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Equilibrium Explanation as Structural Non-Mechanistic Explanations: The Case of Long-Term Bacterial Persistence in Human Hosts

Javier Suárez and Roger Deulofeu

RESUMEN

Philippe Huneman ha cuestionado recientemente los límites en la aplicación de los modelos mecanicistas de la explicación científica en base a la existencia de lo que denomina “explicaciones estructurales”, en las que el fenómeno se explica en virtud de las propiedades matemáticas del sistema en que el fenómeno ocurre. Las explicaciones estructurales pueden darse en formas muy diversas: en virtud de la forma de *pajarita (bowtie)* de la estructura, de las propiedades topológicas del sistema, de los equilibrios alcanzados, etc. El papel que juegan las matemáticas en las explicaciones que apelan a la estructura de pajarita o a las propiedades topológicas del sistema ha sido recientemente examinado en varios trabajos. Sin embargo, el papel exacto que juegan las matemáticas en el caso de las explicaciones en términos de equilibrio aún no ha sido totalmente clarificado, y diferentes autores defienden interpretaciones contradictorias, algunas de las cuales las asemejarían más al modelo defendido por algunos filósofos mecanicistas que al modelo estructural de Huneman. En este trabajo, tratamos de cubrir ese déficit estudiando el papel que juegan las matemáticas en el modelo de equilibrio anidado (*nested equilibrium*) elaborado por Blaser y Kirchner para explicar la estabilidad de las asociaciones ontogenética y filogenéticamente persistentes entre humanos y microorganismos. De nuestro análisis se desprende que su modelo es explicativo porque i) se identifica una estructura matemática del sistema que viene dada por un conjunto de ecuaciones diferenciales que satisfacen una estrategia evolutivamente estable; ii) la estructura anidada del modelo hace que la estrategia evolutivamente estable sea robusta ante posibles perturbaciones; iii) esto es así porque las propiedades del sistema empírico son isomorfas a, pero no causalmente responsables de, las propiedades de la estrategia evolutivamente estable. La combinación de estas tres tesis hace que las explicaciones en términos de equilibrios se asemejen más al modelo estructural de explicación que al modelo mecanicista.

PALABRAS CLAVE: *explicación científica; mecanismos; explicación en términos de equilibrio; explicaciones estructurales; explicaciones no causales; estrategia evolutivamente estable.*

ABSTRACT

Philippe Huneman has recently questioned the widespread application of mechanistic models of scientific explanation based on the existence of structural explanations, i.e. explanations that account for the phenomenon to be explained in virtue of the mathematical properties of the system where the phenomenon obtains, rather than in terms of the mechanisms that causally produce the phenomenon. Structural explanations are very di-

verse, including cases like explanations in terms of bowtie structures, in terms of the topological properties of the system, or in terms of equilibrium. The role of mathematics in bowtie structured systems and in topologically constrained systems has recently been examined in different papers. However, the specific role that mathematical properties play in equilibrium explanations requires further examination, as different authors defend different interpretations, some of them closer to the new-mechanistic approach than to the structural model advocated by Huneman. In this paper, we cover this gap by investigating the explanatory role that mathematics play in Blaser and Kirschner's nested equilibrium model of the stability of persistent long-term human-microbe associations. We argue that their model is explanatory because: i) it provides a mathematical structure in the form of a set of differential equations that together satisfy an ESS; ii) that the nested nature of the ESSs makes the explanation of host-microbe persistent associations robust to any perturbation; iii) that this is so because the properties of the ESS directly mirror the properties of the biological system in a non-causal way. The combination of these three theses make equilibrium explanations look more similar to structural explanations than to causal-mechanistic explanation.

KEYWORDS: *Scientific Explanation; Mechanisms; Equilibrium Explanations; Structural Explanations; Non-Causal Explanations; Evolutionarily Stable strategy.*

In the last few years, a new trend in the debates about scientific explanation has flourished in philosophy of science. This new trend, “new-mechanism,” emphasizes the role of mechanisms in scientific discourse in general, and in scientific explanation in particular [Machamer et al. (2000); Glennan & Illari (2017)]. Inspired by the developments in molecular biology, new-mechanists redefine causalism and argue that to explain a phenomenon consists in providing the mechanism that produces it. In the new-mechanist tradition, mechanisms are taken to be a set of *entities* (parts) and *activities* (operations) with a particular *organization* such that their causal interactions bring the phenomenon to be explained about [Glennan (2002); Bechtel & Abrahamsen (2005); Craver & Darden (2013); Craver (2007); Nicholson (2012); Issad & Malaterre (2015); Deulofeu & Suárez (2018)]. Thus, for a scientific explanation to be mechanistic, it must fulfill two necessary and sufficient conditions. First, it must identify a *model of mechanism* in which the mechanism is individuated by its parts, operations and organization. Second, it must provide a story of how the components of the mechanism are causally connected in such a way that they produce the *explanandum*.

New-mechanists share a basic commitment to a causal view of the world combined with: 1) the rejection of the Hempelian idea that explanations take the form of logical arguments, either inductive or deductive, and 2) the notion that mechanisms provide the causal “ingredient” that scientific explanations require to be genuinely explanatory¹. Furthermore, they often assume a hierarchical view of mechanisms, acknowledging the existence of a diversity of scientific explanations in every science, thus

neither renouncing to the explanatory role of the special sciences, nor to the possible existence of mechanistic inter-level (hierarchical) explanations among different sciences [Krickel (2018)].

