; Tennant *et al.*, 2015). Regarding the immune response, it is evident that neutrophils are the most abundant ones and the first one to fight infection, although since they have a short lifespan their response is hindered in the long run. In contrast, monocytes are seen to have a more steady production over time, which may be due to the differentiation into macrophages and dendritic cells instead of fighting the infection directly by themselves. Interestingly, Peyer's patches, the mesentheric lymph node and organ reservoirs have a small peak shortly after infection, which is rapidly reduced just to grow exponentially afterwards. This effect could be due to the rapid bacterial growth in infection sites that act as reservoirs for *S. enterica*, suggesting that the process of initial infection and shortly after, the dissemination of those bacteria to other tissues, is a key process for persistent systemic infection.

In the modern world, efforts for the development of antimicrobial treatments as well as immunization alternatives have reduced the threat of *S. enterica*. Given that non-typhoidal infection of *S. enterica* is much less lethal than typhoidal infections (30% mortality without antibiotic treatment), the progression of the disease in a common individual may look different. In Figure 4 it is possible to see that the clearance of infection is fast due to the greater immune response in these simulations. Even though *S. enterica* still achieved a systemic infection, the concentration in contrast with Figure 3 is minimal.

From this model we can extract the following points. 1) The infection process of *S. enterica* is a complex process that is filled with many host-pathogen interactions. 2) These interactions are affected by the dynamics of the immune response and the possibility of reinfections due to reservoirs. 3) Even though the presented model is a simplification of what is happening in a real situation, it can help us notice key processes of infection, such as the invasion of Peyer's patches and the dissemination through the mesenteric lymph node and organ reservoirs.

This model goes to show that RNs are a helpful way to

visualize and understand how multilevel processes like this happen.

6 DISCUSSION

We found that the systemic pathogenesis model brings up information that other modelling approaches fail to do. This is due to the nature of RNs where components are only a part of the model and for it to be fully functional, interactions or reactions are needed to control and understand how the dynamics of the system change at different parts of the infection process.

With the above results, it is possible to see some key processes of the host-pathogen interaction between *S. enterica* and the host. One of those key processes is the spread of *S. enterica* through the Peyer's patches and the mesenteric lymph node, mostly due to the amount of intermediaries that can allow bacteria to travel from the site of infection to organ reservoirs. The dynamics of these interactions suggest that it is at the very least, a very common path of *S. enterica* to disseminate to reservoirs.

These interactions have been modeled through biological phenomena that has been researched throughout the years. *S. enterica* is a well known pathogen and model of study for host-pathogen interaction and what we show is a simplification of complex interactions. These interactions show that *S. enterica* is a specialized bacterium that can suppress the immune response of the host cells and that it correlates with the available data.

The data available usually corresponds to genomic analysis, systems biology techniques and reaction rate models (Styles *et al.*, 2021; Stelling, 2004). These models usually are specific to gene regulatory networks of a determined species or interaction processes in a controlled environment. These models usually lack the different layers of complexity found in biological systems.

Specifically to *S. enterica*, systems of ordinary differential equations, metabolic network analysis and others has been done (Bumann, 2009; Lo, 2007; Sweilam *et al.*, 2022). These models are usually used in the area of epidemiology for disease spread in a specific situation. That is the case of typhoid fever, where a few studies have reported the emergence, spread and control of the disease by using mathematical models (Gauld *et al.*, 2018; Pitzer *et al.*, 2015).

These reports show that the insights gained from modelling dynamics allow for unexpected results. That is the case of Pitzer *et al.* (2015) where population density and cross-immunity was not enough to explain typhoid emergence in Blantyre, but increase in the duration of infectiousness and transmission rate did. This goes to show that data on its own is not enough to get the full picture of the processes and dynamics of a system, and that computational efforts are needed to uncover them.

In a similar manner, Gauld *et al.* (2018) developed a mathematical model for typhoid transmission in Santiago, Chile. Their model showed that vaccination and reduced exposure to long-cycle transmission were important factors for the decline of incidence. Although the approach of these two cases are on a disease level and not an infection level. These studies reflect the need of better alternatives to what has been done on mathematical modelling efforts to complement the reports available, specially within the infection process bacteria.

In regards to this problematic, a study built a so called "within-host" mathematical model to understand the pathophysiology of *S. Typhi* from ingestion to the full progression of disease. What they found was that the migration of bacteria to the caecal lymph node was a key step for the dissemination of *S. Typhi* and the progression of disease. Even though the analysis is very robust, it lacks major components and interactions that are crucial in the pathogenesis of *S. enterica*, making it a powerful but simple model. This makes RNs a useful alternative to these types of models.

Even though network analysis is somewhat common in biological sciences, the use of RNs is very limited, even more in host-pathogen interactions. One such case of a network analysis is that of Zhang *et al.* (2022), where they evaluated the network model of a inter-host disease spreading with intra-host evolutionary dynamics. This study is a great example of modelling biological systems at different layers of complexity (inter-host and intra-host) since the components work independently from one another and that can have great impact on the results and comparisons of the model with what is actually happening.

Another example is that of the complex interactions between bacteriophages, bacteria and eukaryotic hosts with the goal of understanding these interactions to develop phage therapies as an alternative to antibiotics. This is another example of host-pathogen interaction at different layers of complexity, where RNs have been used in flux-balance analysis (Styles *et al.*, 2021).

Recent studies regarding endosymbiosis (a type of symbiosis where one species inhabits inside another species) proposed reaction network model to show the interactions between organisms (Veloz and Flores, 2021b,a). This study showed the endosymbiotic relationship between a coral host and its symbiont (*Symbiodinium* sp.). This is another example of host-pathogen interaction but in this case both species cooperate for survival (Veloz and Flores, 2021a). This co-operation is tightly regulated by evolution and biochemical pathways that helps both species live in harmony.

The above mentioned examples suggest that there is an unexplored niche of research to develop new models that can fill the gaps that other studies failed to complete. As such, RNs models, specially those related to host-pathogen interactions are not only an emerging technology for the modelling of host-pathogen interactions, but also a way to model them at the different levels of complexity that they appear in nature.

Some considerations that need to be made in this model are that: 1) it is necessary to refine the organismic and biochemical reactions described, and 2) they can be applied

to other pathogens with similar pathogen-host interactions, or even that these reactions serve as support to describe different cases. Nonetheless, this model shows that the intricate interactions of *S. enterica* can be simplified without losing significant information of the system, all while benefiting from the framework of RNs.

7 CONCLUSION

The complexity of biological processes can be simplified to accommodate a mathematical model using RNs as a modelling framework. This model sets a basis for the future development of modelling technologies for the research of host-pathogen interactions with the goal to understand the key steps in infection and develop strategies to fight pathogens.

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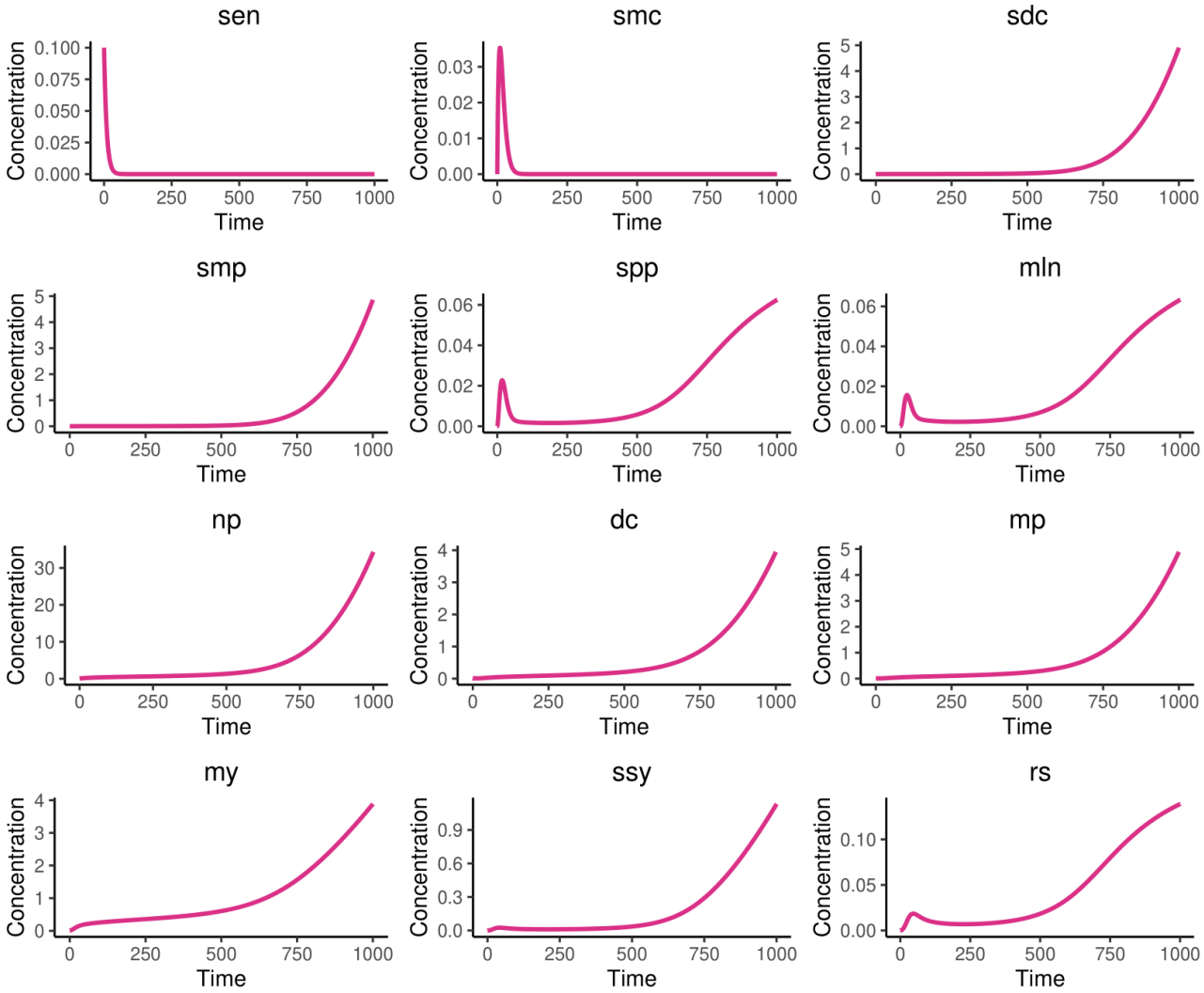

Figure 3: Simulation of the infection process of *S. enterica*. The evolution of the 12 components of the model are shown as the concentration change over time.

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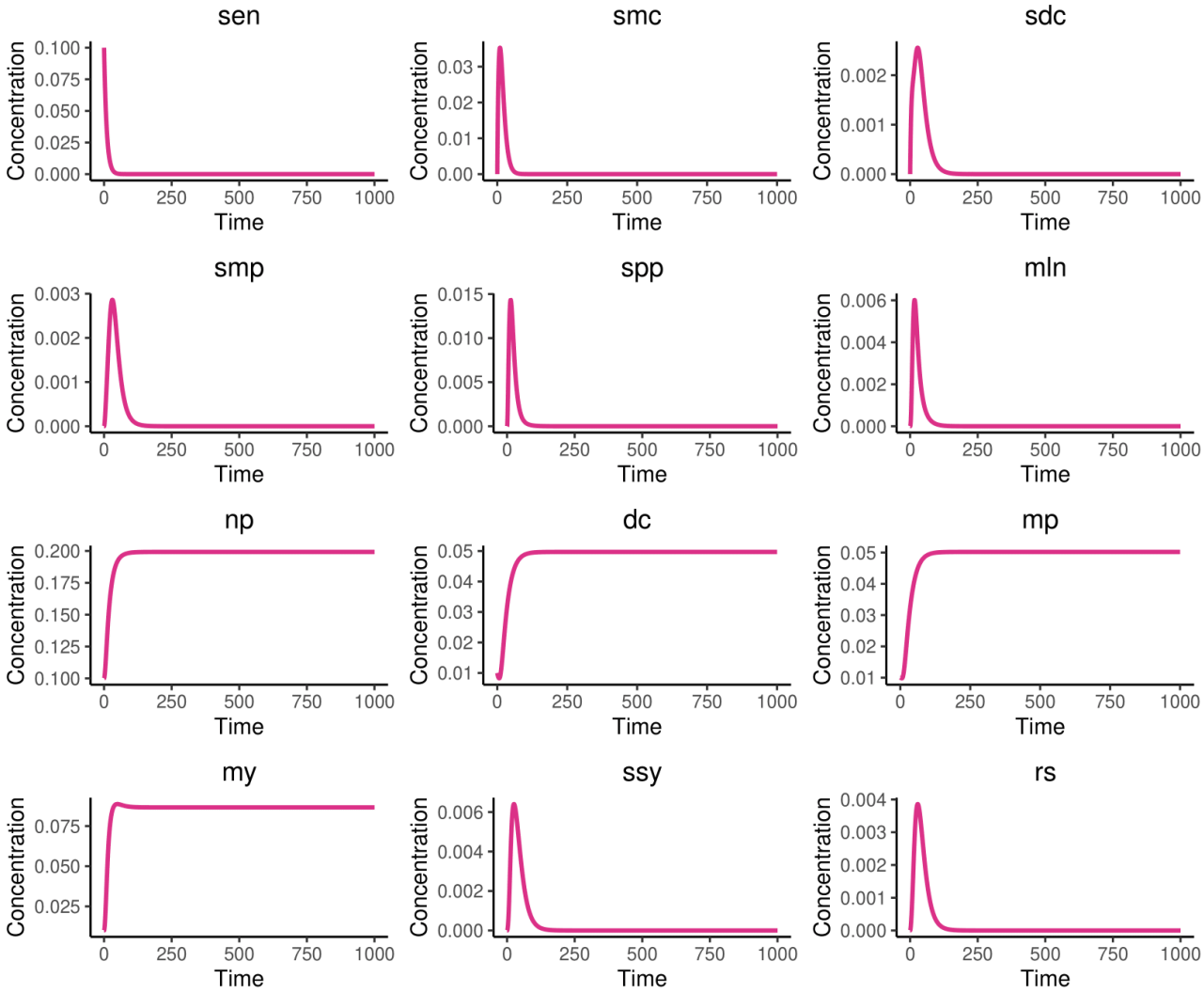

Figure 4: Simulation of the infection process of *S. enterica* in a immunized host. The evolution of the 12 components of the model are shown as the concentration change over time. The parameters of the immune response were increased to simulate a vaccinated host.