The wide scope of the New Mechanism account of scientific explanation in biology has been questioned due to the existence of explanations that seem to lack the causal ingredient that new-mechanists demand. One of the traditional explanatory types where this happens is in equilibrium explanations, where the mathematical properties of the empirical system (i.e. the fact that it reaches an equilibrium point) are taken as explanatory, irrespectively of the causal-mechanistic details of the system. Starting with Sober (1983), equilibrium explanations have been hypothesized to constitute an alternative to purely causal-mechanistic explanations [Batterman & Rice (2014); Rice (2015); Huneman (2018b), (2018c)]. However, it has also been argued that some equilibrium explanations admit a causal interpretation, if “causality” is understood in Woodward’s interventionist terms [Woodward (2003); Kuorikoski (2007); Potochnik (2015)]. If the later were the case, as some new-mechanists are committed to an interventionist Woodwardian view of causation [Craver (2007); Kaplan & Craver (2011)], it could be argued: first, that the mathematical components that are present in equilibrium explanations describe the causal relationships among the entities of the system; second, that equilibrium explanations do not then constitute a real exception to the new-mechanist trend. The existence of these contradictory interpretations of the nature of equilibrium explanations (causal vs. non-causal) creates an important gap to understand how they gain their explanatory force, as well as about the specific role of causality in scientific explanation: is causality — at some level — a necessary ingredient in every scientific explanation, or are non-causal explanations also legitimate in certain cases?

In this paper, we aim to clarify this issue by studying Blaser & Kirschner’s (2007) nested equilibrium model (NEM, hereafter) of the persistence of bacteria in human hosts. Our choice of this case is motivated by two reasons: on the one hand, Blaser & Kirschner’s NEM explains the phenomenon in terms of the existence of an evolutionarily stable strategy (ESS, hereafter) among the different interacting organisms, a feature that makes it sufficiently analogous to most cases of equilibrium explanations reviewed in the philosophical literature so that our conclusion can shed light on the nature of scientific explanation; on the other hand, the explanatory force of their model is also conditional on the existence of a nestedness among different biological scales, i.e. on the

existence of a hierarchy of interrelated ESSs. As the acknowledgment of the existence of a hierarchy of mechanisms is a hallmark of the new-mechanist account of scientific explanation, and, to our knowledge, cases of nested equilibria have never been studied before in the philosophical literature, we believe that our case study could bring new light to the study of the old phenomenon of equilibrium explanations. Our aim is thus to analyse the explanatory role that the appeal to the existence of equilibria at different levels plays in the NEM. In that vein, we intend to provide a better understanding of the nature of equilibrium explanation, and to the role of causality in scientific explanation². To do so, we frame the paper in the context of the debate between Huneman's structural account of scientific explanation and the causal-mechanistic account.

In section I, we introduce the general account of structural explanations presented by Huneman (2018a) and motivate the necessity of discussing the precise nature of equilibrium explanation to understand whether, and if so, to what extent, equilibrium explanations fit Huneman's account, or are rather a special case of causal-mechanistic explanations. In section II, we present our case study. In section III, we present our philosophical analysis. We first argue that the explanatory force of Blaser & Kirschner's NEM is mainly provided by the concept of ESS, plus the mathematical modelling that defines each strategy at each of the levels of the hierarchy, rather than by the causal-mechanistic details of the system. Additionally, the nested nature of the different ESSs plays a role in making the system robust to every possible intervention at different levels. Thirdly, and connected to this last point, we argue that no role is left for any causal element in their model, thus suggesting that their explanation constitutes a case of structural explanation as Huneman has defined it. Finally, in section IV, we present our conclusions.

I. EXPLAINING WITH AND WITHOUT CAUSES: THE ROLE OF MATHEMATICS IN EQUILIBRIUM EXPLANATIONS

In recent years, the universal application of the "new-mechanist" account of scientific explanation in biology has been questioned on the basis of the existence of a family of explanations that do not rely on any causal features of the system whose properties they explain, but rather on its mathematical properties [Huneman (2010), (2018a), (2018b); Woodward (2013); Rice (2015); Kostic (2018), (2019); Deulofeu et al. (2019)]. Huneman has called these explanations "structural", and defines them as follows:

Family of explanations for which the mathematical tools used in the description of an explanandum system belong to a mathematical structure whose properties are directly explanatory of some aspects of the system (such as equilibria, behaviour, limit regime, asymptotic behaviour, etc.) (...) They explain by accounting for the explananda through pinpointing structural relations that are mathematical relations of some sort. Mathematics here are not representing a dependence between structures in the world, but they are constituting the structural dependence itself, (...) and in virtue of that they are explanatory [Huneman (2018a), p. 695].

In contrast with mechanistic explanations, structural explanations do not include any mechanism, nor any causal story in their *explanans*. Furthermore, the inclusion of any of these elements would usually be taken as counterproductive to account for the *explanandum*. Structural explanations are abundant in systems biology, where an extensive amount of data has to be interpreted by using mathematical and computational tools [Green (2016), (2017); Green & Jones (2017); Brigandt et al. (2017)]. Huneman explicitly argues that some of the properties of the biological systems studied under the label of “systems biology” can only be explained by appealing to the formal (mathematical) properties that characterize those systems. A well-known example of this, studied by Jones (2014), is the vulnerability of the immunological system to attacks to the CD4+ T-cells. Drawing upon Kitano & Oda’s (2006) case study, Jones argues that what explains the vulnerability of the human immune system to attacks on this particular component is its bowtie structure: because the human’s immune system has a bowtie structure such that CD4+ T-cells are non-redundant elements in the core of the bowtie, the system is vulnerable to attacks on this type of cells (Figure 1). What is more important is that the vulnerability to attacks on CD4+ T-cells is not a consequence of the causal-mechanistic processes that produce the vulnerability: it is a consequence of the topological properties of the architecture (organization) of the immunological system. These topological properties determine its vulnerability to attacks on its core, as it is the only non-redundant element of the network, which is furthermore a necessary step for every other immunological process. Huneman summarized this kind of explanation as follows: “what is epistemically proper to this network modelling is that the topological properties found in the networks are such that they explain some of the properties one is interested in [vulnerability to attacks on CD4+ T-cells], (...) the instantiation of these properties is explained by the fact that the network is of such topological nature” [Huneman (2018b) p 127].

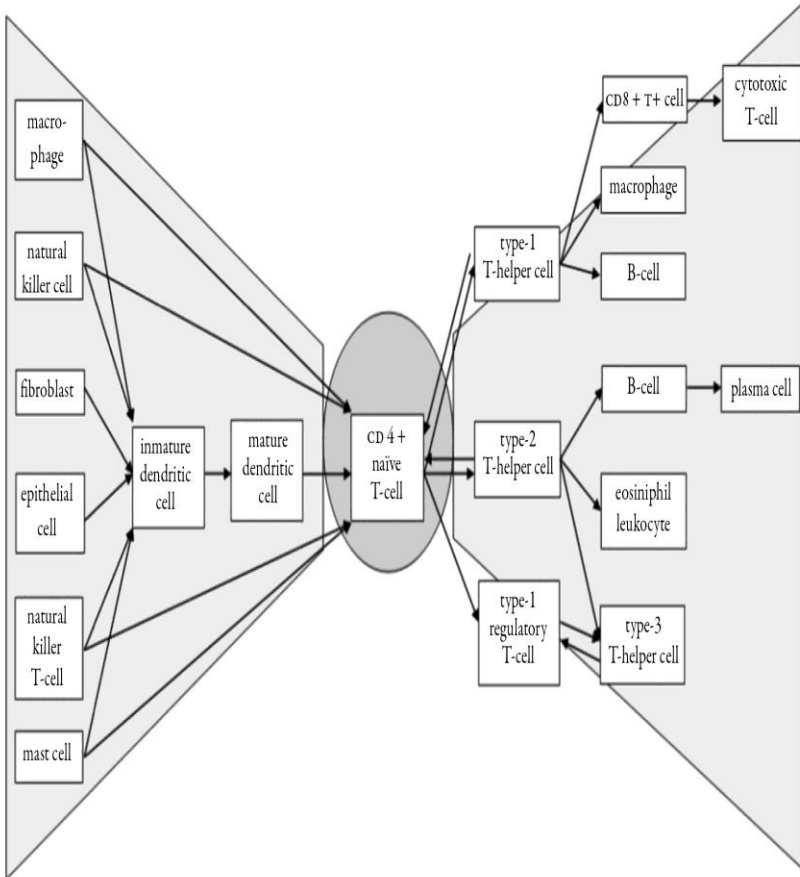


FIGURE 1. Bowtie structure of the immune system, with the CD4+ T-cells in the core of the bowtie. From Jones (2014), p. 1138, Fig. 1.

A second point that is epistemically proper to this kind of explanation is that the mechanisms that “sustain” the realization of such topological properties are irrelevant for explaining those properties (namely, the vulnerability of the network) [Huneman (2018c) pp. 6-8; Deulofeu et al. (2019); Moreno & Suárez, (submitted)]³.

Structural explanations are not restricted to cases of topological explanation, though. In his (2018c), p. 6, Huneman outlines the case of explanations in microeconomics, particularly the “ice cream vendors” problem — a direct application of the theory of Nash equilibrium to

human behaviour. In this situation, we imagine that there are two vendors standing on a beach and need to decide where to situate their stall in order to maximize their sales. Microeconomics, relying on game theory, says that the vendors will situate their stall in the middle of the beach, next to each other, to attract customers both in the area around them and in their extremes. By placing themselves in the middle of the beach, the vendors generate a Nash equilibrium, a situation where none of the players (the vendors) can change their strategy without decreasing their benefits (potential customers). Let us suppose we have to explain a scenario where there are two vendors placed in the middle of the beach. What explains the fact that both of them place their stalls in the middle? Huneman replies: “the fact that it simultaneously maximizes the share of each of them, or in other words, that it instantiates a Nash equilibrium.” And adds: “[t]he mechanisms through which vendors move, decide, sell or buy, etc. are not explanatory relevant to this precise question” [Huneman (2018c), p. 6].

Nonetheless, Huneman just sketches the elements that make the Nash equilibrium explanatory in the case of the “ice cream vendors” but does not specify in detail what explaining with equilibria exactly entails, nor what is his reason to believe that mechanisms do not play any explanatory role in equilibrium explanations. Previous analyses of the role of equilibria in scientific explanations had been presented in Sober (1983) and Kuorikoski (2007). However, both authors reach opposing conclusions about where equilibrium explanations gain their explanatory force from: while the former argues that “equilibrium explanations show how the cause of an event can be (statistically) *irrelevant* to its explanation”, and that their explanatory force comes exclusively from their mathematical structure [Sober (1983), p. 201], the latter believes that “explanations of singular events are indeed causal, even those supplied by equilibrium models” [Kuorikoski (2007), p. 149]. These opposing conclusions are interesting because they leave open whether equilibrium explanations must be considered a subtype of structural explanation (Sober), or a subtype of causal-mechanistic explanation (Kuorikoski), thus creating an important gap in how to understand the role of mathematics in this type of explanation. In addition to that, they leave open a question about the role of causality in scientific explanation in general for, if as Kuorikoski argues, even equilibrium explanations are in the end causal, then it could be argued that causality is a necessary ingredient in every genuine case of scientific explanation.

In the next section, we introduce Blaser & Kirschner's NEM of the persistence of bacteria in human hosts as a case study that we will use to motivate our response to these two questions.