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Beyond R_0: Exploring New Approaches

Más allá de R_0: Explorando Nuevos Enfoques

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ABSTRACT

The basic reproduction number, denoted as R_0, is a crucial parameter in infectious disease modeling and serves as a key element for designing control strategies.
Calculating R_0 can be challenging in certain situations due to the complexity of the model. This complexity often hinders the explicit computation of R_0 and makes it difficult to understand how different populations and parameters influence its value. Recent research has introduced the concept of the target reproduction number as an alternative to R_0 (Shuai *et al.*, 2013).
The target reproduction number demonstrates how it is possible to exert control over the entire system, by analyzing some subsystems that describe the behavior of an infectious disease, it is possible to exert control over the entire system. The target reproduction number offers a framework for making decisions in public health. In this study, we apply it to two models: a model involving incomplete vaccination and a model for leptospirosis. The presented models showcase two fundamental features of the target reproduction number. Firstly, its expression's simplicity compared to the basic reproduction number. Secondly, its behavior analogous to R_0 at 1.

Keywords:

Target reproduction number, Failed vaccination model, Basic reproduction number, Mathematical Epidemiology.

RESUMEN

El número básico de reproducción, en la modelización de enfermedades infecciosas es un valor fundamental para diseñar estrategias de control. Calcular el valor de R_0 puede ser difícil en algunas situaciones debido a la complejidad del modelo. Esta complejidad a menudo obstaculiza el cálculo explícito de R_0 y dificulta la comprensión de cómo diferentes poblaciones y parámetros influyen en su valor. Trabajos recientes han propuesto el número de reproducción objetivo como alternativa al R_0 (Shuai *et al.*, 2013).
El número de reproducción objetivo muestra cómo, a través del análisis de algunos de los subsistemas que describen el comportamiento de una enfermedad infecciosa, es posible ejercer control sobre todo el sistema. El número de reproducción objetivo puede proporcionar un marco para la toma de decisiones en salud pública. En este trabajo lo aplicamos a dos modelos: un modelo con vacunación incompleta y un modelo para la leptospirosis.
Los modelos presentados exhiben dos características fundamentales del número de reproducción objetivo. En primer lugar, la simplicidad de su expresión en comparación con el número de reproducción básico. En segundo lugar, su comportamiento análogo al R_0 en 1.

Palabras Claves:

Número de reproducción objetivo, Modelo de vacunación imperfecta, Número de reproducción básico, Epidemiología Matemática.

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1 INTRODUCTION

On infectious disease modeling, the basic reproduction number (R_0) is crucial. It indicates the average number of secondary infections generated by an infectious individual in a fully susceptible population during its infectious period. Calculating R_0 is essential because it provides vital information for assessing the likelihood of an epidemic outbreak and understanding how diseases will spread. Moreover, it aids in the development of effective strategies to control and prevent infectious diseases (van Den Driessche and Watmough, 2002). In mathematical models involving multiple infectious compartments, computing the basic reproduction number R_0 can be challenging (Saldaña and Barradas, 2018), as it involves intricate parameter relationships resulting in complex expressions. Even if an explicit expression for R_0 is derived, identifying which parameters impact its reduction most significantly is not always straightforward. The expression's complexity often hampers direct analysis. The challenge of calculating and modifying R_0 has direct implications when designing strategies for controlling and preventing infectious diseases. Without a clear understanding of the factors that influence R_0 and how to intervene in them, devising effective measures to contain disease spread becomes more difficult.

The aforementioned challenges highlight the necessity on calculating a value that is easy to determine and enables the design of control strategies in a clear manner. In this way, the work presented by (Heesterbeek, 2007) introduces the concept of target reproduction number. This approach provides a significantly simpler expression in comparison to the originally proposed basic reproduction number.

This perspective concentrates on implementing specific strategies within a subsystem of the disease propagation model, provided that the remaining subsystems are under control. The objective is to exert control over the disease spread.

The target reproduction number estimates the level of effort required to eliminate an infectious disease when control is applied to a specific subpopulation (Driessche, 2017).
An illustrative example could arise in the context of a disease where diverse infection groups coexist, such as in the case of leptospirosis, where infectious groups encompass both animals and bacteria, with humans as the susceptible classes. Assuming that certain transmission routes have been controlled due to prior measures, for instance, transmission between humans and bacteria through interventions like water treatment, the focus might shift to controlling other transmission routes, specifically infections between animals and bacteria. The target reproduction number offers a tool to regulate the subsystem related to the intended control pathways. Consequently, it becomes feasible to achieve control over the entire system, provided the other subsystems associated with the remaining transmission routes have already been managed.

A fundamental property of the target reproduction number resides in its value being 1 when the basic reproduction number is also equal to 1. This characteristic implies that control strategies implemented to attain a value of 1 in the target reproduction number will also place R_0 at 1. Depending on the model's characteristics, for example, if the model does not exhibit a backward bifurcation at $R_0 = 1$, this could lead to disease elimination through control strategies as mentioned.
The target reproduction number is not unique, as it depends on the population to which the control strategy is applied. This implies that the value of the target reproduction number can vary based on the considered population.

In practice, it is recognized that different control strategies can lead to disease eradication. Therefore, it is necessary to evaluate which strategy requires lower implementation costs.
To illustrate the calculation of the target reproduction number, in this work two examples are presented. The first model, proposed in (Gandon *et al.*, 2003), addresses a scenario of failed vaccination where the infectious disease can persist despite vaccination. This model is known as the incomplete vaccination model.
On the other hand, the second model is about leptospirosis, presented in (Baca *et al.*, 2015). In this work an analysis is conducted on a model representing leptospirosis, a disease in which humans become infected through direct or indirect contact with the urine of infected animals, wounds, or other bodily fluids. In this work, numerical simulations will be presented to illustrate the obtained results. These simulations will illustrate how, by implementing control strategies constructed based on the target reproduction number, the infected curves tend towards zero as time increases. This implies the eradication of the disease.

In this article, the emphasis lies on the significance of the target reproduction number as an alternative to the basic reproduction number, facilitating more detailed analyses and employing simpler expressions. We refer to prior investigations conducted by (Roberts and Heesterbeek, 2003) and (Driessche, 2017). This paper is structured as follows. In Section 2 it is elaborated on the concept of the target reproduction number, detailing the steps and calculations required for its construction. In Section 3 it is shown two specific examples in which target reproduction number is employed to underscore its utility in concrete situations. Additionally, this section includes simulations to verify the effectiveness of the target reproduction number as a control strategy. In the last section, the discussion is presented, highlighting the main results obtained in the analyses, along with the effectiveness of implementing the strategy based on target reproduction number.

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2 CONSTRUCTION OF THE TARGET REPRODUCTION NUMBER

In this section, the construction of the target reproduction number will be performed using the methodology proposed by (Roberts and Heesterbeek, 2003) and (Lewis *et al.*, 2019).

In this analysis, the study addresses an infectious disease that spreads among susceptible individuals using a system of differential equations. Specifically, the existence of n infectious compartments is considered. To understand and analyze the disease spreading dynamics, we will start by using the next-generation matrix, referred to as $K = [k_{ij}]$. This matrix, as described in the study by (van Den Driessche and Watmough, 2002), characterizes the interactions and connections among the distinct infectious compartments, playing a fundamental role in determining the target reproduction number.

Each element k_{ij} in the matrix K represents the expected number of secondary infections in the compartment i that can be caused by an infected individual in the compartment j, considering a fully susceptible population during their infectious period. These matrix components reflect the potential for disease the propagation among the different compartments.

To explain the methodology, we will begin with the first infectious compartment. That is in a fully susceptible population, the introduction of an infected individual belonging to compartment 1 will be considered. Subsequently, the matrix K will be used to calculate the expected number of individuals in all infectious compartments in the next generation of infection, due to an infectious individual from the first compartment.

Considering the canonical vector $e_1 = (1,0,\ldots,0)$ of the standard basis in $\mathbb{R}^n$, we will compute Ke_1. The i-th component of this vector represents the expected number of new infections in compartment i produced by an in individual from compartment 1. Specifically, the first component of this vector represents the expected number of new cases in the infectious compartment 1 in the next generation of infection, caused by an infectious individual from compartment 1.

To identify all new infections in compartment 1, it is necessary to consider infections generated by individuals from other compartments. To achieve this, the first position of the vector (Ke_1) is removed. This is accomplished through the expression $(I-P)(Ke_1)$, where $P = [p_{ij}]$ is the projection matrix defined by:

$$\begin{cases} p_{ij} = 1 & \text{if} \quad i = j = 1, \\ p_{ij} = 0 & \text{otherwise.} \end{cases}$$

Subsequently, the matrix K is applied again to the resulting vector $(I-P)(Ke_1)$, allowing us to obtain the expected number of infected individuals from classes 2 to n that are generated by an infectious individual from class 1 during the second generation of infection.

In the third generation of infection, the vector $K(I-P)(Ke_1)$ is calculated. The expected number of infected individuals of type 1 is obtained using the expression $PK(I-P)(Ke_1)$.
On the other hand, the term $(I-P)(K(I-P)(Ke_1))$ represents the expected number of infected individuals of types 2 to n. This term takes into account infections that occur in intermediate generations of the infection without the involvement of infectious individuals of type 1.
After $j+1$ generations of infection, the value $e_1^T K((I-P)K)^{j-1} e_1$ represents the expected number of infected individuals of type 1 that arise during the infection cycle without the intervention of an infectious individual from the same group in an intermediate generation. Therefore, the value representing the number of secondarily infected individuals of type 1 originating from an infected individual of type 1 is:

$$\Gamma_1 = e_1^T K \sum_{j=0}^{\infty} ((I-P)K)^j . \tag{1}$$

The spectral radius of the matrix $(I-P)K$ is denoted as $\rho(I-P)K$. If $\rho((I-P)K) < 1$, then the sum, given in (1), converges to:

$$\Gamma_1 = e_1^T K (I-(I-P)K)^{-1} e_1. \tag{2}$$

In the realm of numerous infectious diseases, different groups of infected individuals are often encountered. Previously, the focus was solely on counting the expected number of infected individuals from the first group. However, it is now possible to generalize this concept by considering the existence of l classes of infected individuals, where l can be less than or equal to n. The following definition is provided:

Definition 1 *The target reproduction number Γ_l is defined as the spectral radius of the $l \times l$ matrix M_l, given by:*

$$M_l = E_l^T K (I-(I-P_l)K)^{-1} E_l. \tag{3}$$

With E_l and P_l are matrices of size $n \times l$ and $n \times n$ respectively, defined as:

$$\begin{cases} (P_l)_{ii} = (E_l)_{ii} = 1 & \text{if} \quad i = 1,\ldots l, \\ (P_l)_{ij} = (E_l)_{ij} = 0 & \text{otherwise.} \end{cases}$$

From this point onward, we will employ the matrices: $D = P_l K$ and $B = (I-P_l)K$, which were used in the equation given in (3). Note that $D+B = K$.