II. A NESTED EQUILIBRIUM EXPLANATION OF THE PERSISTENCE OF BACTERIA IN HUMAN HOSTS

Humans harbour an abundant number of microbes in their guts that constitute the human microbiome [Huttenhower et al. (2012); Lozupone et al. (2012)]⁴. Among those microorganisms, some persist in our guts throughout our entire whole life cycle, whereas others are mainly transient, or appear in specific moments of our development, disappearing afterwards [Chiu & Gilbert (2015)]. Furthermore, some of those are hypothesized to have established long-term associations with humans over millions of years, with some people speculating that they might constitute co-evolved systems or hologenomes [Rosenberg & Zilber-Rosenberg (2014), (2016); Díaz (2015); Suárez (2018); Suárez & Triviño (2019); cf. Moran & Sloan (2015); Douglas & Werren (2016)]. Irrespectively of the evolutionary nature of those associations, the fact that organisms from different species engage in persistent long-term associations with each other is paradoxical from the perspective of the neo-Darwinian model of life and evolution. According to this model, when two individuals of different species associate, i.e. when they share the same habitat or niche, each one will pursue its own fitness interests. In this scenario, it might happen that the two organisms coexist peacefully for a period of time but, normally, peaceful coexistence will tend to break down: on the one hand, in the moment in which an opportunity for one of the organisms to benefit in detriment of the other appears, it will tend to grow to maximize its fitness until the other organism is destroyed (appearance of cheaters); on the other hand, it is also not infrequent that in a stable biological population where one out of two different survival strategies has been adopted among the members, the population becomes invaded by individuals that adopt an alternative strategy, until the point where the population collapses (external invasion). For these reasons, peaceful associations among organisms of different species are rare and will normally be short-term. Then, how is it possible that humans and some of their microbes establish persistent infections that are not disrupted by cheaters⁵? And which are the mechanisms that allow long-term associations that survive the challenges of sharing a habitat and are not perturbed by external invaders?

Blaser and Kirschner have recently developed a model “to explain the common features of microbial persistence in their human hosts” [(2007), p. 847, emphasis added)], i.e. to explain why humans and some specific microorganisms have overcome the difficulties of co-habitation⁶. They speculate that those situations represent a successful phenotype that must be maintained according to certain eco-evolutionary rules. In their view:

persistence represents the evolved selection for balancing host and microbial interests, resulting in an equilibrium that, by definition, is long-term but not necessarily forever stable. We hypothesize that maintenance of this equilibrium requires a series of evolved, nested equilibria to achieve the overall homeostasis [Blaser & Kirschner (2007), p. 843].

They argue that such nested equilibria will be observed at different time-scales: microscopic, at the level of the interactions between the immunological system of the host and cell-receptors of the microbes; mesoscopic, at the level of tissue function; tissue in which the microbe population inhabits; macroscopic, where evolutionary changes in the host and the microbe will occur to guarantee microbe transmission⁷. Blaser and Kirschner believe that any of these levels conforms to Nash equilibria in the form of an ESS that allows the persistence of the relationship. This is so because both the host and the microorganism will have developed a very specific hierarchy of cross-signalling mechanisms that generate a set of positive and negative feedback loops with each other that guarantee that the overall equilibrium is not disrupted.

Blaser and Kirschner’s model begins by defining five populations at the microlevel whose changes with respect to certain variables are followed over time [see also Blaser & Kirschner (1999); Blaser & Atherton (2004); Blaser (2006)]. In the case of *Helicobacter pylori*, the variables include: M , which represents the population of mucus-living *H. pylori* (rate of change); A , which represents the *H. pylori* population that adhere to epithelial cells; N , which represents the concentration of nutrients available to bacteria derived from inflammation; E , which represents the concentration of effector molecules (molecules that the microbes generate to achieve some aims, such as suppressing immune response by the host); and I , that stands for the host response. Blaser and Kirschner’s NEM includes five differential equations that track the changes in the variables of their model, as well as how they interact with each other⁸.

For instance, to study how the concentration of mucus-living *H. pylori* varies over time due to the interaction with the other populations, they introduce the following differential equation:

$$\frac{dM}{dt} = g_m \alpha N(t) - \mu_m M(t) - \alpha M(t)(K - A(t)) + \delta A(t) \quad (1)$$

where, g_m, α, μ_m and δ are parameters, whose value will depend on the situation; N, M, A (mentioned above) and K (the epithelial carrying capacity) are variables that together will determine the rate of change of the mucus-living population M . In (1), $g_m \alpha N(t)M(t)$ represents the potential growth of the population in virtue of the nutrient availability; $\mu_m M(t)$, represents the loss of *H. pylori* due to the process of mucus shedding; and $\alpha M(t)(K - A(t)) + \delta A(t)$ represents the potential loss/gain of *H. pylori* due to migration between the epithelial and the mucus-living populations. Obviously, migration from M to A can only happen when $A < K$, namely, when there is still room for more adherence to epithelial cells, and the opposite is the case for migration from A to M . Adherent sites are always limited or otherwise *H. pylori* would grow too much, risking the stability of the symbiotic association.

The inflammation induced by the bacteria on the host is captured by measuring the change of nutrient concentration over time:

$$\frac{dN}{dt} = \frac{b}{(b + I(t))} \beta E(t) - g_m N(t)M(t) - g_\alpha N(t)A(t) \quad (2)$$

In (2), b, β, g_m and g_α are parameters. $N(t)$ is characterized by a gain term that is a function of the concentration of effector molecules, E , and the host response I . The equation shows the direct proportionality that exists between E and N , and the inverse proportionality between I and N . In other words, it shows the limiting effect that the host response has over the nutrient concentration, as well as the inducing effect of the bacteria on the nutrient concentration. (2) also specifies the rate of assimilation of nutrients of the mucus-living bacterial population and of the adherent epithelial populations.