A related method regarding the matrices D and B, as proposed by (Driessche, 2017), is presented in the next. Suppose that a control strategy is to be applied and the parameters describing the infection behavior in the next-generation matrix

K are modified. Let S be the set of entries in K that will be modified by the control strategy τ. Additionally, let l be the classes of infectives from which Γ_l was constructed. In this context, the matrix $P_l = [p_{ij}]$ is:

$$\begin{cases} p_{ii} = 1 & \text{if} \quad i = 1, ...l, \\ p_{ij} = 0 & \text{otherwise.} \end{cases}$$

The matrix $D = [d_{ij}]$ will be referred to as the target matrix. It contains the entries that will be modified in the matrix K through the control strategy τ. On the other hand, $B = [b_{ij}] = (I - P_l)K$ contains the entries of K that will not be modified. To ensure an effective control strategy over the terms of the matrix K that will not be modified, it is required that the spectral radius of the matrix $B = (I - P_l)K$, denoted as $\rho(B) = \rho((I - P_l)K)$, be less than 1, as established in (1). This ensures that the non-modified terms do not significantly contribute to the disease's spread. The target reproductive number can be defined based on the aforementioned matrices B and D as follows (Driessche, 2017):

$$\Gamma_l = \rho\left(D(I - B)^{-1}\right). \tag{4}$$

With $\rho\left(D(I - B)^{-1}\right)$ being the spectral radius of the matrix $D(I - B)^{-1}$, and I being the identity matrix of size $n \times n$. Associated with the target reproduction number, the control matrix is constructed as defined below.

Definition 2 (Control Matrix) *The control matrix associated with the target matrix D is defined as $K_{C(\tau)} = B + \frac{D}{\tau}$. τ represents a control applied to the matrix D, which in turn represents the implementation of a control policy within the population.*

According to the above definition, the components d_{ij} of the matrix D are transformed to $\frac{d_{ij}}{\tau}$. The following theorem describes some characteristics of the target reproduction number as a threshold parameter, as well as its effectiveness as a control policy. The complete proofs of these theorems can be found in (Driessche, 2017).

In this section, we make use of the definition of a non-negative matrix, where all its entries are greater than or equal to zero. Additionally, we consider an irreducible matrix, characterized by the property that all its elements can be related to one another, either directly or indirectly, through a finite number of steps. This implies that there are no isolated submatrices where there is no connection between rows and columns. The main characteristic of the target reproduction number is manifested through the following theorem, which explicitly establishes the relationship between the control strategy τ applied to the population and the reproduction objective number. Γ_l, defined in equation (4).

Theorem 1 *Let K, B, D be non-negative $n \times n$ matrices with $K = B + D$ is irreducible, $D \neq 0$, and $\rho(B) < 1$. Then, $\rho(K_{C(\tau)}) = 1$ if and only if $\tau = \Gamma_l$.*

The following theorem demonstrates that the target reproduction numbers associated with different control strategies share similar characteristics, as they are threshold parameters at 1. Additionally, they offer the advantage of having much simpler expressions compared to the basic reproduction number, R_0.

Theorem 2 *Let K, B, and D be non-negative irreducible matrices with $K = B + D$, $D \neq 0$, and $\rho(B) < 1$. Then, the following propositions hold:*

i) $\rho(K) < 1$ *if and only if* $\Gamma_D < 1$.

ii) $\rho(K) = 1$ *if and only if* $\Gamma_D = 1$.

iii) $\rho(K) > 1$ *if and only if* $\Gamma_D > 1$.

This theorem establishes a relationship between the target reproductive numbers and their behavior around the threshold value of 1.

Theorem 3 *Let K, B, B', D, and D' be non-negative matrices, with $K = B + D = B' + D'$, and all of them are irreducible. $D \neq 0$, $D' \neq 0$, $\rho(B) < 1$, and $\rho(B') < 1$. If $D' < D$, then one and only one of the following propositions holds:*

i) $1 < \Gamma_D < \Gamma_{D'}$.

ii) $1 = \Gamma_D = \Gamma_{D'}$.

iii) $\Gamma_{D'} < \Gamma_D < 1$.

3 THE TARGET REPRODUCTIVE NUMBERS

In this section, we will apply the methodology proposed in (Shuai *et al.*, 2013) to calculate the target reproductive numbers for different epidemiological models in order to demonstrate the advantages of this technique.

Example 1**.** In this example, we examine the model proposed in (Gandon *et al.*, 2003). The model describes the dynamics of an infectious disease when a vaccination strategy is being implemented in the susceptible population. In this model, it is assumed that the vaccine is imperfect. The model is presented below:

$$\begin{aligned} S' &= \Lambda(1-p) - \mu S - (\beta_{uu} I + \beta_{vv} I_v) S, \\ S'_v &= -p\Lambda - \mu S_v - (\beta_{uv} I + \beta_{vu} I_v) S_v, \\ I' &= (\beta_{uu} I + \beta_{vv} I_v) S - (\mu + \nu) I, \\ I'_v &= (\beta_{uv} I + \beta_{vu} I_v) S_v - (\mu + \nu_v) I_v. \end{aligned} \tag{5}$$

In the design of control strategies, it is useful to have a tool that allows me to determine whether an epidemic outbreak will occur. In the introduction of this paper, it is mentioned that the basic reproductive number is the commonly used epidemiological threshold parameter to determine infectious dynamics at the onset of the disease.

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The next-generation matrix for model (5) is shown below.

$$K = \begin{bmatrix} \dfrac{\beta_{uu}S_0^*}{\mu+\nu} & \dfrac{\beta_{uv}S_0^*}{\mu+\nu_v} \\ \dfrac{\beta_{vu}S_{0v}^*}{\mu+\nu} & \dfrac{\beta_{vv}S_{0v}^*}{\mu+\nu_v} \end{bmatrix}, \tag{6}$$

When calculating the spectral radius of matrix K with $E_0 = (S_0, S_{0v}, 0, 0) = \left(\frac{\Lambda(1-p)}{\mu}, \frac{p\Lambda}{\mu}, 0, 0\right)$, the basic reproductive number associated with the model given in (5) is:

$$R_0 = \frac{1}{2}\left(\frac{\beta_{uu}S_o^*}{(\nu+\mu)} + \frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)} + \sqrt{\left(\frac{\beta_{uu}S_o^*}{(\nu+\mu)} + \frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)}\right)^2 - 4\left(\frac{\beta_{uu}S_0^*\beta_{vv}S_{ov}^* - \beta_{uv}\beta_{vu}S_{ov}^*S_{ou}^*}{(\nu+\mu)(\nu_v+\mu)}\right)}\right). \tag{7}$$

Consequently, the disease-free equilibrium E_0 is locally asymptotically stable if and only if $R_0 < 1$. Therefore, a control strategy involves adjusting one or more parameters of the model in such a way that the value of R_0 decreases below 1.

Note that the effects on R_0 when applying a control strategy to reduce the transmission rate among the non-vaccinated population β_{uu} are not clear. The same ambiguity applies to the other effective contact rates β_{vv}, β_{vu}, and β_{uv}. Let us consider a control strategy aimed at decreasing the spread of infections among the non-vaccinated individuals, assuming that transmissions among vaccinated individuals are under control.

This strategy can be implemented by reducing mobility among the non-vaccinated individuals. Next, we proceed to calculate the value of target reproductive number associated with this strategy, as per the definition established in equation (4). However, before performing this calculation, it is necessary to obtain the matrix $D(I-B)^{-1}$.

The expression that defines $D(I-B)^{-1}$ is as follows:

$$\begin{bmatrix} \dfrac{\frac{\beta_{uu}S_o^*}{(\nu+\mu)}\left(1-\frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)}\right)}{1-\frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)} - \frac{\beta_{uv}S_o^*}{(\nu_v+\mu)}\frac{\beta_{vu}S_{ov}^*}{(\nu+\mu)}} & \dfrac{\frac{\beta_{uu}S_o^*}{(\nu+\mu)}\frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)}}{1-\frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)} - \frac{\beta_{uv}S_o^*}{(\nu_v+\mu)}\frac{\beta_{vu}S_{ov}^*}{(\nu+\mu)}} \\ 0 & 0 \end{bmatrix}. \tag{8}$$

Let the set of indices $S = \{(i,j) \mid 0 \le i,j \le n\}$ correspond to the entries of the matrix K given in (6). According to the definition established in (4), the target reproduction number Γ_l for (5), associated with the index set $S = \{(1,1)\}$, is given by the following expression:

$$\Gamma_l = \frac{\frac{\beta_{uu}S_o^*}{(\nu+\mu)}\left(1-\frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)}\right)}{1-\frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)} - \frac{\beta_{uv}S_o^*}{(\nu_v+\mu)}\frac{\beta_{vu}S_{ov}^*}{(\nu+\mu)}}. \tag{9}$$

It is essential to highlight the simplicity of the target reproduction number as defined in equation (9), compared to the basic reproduction number established in equation (7). Although the expression for the target reproduction number is much simpler, its value equals is 1 when the basic reproduction number R_0 is also equal to 1. However, another important aspect is to consider its effectiveness in guiding the control of disease spread. This happens once a specific control strategy that modifies transmission rates has been implemented.

To demonstrate the effectiveness of the target reproduction number, numerical simulations will be conducted. The expression given in (1) asserts that by applying a control strategy to the parameters related to disease transmission in the entries of the next-generation matrix K and adjusting these parameters through the control strategy to make τ equal to the target reproduction number, the new basic reproduction number associated with the control matrix $K_{C(\tau)}$ will be equal to 1.This condition, in turn, ensures that the solution curves of system (5) approach to zero as time approaches to infinity, provided initial conditions are near the equilibrium point. Additionally, it is essential that system (5) has no endemic points in order to develop the strategy associated with the target reproduction number, the following set of parameters is considered: $\theta = (\beta_{uu}, \beta_{vv}, \beta_{uv}, \beta_{vu})$ that are related to the target reproduction number Γ_l defined in equation (9). The implementation of the control strategy involves dividing certain parameters associated with the next-generation matrix of the model by the value of the target reproduction number. In practice, this represents the minimum value to which infections must be reduced to ensure the epidemic's extinction (Saldaña and Barradas, 2018).

Contemplating controlling transmission within the unvaccinated population, entailing an adjustment to the parameter β_{uu}. Contemplating controlling transmission within the unvaccinated population, entailing an adjustment to the parameter β_{uu} will be made. This modification is defined by the new value βuu, which is calculated as $\beta uu^* = \frac{\beta_{uu}}{\Gamma_l}$. The following graphs show the temporal evolution of the curves of infected individuals before and after the implementation of the control strategy through parameter modification. These graphs illustrate the curves of infected individuals both before and after the parameter modification.

Figure (1) shows the impact on the spread of the epidemic in the unvaccinated population. It can be observed that as control is implemented, the curve showing the evolution of the infected population tends to zero as time approaches to infinity. This result is explained by the expression given in (1), which states that the control measure is effective if the transmission rate is reduced in accordance with the values specified by the target reproduction number (Saldaña and Barradas, 2018). According to the theorem presented in (3),

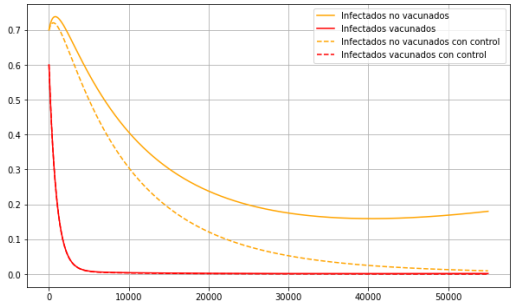

Figure 1: The graph depicts the prevalence of the infection in the non-vaccinated population over time, represented by a continuous curve in the absence of control and a dashed curve in the presence of control.
The parameter values used are: $\beta_{uu} = 0.0002$, $\beta_{vv} = 0.00009$, $\beta_{uv} = 0.000009$, $\beta_{vu} = 0.000003$, $v = 0.0001$, $v_v = 0.00011$, $p = \frac{1}{5}$, $\mu = \frac{1}{365\times 20}$, $\Lambda = 3\times\mu$

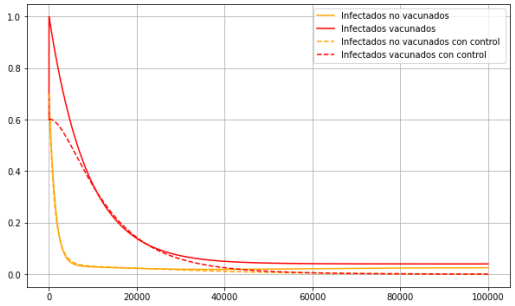

Figure 2: The graph depicts the prevalence of the disease infection in the vaccinated and unvaccinated populations over time, represented by continuous curves in the absence of control and dashed curves in the presence of control. The parameter values used are: $\beta_{uu} = 0.00000002$, $\beta_{vv} = 0.9$, $\beta_{uv} = 0.000009$, $\beta_{vu} = 0.000003$, $v = 0.001$, $v_v = 0.0001$, $p = \frac{1}{5}$, $\mu = \frac{1}{36520}$, $\Lambda = 3\mu$

when considering a different index set for the matrix K, the associated target reproductive number for that index set exhibits the same behavior around 1 as any other reproductive number associated with a different strategy.
In this context, let us consider the index set $S = \{(2,2)\}$. This index set is related to a new control strategy linked to the vaccinated population. Imagine a scenario where the epidemic spread in the non-vaccinated population is already under control, possibly due to the isolation of this population. However, the vaccinated population is allowed to circulate freely. Despite this situation, there still exists a possibility of transmission within this vaccinated group. Now, let us proceed to calculate the target reproductive number $\Gamma_{D'}$ for infections generated by a vaccinated individual in the vaccinated susceptible population. We follow a similar process as shown the previous steps for the model given in (5) with the values provided in (7), and with the matrix $D = [d_{ij}]$ with:

$$\begin{cases} d_{ij} = k_{ij} & \text{if} \quad i = j = 2, \\ d_{ij} = 0 & \text{otherwise.} \end{cases}$$

If $\rho(B) < 1$, the objective reproductive number $\Gamma_{D'}$ exists and is given by:

$$\Gamma_{D'} = \frac{\frac{\beta_{vv}S^*_{ov}}{(v_v+\mu)}\left(1 - \frac{\beta_{uu}S^*_o}{(v+\mu)}\right)}{1 - \frac{\beta_{uu}S^*_o}{(v+\mu)} - \frac{\beta_{uv}S^*_o}{(v_v+\mu)}\frac{\beta_{vu}S^*_{ov}}{(v+\mu)}}. \tag{10}$$

The target reproductive number $\Gamma_{D'}$ represents the average number of vaccinated individuals infected by another vaccinated individual in a population that is completely susceptible to the disease. The infection can spread from one vaccinated individual to another or through unvaccinated individuals.

In this context, the goal is to put in place a control strategy to reduce the spread of the epidemic among the vaccinated population, assuming that the epidemic is already under control among the unvaccinated population. To achieve this, a set of parameters $\theta = (\beta_{uu}, \beta_{vv}, \beta_{uv}, \beta_{vu})$ related to the target reproductive number $\Gamma_{D'}$ defined in (4) is taken into consideration.

Firstly, a study was conducted on the effect of vaccination on the disease spread. For this purpose, the dynamics of the epidemic in the absence of control measures on the population were analyzed, and the parameters $\theta = (\beta_{uu}, \beta_{vv}, \beta_{uv}, \beta_{vu})$ corresponding to the initial situation were obtained. Subsequently, a numerical simulation of the epidemiological model was performed using the parameters θ, in order to obtain the prevalence curves of the disease both in the vaccinated and unvaccinated populations.

Once these curves were obtained, the control strategy was implemented by adjusting the parameters $\theta_0 = (\beta_{uu}, \beta^*_{vv}, \beta_{uv}, \beta_{vu})$, where $\beta^*_{vv} = \frac{\beta_{vv}}{\Gamma_{D'}}$, with the aim of reducing the reproductive number of the disease. In practice, this could be achieved by implementing specific control measures, such as reducing the mobility of the vaccinated population, among other strategies.

Figures 1 and 2 show how, by applying control strategies based on target reproductive numbers, the curves representing the behavior of the infected individuals experience a significant decrease. This implies that, in the context of the model, the disease tends to disappear.

Example 2. The following example, presented in (Baca *et al.*, 2015), deals with human infection caused by bacteria from the environment or contact with infected animals. The mathematical model describes how an epidemic spreads, with contact with infected animals and environmental bacteria being the main sources of new infections in both animals

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and humans. Below is the detailed model:

$$\begin{aligned} S_A' &= -(C_1 I_A + C_2 B) S_A + \beta N_A - \alpha_2 S_A, \\ I_A' &= (C_1 I_A + C_2 B) S_A - \alpha_2 I_A, \\ S_H' &= -(C_3 I_A + C_4 B) S_H + \alpha_1 I_H, \\ I_H' &= (C_3 I_A + C_4 B) S_H - \alpha_1 I_H, \\ B' &= C_5 I_A + C_6 I_H - kB. \end{aligned} \tag{11}$$

By setting the direction field given in (11) equal to zero, an infection-free equilibrium is obtained with the following components:

$$X_0 = (S_{A0}, S_{H0}, I_{A0}, I_{H0}, B) = \left(\frac{N\beta}{\alpha_2}, N_H, 0, 0, 0\right). \tag{12}$$

The next-generation matrix K associated with the model described in (11) is displayed.

$$K = \begin{bmatrix} \frac{C_1 N_A}{\beta} & 0 & \frac{C_2 N_A}{K} \\ \frac{C_3 N_H}{\beta} & 0 & \frac{C_4 N_H}{K} \\ \frac{C_5}{\beta} & \frac{C_6}{\alpha_1} & 0 \end{bmatrix}. \tag{13}$$

The characteristic polynomial of (13) is defined as follows:

$$P(\lambda) = -\lambda^3 + R_1 \lambda^2 + \left(R_4^2 + R_6^2\right) \lambda + \overline{R}^3 - R_1 R_4^2. \tag{14}$$

The equation (18) define the values of R_1, R_4, R_6, and $\overline{R}$ in terms of the parameters C_1, C_2, C_4, and C_5. N_A and N_H represent the total populations of animals and humans, respectively.

$$R_1 = c_1 N_A \beta. \tag{15}$$

$$R_4 = \sqrt{\frac{C_4 C_6 N_H}{\alpha_1 k}}. \tag{16}$$

$$R_6 = \sqrt{\frac{C_2 C_5 N_A}{\beta k}}. \tag{17}$$

$$\bar{R} = \sqrt[3]{\frac{C_2 C_3 C_6 N_A N_H}{\alpha_1 \beta k}}. \tag{18}$$

The basic reproduction number R_0 associated with model (11) is defined as follows:

$$R_0 = \frac{1}{3} R_1 + z^{\frac{1}{3}} + \frac{|z|^{\frac{2}{3}}}{z^{\frac{1}{3}}}. \tag{19}$$

With

$$\begin{aligned} z = &\frac{\bar{R}^3}{2} + \frac{R_1^3}{3} + \frac{R_1 R_6^2}{6} - \frac{R_1 R_4^2}{3} + \\ &\sqrt{\frac{\bar{R}^6}{4} + \frac{R_1 R_6^2 \bar{R}_3}{6} + \frac{R_1^3 \bar{R}^3}{27} + \frac{2 R_1^2 R_4^2}{27} - \frac{R_1^4 R_4^2}{27}} \\ &- \frac{5 R_1^2 R_4^2 R_6^2}{27} - \frac{R_1^2 R_6^4}{108} - \frac{R_1^2 R_4^2 \bar{R}^3}{3} - \left(\frac{R_4^2 + R_6^2}{27}\right)^3. \end{aligned} \tag{20}$$

In the current scenario, we consider a situation where the control of transmission between humans and animals, as well as between humans and bacteria, is already controlled, possibly through control campaigns. Now, the focus is on maintaining control both between animals and between animals and bacteria, possibly through hygienic measures involving animal food consumption. With this consideration, we will proceed to calculate the value of the reproduction number associated with this control strategy. It is important to highlight that identifying which parameters are most sensitive becomes significantly more challenging when examining the entire system, due to the complexity of the expressions involved, as shown in the equation given in (20). However, by focusing the analysis on the subsystem related to a specific strategy, this task simplifies, especially if the other subsystems are already under control. Using the previous definition given in (4), the matrix B is defined as:

$$B = \begin{bmatrix} 0 & 0 & 0 \\ \frac{C_3 N_H}{\beta} & 0 & \frac{C_4 N_H}{k} \\ \frac{C_5}{\beta} & \frac{C_6}{\alpha_1} & 0 \end{bmatrix}.$$

According to the definition given in equation (4), the target reproduction number Γ_l, for (11), associated with the index set $S = \{(1,1), (1,2)\}$, is given by the following expression:

$$\rho(D(I-B)^{-1}) = \frac{(C_1 k + C_2 C_5) N_A \alpha_1 + (C_2 C_3 - C_1 C_4) C_6) N_A N_H}{(k\alpha_1 - C_4 C_6 N_H)\beta}. \tag{21}$$

It is important to highlight the simplicity of the target reproduction number in comparison to R_0 given by (20). This expression remains valid whenever the condition $\rho(B) < 1$ is satisfied, which is equivalent to:

$$\sqrt{\frac{C_4 C_6 N_H}{k\alpha_1}} < 1.$$

Next, numerical simulations will be permormed. These simulations will be carried out before applying the control strategy and after applying the control strategy using the target reproduction number. Given the target reproduction number Γ_l, as defined in equation (21), the set of parameters $\theta = (C_1, C_2, C_3, C_4, C_5, C_6)$ is taken into consideration. The strategy involves controlling the transmission rates between animals and bacteria, which leads to the modification of the parameters C_1 and C_2. New parameters are derived from the value of target reproduction number using the following expressions for C_1 and C_2, denoted as $C_1^* = \frac{C_1}{\Gamma_l}$ and $C_2^* = \frac{C_2}{\Gamma_l}$. In Figure presented show the temporal evolution of the infected individuals, including the curves of infected individuals before and after of the parameter modification.

Figure 3 illustrates how the application of combined control strategies, based on target reproduction number, manages to reduce infections in both animals and humans. The curves representing the behavior of infected individuals tend to zero, indicating that the disease tends to disappear.

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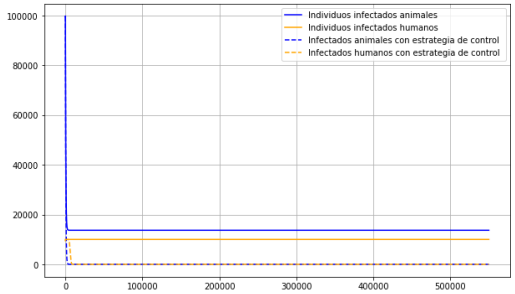

Figure 3: The graph displays the prevalence of infection by the disease in the population over time, represented by continuous curves in the absence of control and dashed curves in the presence of control. The simulation uses the following parameter values: $\beta = \frac{1}{3560}$, $C_1 = 5 \times 10^{-3}$, $C_2 = 5 \times 10^{-3}$, $C_3 = 65 \times 10^{-2}$, $C_4 = 6 \times 10^{-2}$, $C_5 = 2 \times 10^{-2}$, $C_6 = 2.15 \times 10^{-6}$, $\alpha_1 = \frac{1}{20}$, $\alpha_2 = \frac{1}{500}$, and $k = \frac{1}{18}$.

It is noteworthy how it is possible to exert control over the entire system by regulating the subsystem related to transmission between animals and bacteria. This objective is valid as long as the subsystems associated with transmission pathways involving humans are under control. Clearly, this subsystem has a considerably simpler mathematical formulation for analysis compared to the complexity of the entire system. The simplicity in its formulation represents greater efficiency when designing control strategies.

4 Discussion

Calculating the basic reproduction number in situations involving complex interactions among multiple infectious compartments poses significant challenges. The diverse interactions among these compartments, represented by different rates, complicate the derivation of simple formulas for computing R_0. This, in turn, hinders the identification of strategies for controlling the spread of an infectious disease.

In response to this complexity, the concept of the target reproduction number is suggested as a simpler alternative to the original R_0. This strategy focuses on analyzing subsystems related to transmission pathways within an infectious disease system. It shows that by controlling these subsystems, overall system control can be achieved. The target reproduction number facilitates the formulation of more specific control strategies.
By directing efforts towards a subgroup of the population, the target reproduction number provides a tool to control the outbreak of an infectious disease. The target reproduction number offers a clearer understanding of how changes in one part of the system can influence disease spread, thereby enabling more informed decision-making in the implementation of preventive measures.

It is important to highlight that the target reproduction number is supported by results that ensure a similar behavior to R_0 when its value is equal to 1. These results underscore a fundamental aspect: regardless of the strategy used to calculate the target reproduction number, when one of them reaches a value of 1, the others also become 1. Therefore, this property enables the evaluation of various control strategies and their effectiveness. The choice of which strategy to apply should be based on minimizing costs when implementing a control strategy.

To illustrate the applicability of the target reproduction number, two specific models have been used. In the first model, the scenario of incomplete vaccination is addressed, where the infectious disease can persist despite vaccination. In this model, two types of strategies are modeled: the first strategy is linked to controlling the non-vaccinated population. The effectiveness of this control strategy depends on controlling the other subsystem represented by the vaccinated population. Conversely, a control strategy is developed associated with the vaccinated population, assuming control over the non-vaccinated population. The effectiveness of both strategies occurs because changes in the rate values, which are adjusted by the target reproduction number, allow it to reach the threshold of 1. This implies that the respective basic reproduction number for the adjusted system is equal to 1.

Through a detailed calculation of the target reproduction number and the performance of simulations, the effectiveness of this approach as a control strategy in the proposed scenario has been shown. The choice of the most suitable strategy is based on the costs required to control the regulated subsystem. In the second model, an analysis of leptospirosis, a disease with infectious agents including animals and bacteria in the environment, is carried out. A control strategy is proposed that addresses infections between animals and bacteria, assuming transmission to humans is under control. The target reproduction number related to this control strategy is significantly simpler than R_0. The target reproduction number presents itself as an alternative for developing control strategies to contain an epidemic outbreak. It is important to emphasize that by solely controlling the subsystem related to infections between animals and bacteria, it is possible to exert control over the entire system that includes all transmission pathways.