Furthermore, for a microbe-host association to be *evolutionarily* persistent, the microbe needs to develop strategies for transmission. R_0 captures this concept, quantifying “the transmission potential of a microparasite as the average number of secondary infections occurring when a single infectious host is introduced into a universally susceptible host population” [Blaser & Kirschner (2007) p. 844].

$$R_o = \frac{BN}{(x + b + v)} \quad (3)$$

In (3), BN measures the transmission rate as a function of the population size, x measures the rate of host mortality due to the microbe (measure of virulence), b is the rate of mortality of the host population independently of the microbe (measure of lifespan), and v is the rate at which the host recovers from the microbe infection (measure of immunity). Usually, for $R_o > 1$ microbial transmission is sustained whereas for $R_o < 1$ microbial transmission goes extinct.

Blaser and Kirschner show that in a persistent microbe-host association those five differential equations remain constant, and any deviation in one of the equations gets immediately counter-balanced by the adjustment of the other equations, keeping the equilibrium stable. Thus, Blaser and Kirschner claim this can only be possible if the system behaves according to a Nash equilibrium, and if the strategies followed by microbe and host conform to an ESS. Let us now see how an ESS can account *explanatorily* for observed constancy.

II.1. *The Role of the Evolutionarily Stable Strategy in Blaser and Kirschner's Model*

Nash equilibrium is a very common situation in game theory. It obtains when two players in a non-cooperative game adopt a strategy such that no individual change will render greater benefits to any of them, i.e. such that every change in the strategy that one of the players adopts independently will result in lower individual profit for that player. Nash equilibria are not necessarily, however, optimal strategies. It is sometimes possible to obtain a better net result if both players change their strategy simultaneously and a new equilibrium is reached. Nonetheless, this will only occur if *both partners* modify their strategy co-ordinately, but not if they do so independently. Therefore, no player has any incentive to modify his strategy individually. The prisoner's dilemma constitutes a typical example of a game whose solution is provided by a Nash equilibrium (Table 1). In this situation, two individuals — A and B — are accused independently of a crime, and each of them is interrogated separately and offered a deal: 1) if A betrays B and accuses her of having committed the crime, while B stays silent, A will have 4-years reduction of sentence and B will have no reduction (and the same, but inverted, occurs if B betrays A while A remains silent); 2) if both stay silent, each

of them will have a 3-years reduction of sentence; 3) if both betray each other, each will have a 1 years reduction of sentence. In this scenario, the Nash equilibrium is reached in situation 3), when both players betray each other. Of course, the result that they obtain is not optimal (each of them will only get 1 year reduction of sentence), but is such that none of them has any incentive to change her strategy individually, unless the other also does so, as otherwise she will have a bigger individual cost, i.e. she will have less years of reduced sentence [Nash (1950a), (1950b); Gintis (2000)].

A \ B	Betrays	Remains silent
Betrays	1, 1	4, 0
Remains silent	0, 4	3, 3

TABLE 1. Payoff matrix for the prisoner’s dilemma. The numbers represent the amount of years that each subject would have as reduction of sentence. The optimal strategy is that where both remain silent (italics). Only the strategy where both betray constitutes Nash equilibria (bold).

An ESS is a biological strategy that, when it is adopted in a population, natural selection alone will keep the population safe from “intruder populations”, in so far as the organisms that adopt an alternative strategy will be selected against. All ESSs are cases of Nash equilibria, but the opposite is not the case. If a solution to a non-cooperative game represents Nash equilibrium that is not an ESS, the solution could be disrupted by an alternative strategy that drives the population towards an alternative Nash equilibrium that constitutes an ESS [Smith & Price (1973); Smith (1974); Easley & Kleinberg (2010), pp. 209-227]. For instance, take the case of the stag hunt game (Table 2). This is a two players’ game, where each player has two possible exclusive strategies: hunt-hares or hunt-stags. In this situation, there are three possible scenarios: 1) that both individuals are hare-hunters (case where both obtain a fitness benefit of 2); 2) that both individuals are stag-hunters (both obtain a fitness benefit of 3); 3) that one of the individuals is a hare-hunter whereas the other is a stag-hunter (in which case the hare-hunter obtain a fitness benefit of 3, whereas the stag-hunter obtains a fitness benefit of

0). In this situation, strategies 1) and 2) constitute a Nash equilibrium, for none of the players could get a better payoff by changing strategy. However, only 1) constitutes an ESS: while a hare-hunter and a stag-hunter do equally well when they are paired with a stag-hunter (fitness benefit of 3), hare-hunters score better than stag-hunters when they are paired with hare-hunters (hare-hunters score 2, while stag-hunters score 0). That means the stag-hunting strategy is not an ESS because if a hare-hunter is introduced in a population of stag-hunters, the population will evolve towards a population of hare-hunters. On the other hand, a population where all the individuals are hare-hunters represents an ESS, because if a stag-hunter is introduced in the population, it will be eventually extinct, for its fitness benefit will be lower than the fitness benefit of hare-hunters.

	Stag-hunter	Hare-hunter
Stag-hunter	3, 3	0, 3
Hare-hunter	3, 0	<i>2, 2</i>

TABLE 2. Payoff matrix for the stag hunt game. The numbers represent the net benefit for the individuals in the population that engage in the game. Cases where all the individuals in the population hunt exclusively stags or exclusively hares represent Nash equilibria (bold). However, only the case where both individuals hunt hares represent an ESS (italics).