The simulations carried out in the examples have supported the effectiveness of the target reproduction number as a control strategy. In each of the examples, it is illustrated how the curves of infected individuals undergo changes before and after applying the strategy based on the target reproduction number. It is clear that after implementing this strategy, the curve decreases significantly. This contrast highlights the utility of this approach as a control strategy.

A consequence that can be inferred from applying the target reproduction number to the model of incomplete

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vaccination is that when implementing different control strategies based on the target reproduction number, first in the unvaccinated population and then in the vaccinated population, these strategies efficiently achieve disease eradication as time approaches infinity.
An observation that can be made from the analysis of second model is that, despite the simplicity of the target reproduction number, using it as a control strategy on a subpopulation also leads to disease elimination as time tends to infinity.

In conclusion, the target reproduction number provides a valuable alternative to the traditional calculation of R_0 in situations involving complex interactions among multiple infectious classes. Its simplicity make this approach a promising tool for addressing the spread of infectious diseases and designing more effective interventions. By focusing on a specific population group, the target reproduction number allows for a more precise assessment of intervention effectiveness and facilitates informed decision-making regarding prevention and control strategies.

A pathway for future research could involve determining the target reproduction number in models of multiple cities, thus enabling a comparison between the target reproduction number approach for the entire multi-city model and the proposed numbers for each individual city.

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DECLARATION OF USE OF ARTIFICIAL INTELLIGENCE

The autors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

CONTRIBUTION OF THE AUTHORS (CREDIT)

The authors contributed equally to this work.

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A strategic mathematical model of waste disposal

Un modelo matemático estratégico de la disposición de residuos

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ABSTRACT

The impact of human actions on the environment poses several challenges at the global level, with solutions that deserve the productive and political sectors and civil society to be jointly involved. Resource scarcity, ecosystem degradation, and climate change must be addressed urgently; this is a paradigm change in the forms of production and consumption. This is a transition from a linear economy to a circular economy, which allows responsible disposal and reuse of waste along the links of production and use. However, despite notable advances in recycling and upcycling, landfill and dump disposal remain the primary waste disposal worldwide. Furthermore, a significant amount of waste is disposed of illegally, affecting the quality of life of communities that live in nearby areas. This work studies the trade-off between waste container removal and illegal micro-dumps cleaning using impulsive control. A type of strategic mathematical model is formulated, one that captures the minimal but relevant aspects of the phenomenon, to describe the dynamics of garbage.

Keywords:

Circular economy, Waste containers, Illegal dump, Impulsive control, Security factor.

RESUMEN

El impacto de las acciones humanas sobre el medio ambiente plantea varios desafíos a nivel global con soluciones que merecen la participación conjunta de los sectores productivos, políticos y de la sociedad civil. La escasez de recursos, la degradación de los ecosistemas y el cambio climático deben ser abordados con urgencia, siendo necesario un cambio de paradigma en las formas de producción y consumo. Sin embargo, a pesar de los notables avances en el reciclaje y el suprareciclaje, los rellenso sanitarios y vertederos siguen siendo la principal forma de eliminación de residuos en todo el mundo. Es más, una cantidad importante de residuos se elimina de manera ilegal afectando la calidad de vida de las comunidades que viven en zonas cercanas. Este trabajo estudia la compensación entre el retiro de contenedores de residuos y la limpieza de micro-vertederos ilegales mediante el control impulsivo. Se formula un modelo matemático de tipo estratégico, aquel que capta aspectos mínimos pero relevantes del fenómeno, para describir la dinámica de la basura.

Palabras Claves:

Economía circular, Contenedores de residuos, Vertederos ilegales, Control impulsivo, Factor de seguridad.

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1 INTRODUCCIÓN

Waste is generated by human action and as a subproduct of satisfying consumer and production needs. This fact is structured by the linear economy, a model that is defined from the chain: take, make, use, and destroy (Ghisellini *et al.*, 2016). Indeed, the quantity of municipal solid waste (MSW) is increasing worldwide as human societies move toward an urban future. Recent estimates suggested that 1.3 billion tonnes of MSW are generated each year; however, this quantity is projected to increase to around 2.2 billion in 2025 (Hoornweg and Bhada-Tata, 2012). As in most countries, in Chile waste is disposed of in legal and illegal dumps, corresponding to 69.4% and 30.6%, respectively (Ministerio de Medio Ambiente, 2022). Although these final disposal places are far from the central area of the city, they represent a sociosanitary problem for the populations living in adjacent areas, such as rural and urban communities. Indeed, residents living close to waste disposal places are typically affected by contamination of water and ground, jointly with bad smells, visual displeasure, and the potential propagation of diseases and plagues (Cárdenas *et al.*, 2016; Ossio and Faúndez, 2021; Escobar, 2021). Eradicating this vulnerability is the long-term seventh goal of Chile's transition to the circular economy 2040, termed "Recovery of sites affected by illegal waste disposal" (Ministerio de Medio Ambiente, 2021), for this reason, it is important to understand the dynamics of waste disposal and removal to detect critical control points and optimize the local resources for its management.

To achieve this important paradigm change, a challenge of the utmost urgency at the global level, it is necessary to work together with the productive and political sectors and civil society (Govindan and Hasanagic, 2018; Ossio *et al.*, 2020; Ministerio de Medio Ambiente, 2021) to avoid the several negative effects that waste disposal generates on the environmental, social and economic dimensions. In this regard, four axes have been outlined to achieve the desired transformation: Circular Innovation, Circular Culture, Circular Regulation, and Circular Territories in relation to each dimension and their interrelation through the government and/or municipal council directions (Ministerio de Medio Ambiente, 2021).

Since it is a transversal problem, illegal disposal of waste aggravates environmental, social, and economic impacts. For example, Vergara and Tchobanoglous (2012) showed that, relative to the areas surrounding dumping sites, stream ecology, flora and fauna, habitat depletion, and land use change dominated the concerns of the stakeholders. This contingency is not unfamiliar among Chilean communities; indeed, according to Ossio and Faúndez (2021), in Chile, there are 3.735 illegal sites of final waste disposal formed by 3.492 dumps and 243 micro-dumps, distributed throughout the country; however, these are concentrated in the Región Metropolitana which generates the largest amount of waste (Ministerio de Medio Ambiente, 2022; Vivanco Font, 2023). Several strategies have been proposed to recover sites affected by illegal waste disposal, such as zero waste industries, educating the civil society to promote recycling/upcycling behaviors, and strengthening control to avoid illegal waste disposal (Ministerio de Medio Ambiente, 2021).

In this work, a strategic mathematical model (Jiliberto, 2020) is formulated to describe the dynamics of waste that is deposited both in legal waste containers and littering in clandestine or illegal micro-dumps. Assuming that waste container removal and illegal micro-dump cleaning are carried out simultaneously and regularly, a trade-off occurs. In addition, depending on the rate at which wastes are littered, the waste containers can collapse, and thus the waste in the illegal micro-dumps increases and maintains. This situation is modeled from the level of filling waste containers, a fraction between availability and occupied capacity.

2 MATHEMATICAL MODELING

Let be $G = G(t)$ the total waste at time $t \geq 0$. Assuming that the waste is deposited by individuals on the municipal council waste containers or sites such as hillsides and rural roads on the periphery of the city giving rise to micro-dumps, their amounts are represented respectively by $G_{\oplus} = G_{\oplus}(t)$ and $G_{\ominus} = G_{\ominus}(t)$. Then, $G = G_{\oplus} + G_{\ominus}$. In addition, the total capacity of municipal council waste containers is given by the density of these, represented as $N = N(t)$, and their specific capacity c. Therefore, when $G_{\oplus} = cN$ is obtained, the municipal council waste containers are filled. However, since this notion can be subjective, the occupancy fraction $\gamma \in (0,1)$ equivalent to $G_{\oplus}/cN$ is proposed. Consequently, when the municipal council waste containers have availability, being fulfilled $G_{\oplus} < \gamma cN$, then these are occupied at a rate proportional to available capacity: $r(1 - G_{\oplus}/cN)$. Conversely, when $G_{\oplus} \geq \gamma cN$ is obtained, the inflow waste that cannot be deposited due to lack of space is dumped, in addition to rate $r_{\ominus}$, in peripheral sites, and then, forms the illegal micro-dumps. In turn, considering a population increase or constant container theft at a rate μ, the density of municipal waste containers decreases. This waste dynamics' occurs each $\tau > 0$ unit of time, in concordance with the municipal council waste container removal by the cleaning and maintenance department. At these moments, a fraction $\lambda = 1 - e^{-\mu\tau}$ of stolen waste containers are replenished, jointly with the cleaning of illegal micro-dumps and the container waste removal in a trade-off fractions $\delta \in (0,1)$ and $1 - \delta$, respectively. In fact, municipal council waste containers are removed and their capacity is restored to cN when $\delta = 1$. However, the illegal micro-dumps were not cleaned. Conversely, when $\delta = 0$, the illegal micro-dumps were cleaned but the waste containers were not removed, which promotes the emergence of illegal micro-dumps. Consequently, a trade-off is obtained between these clean spaces. Therefore, the following mathematical model is proposed:

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$$\left\{\begin{array}{rcl} N'(t) &=& -\mu N(t) \\ G'_{\oplus}(t) &=& r_{\oplus}\left(1-\dfrac{G_{\oplus}(t)}{cN(t)}\right) \\ G'_{\ominus}(t) &=& \left\{\begin{array}{lll} r_{\ominus} & , \text{ if } & G_{\oplus}(t) < \gamma cN(t) \\ r_{\ominus}+r_{\oplus}\dfrac{G_{\oplus}(t)}{cN(t)} & , \text{ if } & G_{\oplus}(t) \geq \gamma cN(t) \end{array}\right. \end{array}\right\} \; t \neq k\tau$$

$$\left\{\begin{array}{rcl} N(t^+) &=& N(t)+(1-e^{-\mu\tau})(N_*-N(t)) \\ G_{\oplus}(t^+) &=& (1-\delta)G_{\oplus}(t) \\ G_{\ominus}(t^+) &=& \delta G_{\ominus}(t) \end{array}\right\} \; t = k\tau \tag{1}$$

with $N(0)=N_*$, $G_{\ominus}(0)>0$, and $G_{\oplus}(0)>0$. Importantly, if $\mu=0$ then $N(t)=N_*$ for any $t\geq 0$.

3 RESULTS

The mathematical study of the model (1), described by a system of impulsive differential equations, investigates the long-term patterns of waste dynamics and focuses on the relationship between the instant at which the waste containers are filled and when they are removed, and jointly when the illegal micro-dumps are cleaned. The synchrony between activities plays a key role in the illegal micro-dumps' non-persistence.

THRESHOLD CONDITION AND TEMPORAL DYNAMICS

Let be $\{t_k\}$ an increasing and non-bounded sequence such that $t_{k+1}=t_k+\tau$, which is related to the removal of the waste containers and cleaning the illegal micro-dumps. Then, solving the model (1) for $t\in(t_k,t_{k+1}]$, follows that

$$N(t)=N(t_k^+)e^{-\mu(t-t_k)}.$$

Taking $t=t_{k+1}$, the stroboscopic map

$$N(t_{k+1})=[N(t_k)+(1-e^{-\mu\tau})(N_*-N(t_k))]e^{-\mu\tau}$$

is obtained, whose equilibrium point is given by

$$\overline{N}=\frac{\lambda}{e^{\mu\tau}-1+\lambda}N_*,$$

where $\lambda=1-e^{-\mu\tau}$. Consequently,

$$G'_{\oplus}(t)+\frac{r_{\oplus}}{cN(t_k^+)e^{-\mu(t-t_k)}}G_{\oplus}(t)=r_{\oplus},$$

has by solution

$$G_{\oplus}(t)=\exp\left\{-\frac{r_{\oplus}(e^{\mu(t-t_k)}-1)}{cN(t_k^+)\mu}\right\}\left(G_{\oplus}(t_k^+)+\int_{t_k}^{t} r_{\oplus}E(s)ds\right),$$

where

$$E(s)=\exp\left\{\frac{r_{\oplus}(e^{\mu(s-t_k)}-1)}{cN(t_k^+)\mu}\right\}$$

for any $t\in(t_k,t_{k+1}]$. Taking $t=t_{k+1}$, we have the stroboscopic map

$$G_{\oplus}(t_{k+1})=(1-\delta)\exp\left\{-\frac{r_{\oplus}(e^{\mu\tau}-1)}{cN(t_k^+)\mu}\right\}G_{\oplus}(t_k)+$$
$$+\underbrace{\exp\left\{-\frac{r_{\oplus}(e^{\mu\tau}-1)}{cN(t_k^+)\mu}\right\}\int_{t_k}^{t_{k+1}} r_{\oplus}\exp\left\{\frac{r_{\oplus}(e^{\mu(s-t_k)}-1)}{cN(t_k^+)\mu}\right\}ds}_{\mathscr{I}},$$

whose equilibrium point is given by

$$\overline{G}_{\oplus}=\frac{r_{\oplus}\exp\left\{-\dfrac{r_{\oplus}(1-e^{-\mu\tau})}{c\overline{N}\mu}\right\}}{1-(1-\delta)\exp\left\{-\dfrac{r_{\oplus}(1-e^{-\mu\tau})}{c\overline{N}\mu}\right\}}\cdot\mathscr{L},$$

where $\mathscr{L}$ exist due to $0<\mathscr{I}\leq r_{\oplus}\tau$.