Blaser and Kirschner apply this type of reasoning to persistent long-term host-microbe associations to argue that the situation must be the one that is obtained in Nash equilibrium, particularly in ESSs, where both positive and negative feedback between the host and the microbe occur, so that the equilibrium persists over time. The core idea of their model is that the equilibrium obtained at the microscopic level immediately affects the equilibrium at superior levels (mesoscopic and macroscopic). At the same time, the equilibrium at the higher levels affects in a specific way the possibility of new microbe-host persistent associations. The equilibria are nested and the association does not get in principle disrupted. The interaction among levels, partially captured by the equations (1)-(3), is as follows:

first, on the microscopic level one would find the microbial population, localized on an organ or tissue of the host, and the population of immune host cells responsible of recognizing the microbe population. The structure of both populations will depend on the nature of the original founder strain, the possibility for generating genetic variants, the selective pressures from other microbial cells in the same tissue and, more importantly, from the selection that the persistent microbe and the immune cells exert on each other [e.g. (Pradeu et. al 2013); Pradeu & Vivier (2016); Eberl (2016)]. The nature of the interactions between the organisms in the microscale will shape tissue function (or malfunction), and thus will partially determine the viability of the host, as well as the opportunity for microbial transmission (mesoscale). Finally, the effects of the microbe on the viability of the host will determine the host population structure (macroscale) that in return will affect microbial transmission (mesoscale) (Figure 2).

Even if the model illustrated in Figure 2 looks like a multilevel mechanism, for it appeals to a model of mechanism, it lacks the adequate type of causal stories that new-mechanists demand to have a proper explanation. First, because multilevel causation is mysterious, as Craver and Bechtel illustrate (2007), since causal relations happen exclusively intra-level. Second, because the type of inter-level readjustments of the system are symmetrical, occurring both top-down (e.g. from the macroscale to the mesoscale, or from the latter to the microscale), and bottom-up (e.g. from the microscale to the mesoscale, or from the latter to the macroscale), while relations between cause and effect are always asymmetrical. Third, because even if there could be a way to capture inter- and intra-level causal relations, this would be at odds with the information that NEM conveys and appeals to. NEM does not specify the causal way in which the entities at one level affect the entities at another level. It only specifies that the disruption of the equilibrium at one level will either prompt the collapse of the system (i.e. its death), or it will prompt the re adjustment of the equilibrium at that level due to the equilibria that exist in the other scales. In other words, NEM is not specific about how the equilibrium will be readjusted, it only predicts that it will be readjusted, provided that the other levels keep their equilibrium states. The causal elements (if any) that will bring this readjustment are irrelevant for the explanation of this behaviour in terms of NEM. What matters is exclusively the nested structure of the host-symbiont system (see section 4 for the full details).

In that vein, the nested structure of the model and the level of complex interactions between the different elements at the three scales (Nash equilibria, ESS) grant the persistence of the association. As it was

said before, one of the reasons why host-microbe associations do not normally last long is due to the presence of cheaters, organisms that enjoy the profits of the associations without paying the cost. Nash equilibria avoid the appearance of cheaters: cheaters are players that change their strategy unilaterally; in Nash equilibria, every player that does so is condemned to failure, and thus will be removed from the population. Furthermore, as the Nash equilibria that are reached in the population adopt the form of an ESS, it is not possible that an external invader adopting an alternative strategy disrupts the persistence of the association.

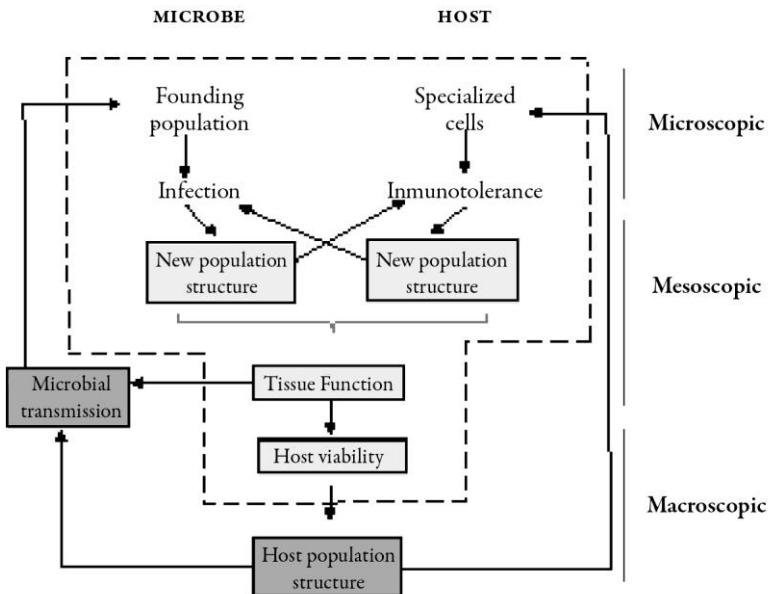


FIGURE 2. Nested equilibrium model. The dashed box represents those events that occur within the host. Adapted from Blaser & Kirschner (2007), p. 845, Fig. 2).

III. EQUILIBRIUM EXPLANATIONS AS STRUCTURAL AND NON-MECHANISTIC EXPLANATIONS

Blaser and Kirchner’s NEM was developed to account for the persistence and the long-term character of certain human-microbe associations. Concretely, the authors seek to explain two paradoxes: first, why the association is not disrupted by the appearance of cheaters, i.e. entities that ben-

efit from the association without paying the costs; second, why the bacterial population is not entirely substituted by an intruder/external invader that deploys a different strategy. Only if those two phenomena are avoided, persistent host-bacterial associations can be successful. We will now argue that Blaser and Kirchner's NEM explains how those phenomena are avoided by appealing to mathematical, *but not causal*, properties, of host-microbial associations. In other words, we will argue that the alleged explanatory force of the NEM lies in the fact that: (i) it provides a mathematical structure in the form of a set of differential equations that together satisfy an ESS; (ii) that the nested nature of the ESSs makes the explanation of host-microbe persistence robust to any perturbation; (iii) that this is so because the properties of the ESS directly mirror the properties of the biological system in a non-causal way.