Taking $e^{\mu(t-t_k)}>\mu(t-t_k)+1$ for any $t\in(t_k,t_{k+1}]$, follows that

$$E(t)>\exp\left\{\frac{r_{\oplus}(t-t_k)}{cN(t_k^+)}\right\},$$

and then

$$\begin{aligned}\mathscr{L} &\geq \lim_{k\to\infty}\frac{cN(t_k^+)}{r_{\oplus}}\left(\exp\left\{\frac{r_{\oplus}\tau}{cN(t_k^+)}\right\}-1\right), \\ &= \frac{c\overline{N}e^{\mu\tau}}{r_{\oplus}}\left(\exp\left\{\frac{r_{\oplus}\tau}{c\overline{N}e^{\mu\tau}}\right\}-1\right)\end{aligned} \tag{2}$$

is obtained. Figure 1 illustrates the temporal dynamics of model (1) for $N(t)$ and $G_{\oplus}(t)$ states and the respective stroboscopic maps according to impulsive dynamics.

Figure 2 shows that $d\overline{G}_{\oplus}/d\mu<0$, and thus $\overline{G}_{\oplus}$ tends to

$$\overline{G}_{\oplus *}=\frac{cN_*\left(1-\exp\left\{-\dfrac{r_{\oplus}\tau}{cN_*}\right\}\right)}{1-(1-\delta)\exp\left\{-\dfrac{r_{\oplus}\tau}{cN_*}\right\}} \tag{3}$$

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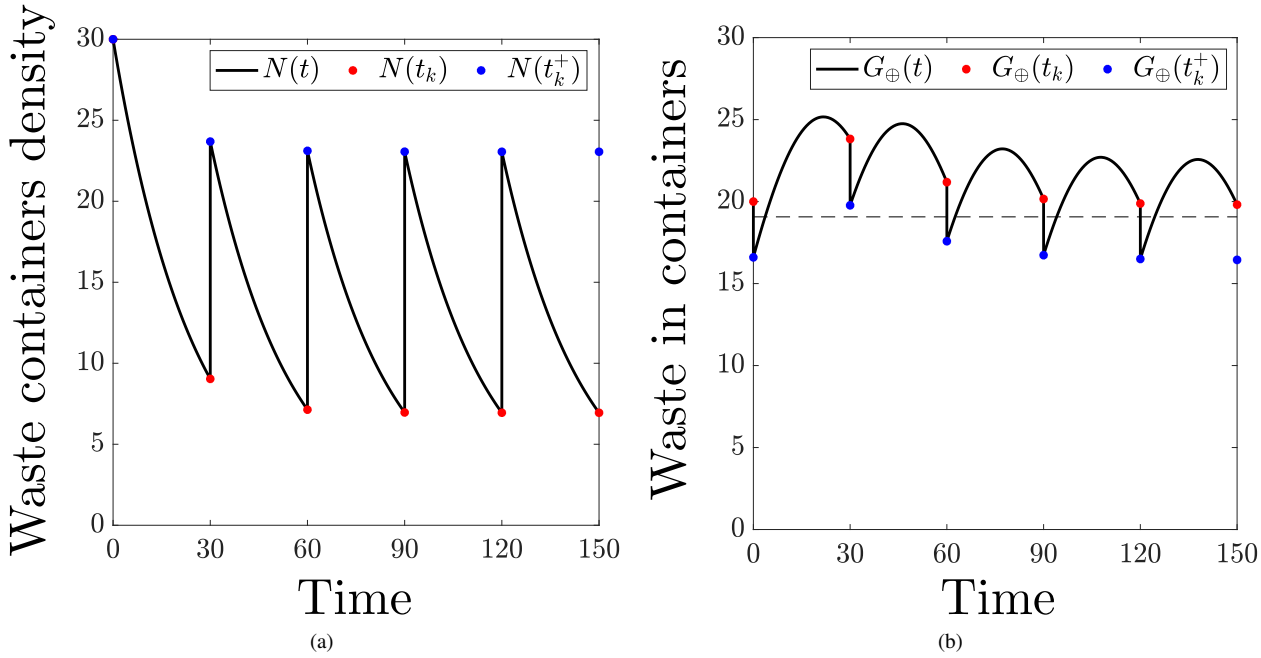

Figure 1: Temporal dynamics of model (1). (a) The waste containers density, $N = N(t)$, and (b) the amount of waste in containers, $G_\oplus = G_\oplus(t)$ for $t \in [0,150]$ and initial conditions $N(0) = 30$, $G_\oplus(0) = 20$. The common parameter values are $\tau = 30$, $\mu = 0.04$, $c = 2$, $\delta = 0.17$, $\gamma = 0.95$, $r_\ominus = 0.01$, $r_\oplus = 1$, and $N_* = 30$. Importantly, the dashed line represents the top-fill level, $G_\oplus := \gamma c N_* = 19$.

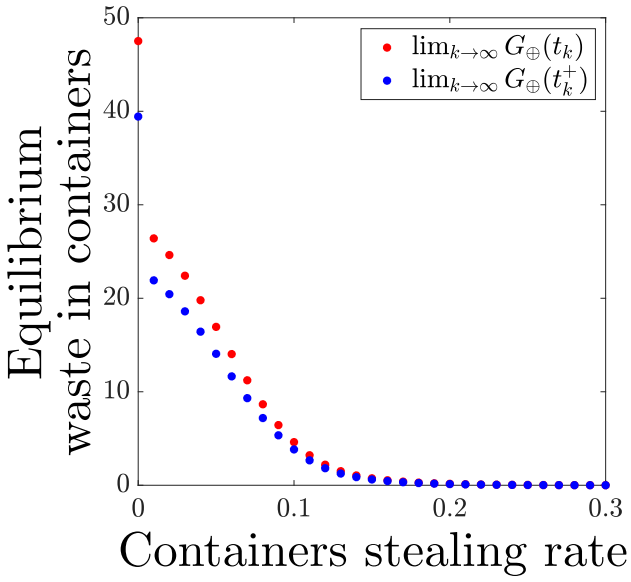

Figure 2: Equilibrium values of the stroboscopic maps $G_\oplus(t_{k+1}) = F(G_\oplus(t_k), N(t_k))$ (red dots) and $G_\oplus(t_{k+1}^+) = \delta G_\oplus(t_{k+1})$ (blue dots) as μ increases, using $\tau = 30$, $c = 2$, $\delta = 0.17$, $\gamma = 0.95$, $r_\ominus = 0.01$, $r_\oplus = 1$, and $N_* = 30$ as parameter values, and initial conditions $N(0) = 30$, $G_\oplus(0) = 20$.

as μ tends to zero, and thus necessarily, $\mathscr{L}$ tends to $cN_*(\exp\{r_\oplus\tau/(cN_*)\} - 1)/r_\oplus$ according to (2).

On the other hand, let be $\{s_k\}$ a sequence such that $G_\oplus(s_k) = \gamma c N_*$, which is related to the waste containers are filled. Therefore, integrating the model (1) on $(s_k, s_{k+1}]$ we have

$$G_\oplus(s_{k+1}) = cN_* + [cN_* - G_\oplus(s_k^+)]\exp\left\{-\frac{r_\oplus(s_{k+1}-s_k)}{cN_*}\right\}.$$

Assuming that $G_\oplus(s_k^+) = 0$, this is, the waste containers are removals, follows that

$$\gamma c N_* = cN_*\left(1 - \exp\left\{-\frac{r_\oplus(s_{k+1}-s_k)}{cN_*}\right\}\right)$$

and thus,

$$s_{k+1} = s_k + \underbrace{\frac{cN_*}{r_\oplus}\ln\left(\frac{1}{1-\gamma}\right)}_{T},$$

which is an increasing and non-bounded sequence. This scenario is the particular case of the model (1) when $\delta = 0$ is proposed.

Therefore, the mathematical model (1) provides a theoretical framework that captures minimal but relevant aspects of the waste dynamics associated with the cleaning of illegal micro-dumps and removal of waste containers based on impulsive control. Specifically, we can derive the following conclusion.

Proposition 1 *Let be* $\mu = 0$ *and*

$$\mathscr{R} = \frac{\delta}{(1-\gamma)\left[\delta + \exp\left\{\frac{r_\oplus\tau}{cN_*}\right\} - 1\right]}.$$

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Therefore,

$$G_{\oplus}(t) = cN_* - [cN_* - (1-\delta)G_{\oplus}(t_k)]\exp\left\{-\frac{r_{\oplus}(t-t_k)}{cN_*}\right\}$$

satisfies the model (1) for any $t \in (t_k, t_{k+1}]$*, where*

$$G_{\oplus}(t_{k+1}) = (1-\delta)\exp\left\{-\frac{r_{\oplus}\tau}{cN_*}\right\}G_{\oplus}(t_k) + cN_*\left(1-\exp\left\{-\frac{r_{\oplus}\tau}{cN_*}\right\}\right)$$

and $k \geq 0$*, so that* $G_{\oplus}(t) \in [(1-\delta)\overline{G}_{\oplus *}, \overline{G}_{\oplus *}]$ *as* t *tends to infinity. In addition, if* $\mathscr{R} \geq 1$ *then*

$$G_{\ominus}(t) \in [r_{\ominus}\tau\delta/(1-\delta), r_{\ominus}\tau/(1-\delta)]$$

as t *tends to infinity. Conversely, when* $0 < \mathscr{R} < 1$ *follows that*

$$G_{\ominus}(t) \in [\delta\overline{G}_{\ominus *}, \overline{G}_{\ominus *}],$$

where $\overline{G}_{\ominus *}$ *is given by (8) when* $(1-\delta)G_{\oplus}(t_k) < cN_*$*, and by (9) when* $(1-\delta)G_{\oplus}(t_k) \geq cN_*$ *are obtained from* $k \geq k_*$*.*

Proof

Let be $\{t_k\}$ and $\{s_k\}$ two sequences given by that $t_{k+1} = t_k + \tau$ and $s_{k+1} = s_k + T_k$ such that $G_{\oplus}(s_k) = \gamma cN_*$. Integrating on $(t_k, t_{k+1}]$ follows that

$$G_{\oplus}(t) = cN_* - [cN_* - G_{\oplus}(t_k^+)]\exp\left\{-\frac{r_{\oplus}(t-t_k)}{cN_*}\right\}, \quad (4)$$

which solve the model (1). Thus, taking $t = t_{k+1}$ we have the stroboscopic map

$$G_{\oplus}(t_{k+1}) = (1-\delta)\exp\left\{-\frac{r_{\oplus}\tau}{cN_*}\right\}G_{\oplus}(t_k) + cN_*\left(1-\exp\left\{-\frac{r_{\oplus}\tau}{cN_*}\right\}\right). \quad (5)$$

Analogously, for $s \in (s_k, s_{k+1}]$,

$$G_{\oplus}(s_{k+1}) = cN_* - [cN_* - G_{\oplus}(s_k^+)]\exp\left\{-\frac{r_{\oplus}T_k}{cN_*}\right\},$$

is obtained, and equivalent to

$$\gamma cN_* = cN_* - [cN_* - G_{\oplus}(s_k^+)]\exp\left\{-\frac{r_{\oplus}T_k}{cN_*}\right\},$$

or

$$G_{\oplus}(s_{k+1}) = cN_* - [cN_* - \gamma cN_*]\exp\left\{-\frac{r_{\oplus}T_k}{cN_*}\right\}$$

depending on the initial condition value. Therefore,

$$G_{\oplus}(s_k^+) = cN_*\left(1-(1-\gamma)\exp\left\{\frac{r_{\oplus}T_k}{cN_*}\right\}\right)$$

with $0 < T_k \leq T$, and

$$G_{\oplus}(s_{k+1}) = cN_*\left(1-(1-\gamma)\exp\left\{-\frac{r_{\oplus}T_k}{cN_*}\right\}\right)$$

with $T_k \geq T$, are obtained.

Considering the equilibrium point of sequence $\{G_{\oplus}(t_k)\}_k$, given by the expression (3), it is necessary to study the parametric conditions that allow it to occur that $\overline{G}_{\oplus *} > G_{\oplus}(s_k^+)$ so that the waste containers to be removals before these are full, and $\overline{G}_{\oplus *} > G_{\oplus}(s_{k+1})$ in the collapse case.