First of all, as shown in section II, Blaser and Kirchner's NEM consists in a series of differential equations that describe how the concentration of bacteria in different host tissues, their effector cells, their nutrient availability, the immunological response and their rate of transmission will change over time. These equations, as we explained, do not contain *a priori* any information about the persistence of the host-microbe relationship. However, they provide information about how the different variables must be related to each other so that persistence obtains. Particularly, the equations measure the impact of host immunological response on bacterial colonization and, in doing so, allow determining the level at which host's response will abruptly disrupt colonization, as well as the levels at which bacterial inflammation will trigger a decrease in nutrient availability that in the end will disrupt colonization. And, in addition, they provide information about the way in which the solutions to these equations that guarantee the persistence of the symbiotic relation relate to: a) the rate of transmission of the symbiont (R_0), b) the viability of the host (tissue function and evolutionary advantages).

The set of equations can be resolved for a concrete host-symbiont system, and the evolution of the variables under study, as well as their interrelation, can be analysed. This will provide information about how they relate and how they are maintained constant, allowing predictions about empirical system⁹. However, notice that they would still provide no information about our *explanandum*, i.e. about what makes the host-microbe relationship persistent. To do so, the set of equations must be embedded in the framework of ESSs, i.e. it must model the biological situation as a non-cooperative game of two players, such that if any of the players (host, microbe) follows a unilateral strategy, the consequences

will be detrimental for the player that does so. That this is so can be seen by studying how changes in the equations that relate the concentration in nutrient availability, immune response, microbial concentration, etc. will relate to each other to make the system collapse if the change is unilateral. However, as we argued, the explanatory character of the equations comes exclusively from the possibility of embedding them in the framework of ESS. In other words, they are explanatory sound because it is possible to realize that no unilateral change that disrupts the system is possible without generating a chain reaction that either reverses the change or destroys the system. The ESS thus explains stability by ruling out two alternative scenarios: one where cheaters spread in the population, and another when an invader population entirely substitutes the actual one.

Second, the explanatory force of the ESS is reinforced in Blaser and Kirschner's NEM due to its nested nature. The nested nature of the equilibria works as a check and balances system which prevents that a disruption of the ESS at one of the levels (microscopic, mesoscopic and macroscopic) spreads across the other levels and destroys the host-microbe association. Let us explain this with an example: take the case of a disruption at the mesoscale that substitutes the microbe population for an invader. As we are at the mesoscale, the invader will disrupt tissue function in its own benefit, e.g. growing more than what the original microbial population would have grown, while at the same time escaping from the barriers of the immunological system. This type of change, totally beneficial for the bacteria at the mesoscale, would trigger two responses: First, a response at the macroscale that would be immediately detrimental for the bacteria. At this level, host viability, which is affected by the tissue function, will be reduced and, as a consequence, bacterial transmission will substantially decrease in relation to the transmission of those bacteria that cause no damage in tissue function. Secondly, at the microscale, where the invader population will not have generated immunotolerance, the invader population will be systematically blocked by the specialized immunological cells, especially the cells of the adaptive immune system. Furthermore, it is expected that the host will reduce nutrient availability, so that it affects in the long-run the intruders' population structure. Remember, as we said in section II, that the key of the ESS is that no player that changes its strategy unilaterally will be better. In this situation, even if the "player" might be better in one particular scale (mesoscale), the same will not be true for the other scales, and thus no possibility for invasion exists¹⁰.

Third, and more concretely about the nature of ESS, we believe that Blaser and Kirschner's NEM, as any explanation that appeals to the existence of an ESS, explains the stability of host-microbe persistent associations in a non-causal way. Let us argue why we believe this to be so.

1) Blaser and Kirschner's NEM appeals to general properties of ESSs, and they make their model explanatory in virtue of the equivalence between the theoretical ESSs framework and the general properties of persistence host-symbiont associations. The strategy is the general strategy of Huneman's structural explanations: first, build a system S' whose properties match the properties of the real system S whose behaviour you aim to track. Second, study the behaviour of S' and attribute its properties to S . In Blaser and Kirschner's NEM, the strategy is applied as follows: first, build the ESS model for host-microbe persistent associations, as a case of a non-cooperative game of two players; second, study the behaviour of the ESS model, i.e. why the existence of an ESS, as the optimal solution for both players (Nash equilibrium), excludes the possibility of cheaters and invasive populations; third, attribute the properties of the ESS model to the empirical phenomenon, i.e. to empirical cases of host-microbe persistent associations. Notice that in this schema the explanatory force comes because the mathematical system that is built, in this case an equilibrium model, behaves in a certain way that (allegedly) is the way in which the empirical system will behave. But, importantly, it is irrelevant how the empirical phenomenon causally realizes the properties that it is attributed. And this is so in a double sense: on the one hand, because the NEM neither mention, nor needs to mention the specific species that interact to generate the ESS; on the other, because the causal connections between the entities (*if any*) are epistemologically irrelevant for the explanation of the phenomenon.

2) Despite the highly problematic way of identifying interlevel causal relations in a multilevel mechanism, as Craver and Bechtel (2007) explain, one could still try to appeal to Woodward's interventionist strategy to identify the supposed causes explaining the persistence of host-microbe associations. However, we believe NEM rules out the possibility of generating or even heuristically imagining any intervention *à la* Woodward, thus contradicting Kuorikoski and Potochnick's interpretation of equilibrium explanations. Let us explore this via an example. Recall that the *explanandum* is the phenomenon of persistence host-microbe associations. How would an intervention look like in Blaser and Kirchner's NEM? The only possibility would be to generate a situation such that the ESS disappears. However, no possible intervention is imaginable without destroying the system. Or,

in other words, any imaginable intervention that would make host-microbe associations non-persistent would directly change the system we are trying to explain, and thus the information it will provide will turn out to be irrelevant to account for the phenomenon. Recall the structure of ESS (Table 2). The only possibility of imagining a significant intervention would be via a change in the expected payoffs for the actions of each player. However, this intervention would not give any relevant information about why the association is stable in certain circumstance, because it would directly shift the focus of attention towards a new system, namely, one where there is not an ESS. Or, in other words, a causal explanation would consist in saying that the ESS is explanatory because if there were not an ESS the host-microbe association would not be stable. But this kind of reasoning is uninformative and, in our view, unexplanatory. The structural interpretation *à la Huneman*, on the contrary, offers a plausible account of how Blaser and Kirschner's NEM gains its explanatory force.