Firstly, $\overline{G}_{\oplus *} > G_{\oplus}(s_k^+)$ is equivalent to

$$\frac{cN_*\left(1-\exp\left\{-\frac{r_{\oplus}\tau}{cN_*}\right\}\right)}{1-(1-\delta)\exp\left\{-\frac{r_{\oplus}\tau}{cN_*}\right\}} > N_*\left(1-(1-\gamma)\exp\left\{\frac{r_{\oplus}T_k}{cN_*}\right\}\right),$$

if and only if,

$$\exp\left\{\frac{r_{\oplus}T_k}{cN_*}\right\} > \frac{\delta}{(1-\gamma)\left[\delta+\exp\left\{\frac{r_{\oplus}\tau}{cN_*}\right\}-1\right]} = \mathscr{R}.$$

Solving for T_k, a value exists whether $\mathscr{R} > 1$. Therefore, $G'_{\ominus}(t) = r_{\ominus}$ for any $t \neq t_k$ and $G_{\ominus}(t_k^+) = \delta G_{\ominus}(t_k)$, so that $G_{\ominus}(t) = \delta G_{\ominus}(t_k) + r_{\ominus}(t-t_k)$ for any $t \in (t_k, t_{k+1}]$, where the sequence $\{G_{\oplus}(t_k)\}_k$ is increasing and satisfies $G_{\ominus}(t_{k+1}) = \delta G_{\ominus}(t_k) + r_{\ominus}\tau$. Consequently, the solution of this difference equation is given by

$$G_{\ominus}(t_k) = \delta^k G_{\ominus}(t_0) + r_{\ominus}\tau\cdot\frac{1-\delta^k}{1-\delta} \quad (6)$$

with tends to $r_{\ominus}/(1-\delta)$ as k increases.

Secondly, from $\overline{G}_{\oplus *} > G_{\oplus}(s_{k+1})$ and by procedures analogous to the first case, $\exp\{-r_{\oplus}T_k/cN_*\} > \mathscr{R}$ is obtained. Solving for T_k, a value exists whether $0 < \mathscr{R} < 1$. Using the expression (4) at $t = s_k$ follows that

$$\gamma cN_* = cN_* - [cN_* - (1-\delta)G_{\oplus}(t_k)]\exp\left\{-\frac{r_{\oplus}(s_k-t_k)}{cN_*}\right\},$$

if and only if,

$$s_k = t_k + \frac{cN_*}{r_{\oplus}}\ln\left(\frac{cN_* - (1-\delta)G_{\oplus}(t_k)}{cN_*(1-\gamma)}\right) \quad (7)$$

when $(1-\delta)G_{\oplus}(t_k) < cN_*$ from $k \geq k_*$. Importantly,

$$\begin{aligned} T_k &= s_{k+1} - s_k, \\ &= \tau + \frac{cN_*}{r_{\oplus}}\ln\left(\frac{cN_* - (1-\delta)G_{\oplus}(t_{k+1})}{cN_* - (1-\delta)G_{\oplus}(t_k)}\right) \end{aligned}$$

tends to τ as k increases. Therefore,

$$G_{\ominus}(t) = \begin{cases} \delta G_{\ominus}(t_k) + r_{\ominus}(t-t_k) & , \text{ If } \quad t \in (t_k, s_k] \\ \tilde{G}_{\ominus}(t) & , \text{ If } \quad t \in [s_k, t_{k+1}] \end{cases}$$

where

$$\tilde{G}_{\ominus}(t) = G_{\ominus}(s_k) + (r_{\ominus} + r_{\oplus})(t - s_k) - \\ - [cN_* - (1-\delta)G_{\oplus}(t_k)] \left(\exp\left\{ -\frac{r_{\oplus}(s_k - t_k)}{cN_*} \right\} - \right. \\ \left. - \exp\left\{ -\frac{r_{\oplus}(t - t_k)}{cN_*} \right\} \right).$$

is obtained. Taking $t = s_k$ and $t = t_{k+1}$, we have

$$G_{\ominus}(s_k) = r_{\ominus}(s_k - t_k) + \delta G_{\ominus}(t_k),$$

and

$$G_{\ominus}(t_{k+1}) = G_{\ominus}(s_k) + (r_{\ominus} + r_{\oplus})(\tau - (s_k - t_k)) \\ - [cN_* - (1-\delta)G_{\oplus}(t_k)] \left(\exp\left\{ -\frac{r_{\oplus}(s_k - t_k)}{cN_*} \right\} - \right. \\ \left. - \exp\left\{ -\frac{r_{\oplus}\tau}{cN_*} \right\} \right).$$

Therefore, substituting the first equation into the second equation, and considering the difference $s_k - t_k$, given by (7), we have

$$G_{\ominus}(t_{k+1}) = \delta G_{\ominus}(t_k) + (r_{\oplus} + r_{\ominus})\tau - \\ cN_* \ln\left(\frac{cN_* - (1-\delta)G_{\oplus}(t_k)}{cN_*(1-\gamma)} \right) - cN_*(1-\gamma) + \\ + [cN_* - (1-\delta)G_{\oplus}(t_k)] \exp\left\{ -\frac{r_{\oplus}\tau}{cN_*} \right\},$$

whose equilibrium point is given by

$$\overline{G}_{\ominus *} = \frac{(r_{\oplus} + r_{\ominus})\tau - cN_* \ln\left(\frac{cN_* - (1-\delta)\overline{G}_{\oplus *}}{cN_*(1-\gamma)} \right) - cN_*(1-\gamma) + + [cN_* - (1-\delta)\overline{G}_{\oplus *}] \exp\left\{ -\frac{r_{\oplus}\tau}{cN_*} \right\}}{1-\delta}. \tag{8}$$

On the other hand, if $(1-\delta)G_{\oplus}(t_k) \geq cN_*$ from $k \geq k_*$ then, integrating on $(t_k, t_{k+1}]$ we have

$$G_{\ominus}(t) = G_{\ominus}(t_k) + (r_{\ominus} + r_{\oplus})(t - t_k) + \\ + [(1-\delta)G_{\oplus}(t_k) - cN_*] \exp\left\{ -\frac{r_{\oplus}(t - t_k)}{cN_*} \right\},$$

and taking $t = t_{k+1}$, follows that

$$G_{\ominus}(t_{k+1}) = \delta G_{\ominus}(t_k) + (r_{\ominus} + r_{\oplus})\tau + \\ + [(1-\delta)G_{\oplus}(t_k) - cN_*] \exp\left\{ -\frac{r_{\oplus}\tau}{cN_*} \right\},$$

whose equilibrium point is given by

$$\overline{G}_{\ominus *} = \frac{(r_{\oplus} + r_{\ominus})\tau + [(1-\delta)\overline{G}_{\oplus *} - cN_*] \exp\left\{ -\frac{r_{\oplus}\tau}{cN_*} \right\}}{1-\delta}. \tag{9}$$

Therefore, $G_{\ominus}(t_k)$ tends to $\overline{G}_{\ominus *}$ given by (8) or (9) as k increases, according on the fulfillment of $(1-\delta)G_{\oplus}(t_k) < cN_*$ or $(1-\delta)G_{\oplus}(t_k) \geq cN_*$ from $k \geq k_*$.

Finally, if $\mathscr{R} = 1$ then

$$\gamma = 1 - \frac{\delta}{\delta + \exp\left\{ \frac{r_{\oplus}\tau}{cN_*} \right\} - 1} = 1 - \frac{\delta \exp\left\{ -\frac{r_{\oplus}\tau}{cN_*} \right\}}{1 - (1-\delta)\exp\left\{ -\frac{r_{\oplus}\tau}{cN_*} \right\}},$$

if and only if,

$$\gamma cN_* = \frac{cN_*\left(1 - \exp\left\{ -\frac{r_{\oplus}\tau}{cN_*} \right\} \right)}{1 - (1-\delta)\exp\left\{ -\frac{r_{\oplus}\tau}{cN_*} \right\}} = \overline{G}_{\oplus *}.$$

Thus, $G_{\oplus}(s_k) = \overline{G}_{\oplus *}$ and $s_k = t_k$ from $k \geq \tilde{k}$. Therefore,

$$G_{\ominus}(t) = \delta G_{\ominus}(t_k) + r_{\ominus}(t - t_k)$$

for $t \in (t_k, t_{k+1}]$. Using the (6) relationship, it follows the result. □

Regarding the threshold value, denoted by $\mathscr{R}$, using the concept of elasticity (Martcheva, 2015), which is defined by $\varepsilon^p_{\mathscr{R}} := (\partial\mathscr{R}/\partial p) \cdot (p/\mathscr{R}) \approx \%\Delta\mathscr{R}/\%\Delta p$ where p is some parameter of interest, follows that

$$\varepsilon^{\gamma}_{\mathscr{R}} = \frac{\gamma}{1-\gamma}, \quad \varepsilon^{\delta}_{\mathscr{R}} = 1 - \frac{\delta}{\delta + e^{\kappa} - 1}, \quad \varepsilon^{\kappa}_{\mathscr{R}} = -\frac{\kappa e^{\kappa}}{\delta + e^{\kappa} - 1},$$

where $\kappa = r_{\oplus}\tau/\{cN_*\}$ is the maximal occupancy ratio. Thus, $\varepsilon^{\gamma}_{\mathscr{R}} > 0$, $\varepsilon^{\delta}_{\mathscr{R}} > 0$ and $\varepsilon^{\kappa}_{\mathscr{R}} < 0$. Therefore, as the subjective occupancy fraction and the removal fraction increase or the maximal occupancy ratio decreases, the available capacity of waste containers is promoted (see Figure 3). However, increasing the removal fraction increases the waste amount range in micro-dump in the long term (see Proposition 1).

Numerical Simulations

To validate our mathematical result, Figure 4 illustrates the Proposition 1 conclusions' based on the varying γ parameter value, and thus, in the filling level γcN_*. Consequently, $\mathscr{R}$ and γcN_* values decrease as γ decreases too, and the inequality fulfillment $(1-\delta)G_{\oplus}(t) < cN_*$ transit to $(1-\delta)G_{\oplus}(t) \geq cN_*$, which can also be promoted as δ increases to one. However, this variation increases significantly the waste amount range in the illegal micro-dumps according to the trade-off between removal and cleaning.

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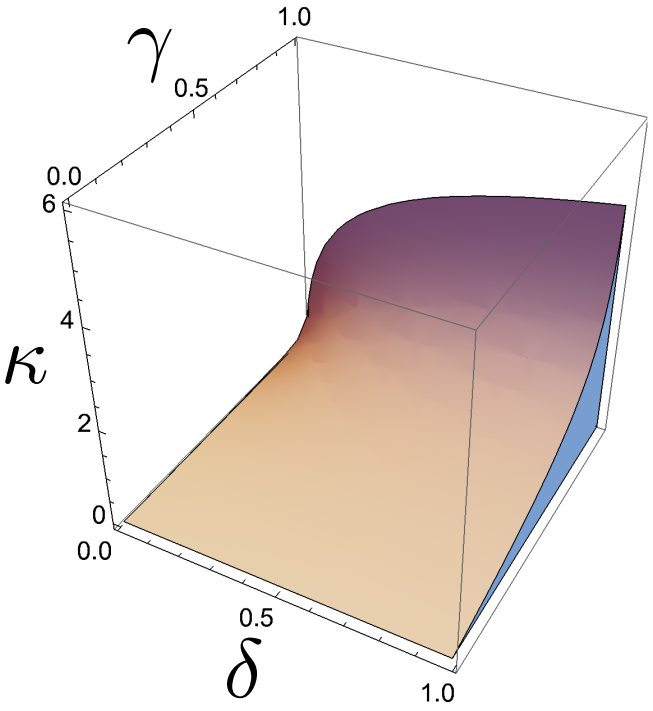

Figure 3: Combinations of $\delta \in (0,1)$, $\gamma \in (0,1)$, and $\kappa \in (0,6)$ so that $\mathscr{R} > 1$, where $\kappa = r_{\oplus}\tau/\{cN_*\}$. Importantly, the complementary region that represents $0 < \mathscr{R} < 1$ is significantly greater than $\mathscr{R} \geq 1$ region.

On the other hand, Figure 5 shows how the temporal dynamics of the model (1) vary as the container stealing rate μ increases, taking as reference the dynamics associated with $\mu = 0$ and a parameter set so that $\mathscr{R} \geq 1$ is obtained (see Fig.5(a)). Here, it is observed the transition among the different scenarios given by Proposition 1, where the capacity of containers in the long term allows a constant waste inflow or not, because these are full, implying waste increases in illegal micro-dumps. Importantly, it is the effect steal of waste containers on garbage dynamics, significantly reducing the containers' top-fill level and promoting their collapse, and thus the illegal micro-dump maintenance.

4 DISCUSSION AND CONCLUSIONS

Our goal was to study the trade-off dynamics between the removal of waste containers and the cleaning of illegal micro-dumps. This dynamics was represented using a mathematical model described by an impulsive differential system at both fixed and variable times (Cordova-Lepe *et al.*, 2015). The findings establish two scenarios in the long term, the containers are full or not, and whose differentiation depends on a threshold that is a function of all model parameters. In particular, when the waste container density does not vary (taking $\mu = 0$), an explicit representation is obtained for this threshold value, denoted by $\mathscr{R}$. Thus, when $0 < \mathscr{R} < 1$ the containers are full in the long term. Conversely, when $\mathscr{R} \geq 1$ the containers have a capacity for waste disposal. Therefore, it is natural to associate $\mathscr{R}$ as a *safety factor* that relates the capacity and demand by a quotient. From the *safety factor* is possible to monitor and guard the integrity of a specific process, particularly of engineering (Hansson, 2009).

Based on elasticity analysis of static quantities (Martcheva, 2015), this *safety factor* increases as the removal (δ) and/or the subjective occupancy (γ) fractions increase too, or by decreasing the maximal occupancy ratio ($\kappa = r_{\oplus}\tau/\{cN_*\}$). As the trade-off result, whose consequence implies that illegal micro-dumps persist, our findings establish that the efforts must be aimed at γ increase or κ decrease. Firstly, we established that γ represents the subjective occupancy fraction, a measure that pretends to consider human behavior faced in the disposition of legal waste disposal, where the location and access to waste containers are keys in the promotion and maintenance of habits with a socio-environmental co-responsibility (Valenzuela-Levi and Flores-Castillo, 2023). Secondly, the decrease of κ, by the reduction of $r_{\oplus}$ or the increase of N_*, is associated with promoting strategies of recycling and upcycling (Ministerio de Medio Ambiente, 2021; Yang *et al.*, 2023; Valenzuela-Levi, 2019).

The illegal disposal of solid waste in urban areas has been found to affect the structure and function of natural ecosystems (Vergara and Tchobanoglous, 2012). As a result, it is crucial to study and simulate waste management practices in cities to create sustainable strategies that can reduce the environmental and health hazards linked with improper waste disposal. In this regard, comprehending the elements contributing to the development of small-scale waste disposal locations and the measures implemented by local government agencies is vital for making informed choices that reduce the occurrence of new dumping sites (Shmelev and Powell, 2006).

Hence, developing models that represent disposal behaviors in these settings is important for devising efficient measures to address the growing issue of municipal solid waste. A future improvement that could be made in this regard might be the incorporation of a spatially explicit analytic framework to the problem of predicting where would be the most probable location of a new micro-dumping area, based on both, the distribution of the collecting containers and the "environmental" characteristics of frequent micro-dumping points.

There are germ or nuclear mathematical models; that is, although they do not fit in detail with each of the observable expressions, that is, the variations of particular phenomena, they come to contain the minimum elements and relationships to characterize the essence of the class in that such phenomena are inserted. This is the case with the logistic model in population dynamics or the SIR (susceptible-infectious-removed) propagation model in epidemiology. These models, called strategic (Jiliberto, 2020), act as platforms since

they have the property that, when assembled or added specificity, they reach a resolution that can be contrasted with a specific reality, and, in general, they become *ad hoc* instruments, that is, with greater descriptive and projection possibilities. In our opinion, the model (1) aspires to be strategic, since considering the complexity that waste disposal processes have *in situ*, its minimalist conceptual structure achieves connections whose mathematical analysis interpreted at sight makes practical sense.

AUTHOR CONTRIBUTIONS STATEMENT

R.G, F.C-L, and I.S.A-R conceived the study. R.G and F.C-L developed the theoretical formalism. R.G performed the analytic calculations and the numerical simulations. All authors discussed the results and contributed to the final manuscript.

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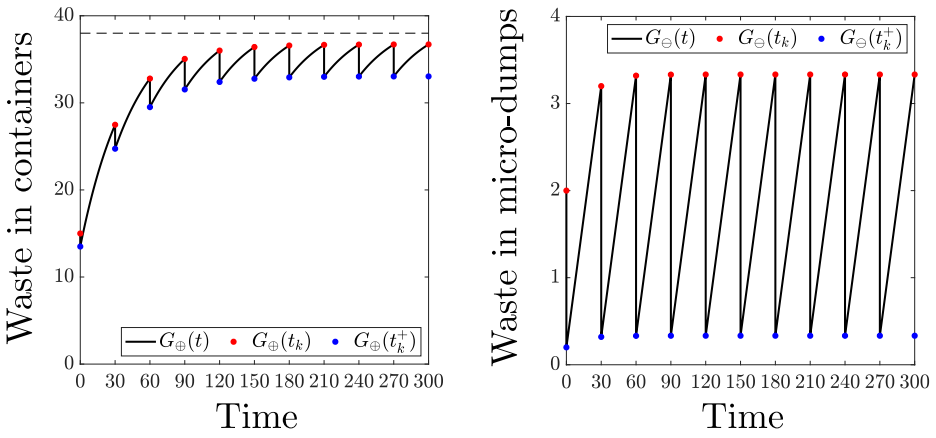
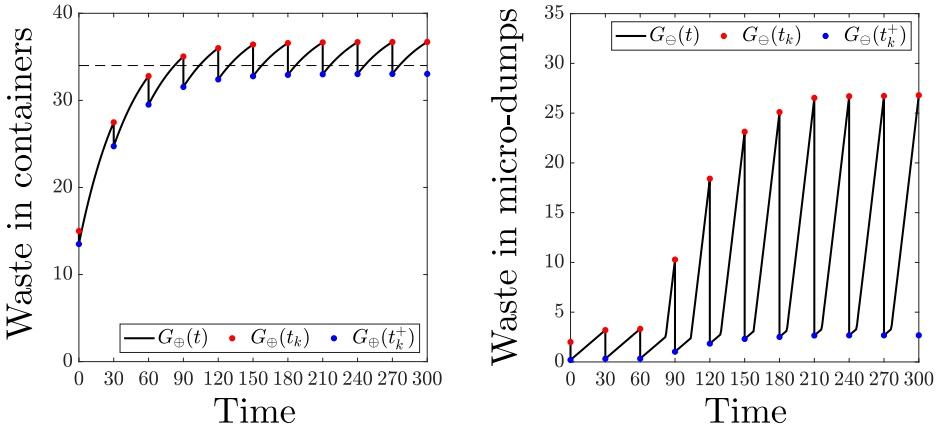
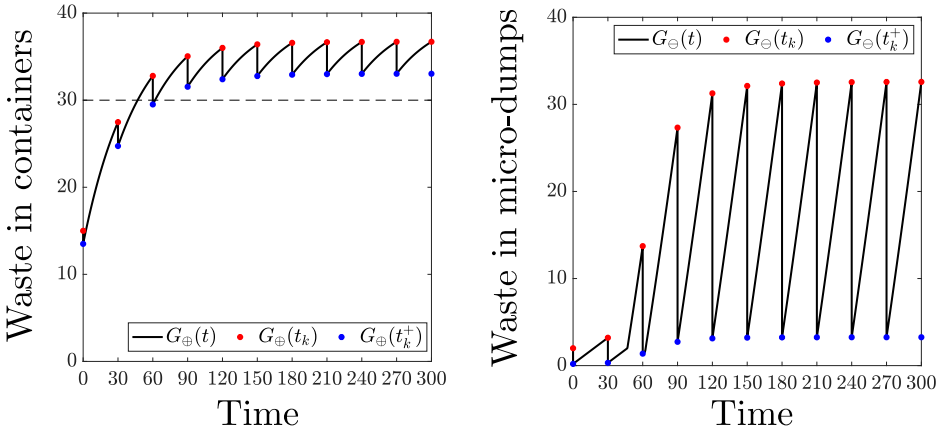


(a)



(b)



(c)

Figure 4: Temporal dynamics of model (1) according to Proposition 1. The common parameter values are $\tau = 30$, $\mu = 0$, $c = 2.0$, $\delta = 0.1$, $r_\ominus = 0.1$, $r_\oplus = 1.0$, and $N_* = 30$. Particularly, (a) $\gamma = 0.95$ with $\mathscr{R} \approx 1.6434$ so that $G_\ominus \in [0.33, 3.33]$, (b) $\gamma = 0.85$ with $\mathscr{R} \approx 0.5478$ so that $G_\ominus \in [2.68, 26.81]$, and (c) $\gamma = 0.75$ with $\mathscr{R} \approx 0.3287$ so that $G_\ominus \in [3.25, 32.58]$. Importantly, the dashed line represents the top-fill level, $G_\oplus = \gamma c N_*$.

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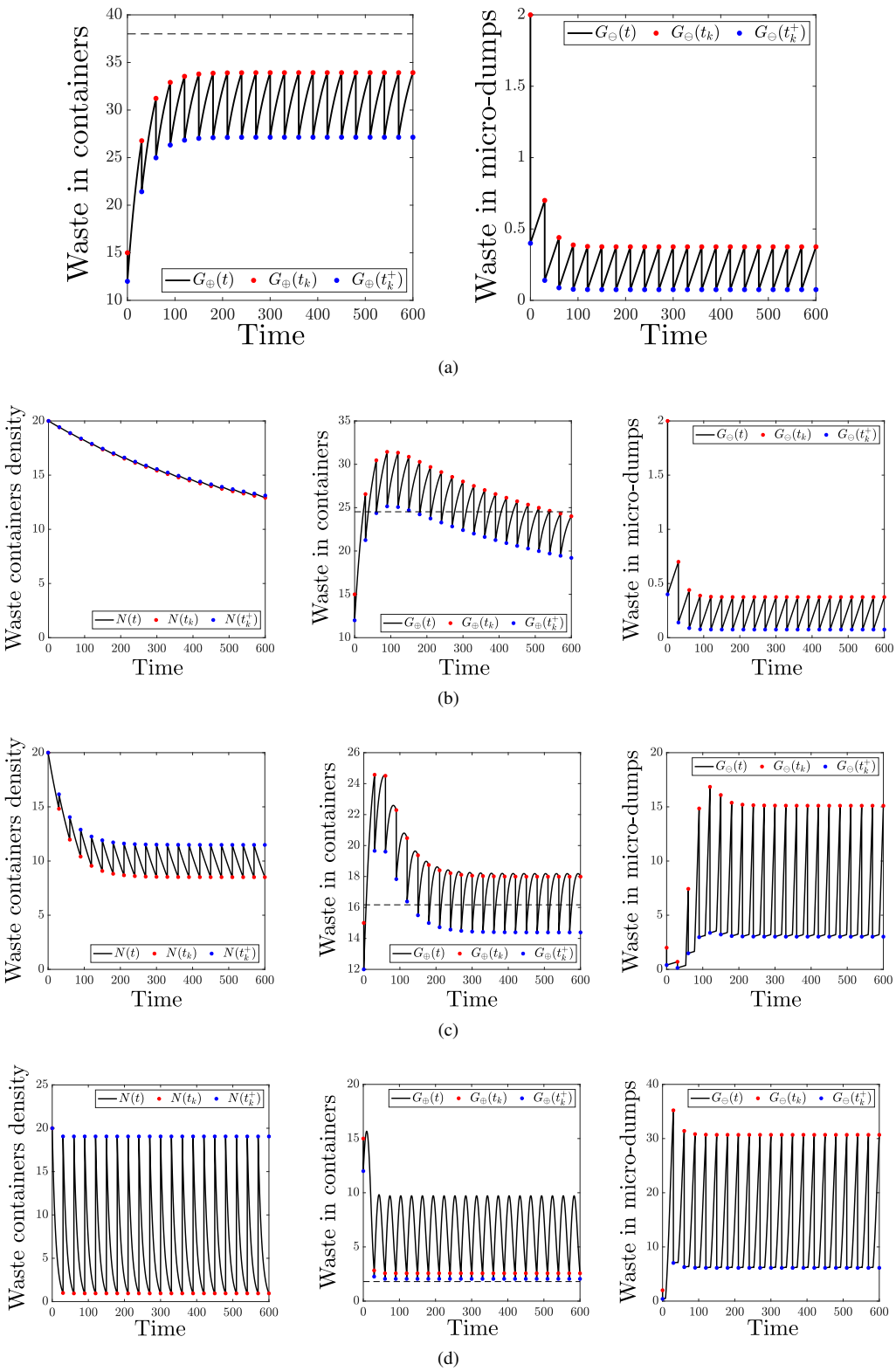

Figure 5: Temporal dynamics of model (1) as parameter value μ increases. The common parameter values are $\tau = 30$, $c = 2.0$, $\delta = 0.2$, $r_\ominus = 0.01$, $r_\oplus = 1.0$, $\gamma = 0.95$, and $N_* = 20$ so that $\mathscr{R} = 3.0372$. In (a) $\mu = 0$, (b) $\mu = 0.001$, (c) $\mu = 0.01$, and (d) $\mu = 0.1$. Importantly, the dashed line represents the top-fill level, $G_\oplus = \gamma c \overline{N}$.

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