More importantly, the nested nature of the model, far from moving its explanatory force in a causal-mechanistic direction, generates the opposite effect. It just makes any possible intervention less imaginable. Because even if one causal intervention could be imagined for one specific level, how would it possibly work, if its effects would be cancelled out due to the existence of ESSs in the other levels? Or, in other words, how is it possible to imagine an intervention that causally escapes the inter-level connection? This connection is just a property of any host-microbe persistent association, and the explanatory power of the nestedness resides, precisely, in its possibility to cancel out the effect of every possible intervention. Therefore, we argue, a causal interpretation of the explanatory power of Blaser and Kirschner's NEM is not possible, since it would simply make the explanatory force of the model completely mysterious.

Of course, one might agree with what we just said, and still believe that our argument does not rule out the fact that the most appropriate interpretation of the explanatory force of Blaser and Kirchner's NEM is indeed causal. For instance, Blaser and Kirschner explicitly argue that specific host-microbe associations (human-*H. pylori*, human-*Salmonella typhi*, etc.) are "not necessarily forever stable" [(2007), p. 843], as obviously context (environment) matters, and in a changing context (environment) it is possible that concrete associations go selected against, simply because the environment selects against that coevolved system [see Díaz (2015); Suárez & Triviño (2019)]. In this context, it is possible to investigate the causes that made the system collapse, and if this is so, then the same must

be true for the cases in which the association is persistent. Nonetheless, we disagree, because that will entail changing the *explanandum* in two senses: first, making it specific to particular species; second, explaining the disruption of the persistence, instead of the persistence itself. And remember that our original *explanandum* was why some host-microbe associations are persistent, and the cases to rule out are the cases of cheaters and invasive populations. In our view, their model should be interpreted counterfactually: if a host-microbe association is persistent throughout the host's life cycle and evolutionarily long-term, then it will satisfy the conditions of the NEM reached through an ESS. And this situation will be so irrespectively of the species that interact, and thus irrespectively of the causal-mechanisms that host and microbe could have developed to reach that equilibrium. As in the case of the ice vendors (section I), where the psychological mechanisms that have driven the vendors to put their stalls in the middle of the beach are explanatorily irrelevant to understand why their stalls are there, in the case of persistent associations causal-mechanistic details are simply superfluous. One can perfectly omit all those details and the explanation would still be epistemically sound.

Alternatively, an enumeration of the causes (if any) that would determine whether a concrete host-microbe association is stable will be irrelevant to explain its persistence if it is not conceived as a consequence of an ESS. This is because it would still be possible to imagine the existence of cheaters or invasive populations that deploy the same causal-mechanistic “machinery” to escape e.g. immunitary controls, without paying the cost of the symbiotic association. However, as we explained, because the host-microbe association constitutes a nested ESS, both the cheater and the invader population will end up disappearing from the population, just because the host-microbe persistent system has the structure that appears in the mathematical formulation of ESSs. Importantly, we are not here saying that Blaser and Kirchner's NEM rules out the possibility of telling a causal story of why concrete host-microbe associations are, sometimes, persistent, although some story about how to speak about interlevel causation should be provided.¹¹ Furthermore, we believe that such causal stories *could* be told to explain specific host-microbe associations, even when these must be complemented with the appeal to ESSs. Our point is rather *epistemological*: causal stories that seek to explain the existence of persistent host-microbe associations are neither required, nor explanatory in themselves. The element that provides the explanatory strength in equilibrium explanations is purely structural (in Huneman's terms), and it is connected with the possibility of accounting for the existence of an equilibrium (in Blaser and Kirchner's NEM, a nested ESS).

IV. CONCLUSION

In this paper, we have examined the explanatory force of equilibrium explanations, and have studied whether the explanatory force of equilibrium explanations can be better justified by applying the causal-mechanistic model of scientific explanation, or Huneman's structural model. Concretely, we have examined the role that mathematical vs. causal properties play in the explanation of the stability of persistent long-term host-microbe associations. Explaining the stability of this type of associations is paradoxical, as it requires explaining two facts: first, the absence of cheaters; second, the impossibility of the population being substituted by an intruder population. We have used Blaser and Kirschner's NEM to illustrate that the explanation of host-microbe persistent associations does not seem to be causal, but structural, relying solely on the non-causal mathematical properties of the association to explain its long-term persistence [Huneman (2018a), (2018b)]. We have argued that Blaser and Kirschner's NEM is explanatory of the long-term persistence of host-microbe associations because (i) it provides a mathematical structure in the form of a set of differential equations that together satisfy an ESS; (ii) that the nested nature of the ESSs makes the explanation of host-microbe persistence robust to any perturbation; (iii) that this is so because the properties of the ESS directly mirror the properties of the biological system in a non-causal way. In this vein, our case study shows how equilibrium explanations, even if nested, gain their explanatory force from the mathematical structure that describes the system, instead of from the causal interactions among its components. Our analysis supports two theses: first, that equilibrium explanations, even if nested (in a hierarchical setting), are structural rather than causal-mechanistic; second, that causality, even if necessary in some explanations, is not a universally necessary requirement of every scientific explanation.

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NOTES

¹ The commitment to a causal view of the world does not entail either a physical reductionism [as in Salmon (1984)] or an “ontic” interpretation of scientific explanation [as in Craver (2014)]. Cf. Glennan (2002), Bechtel & Abrahamsen (2005), for a model-based interpretation of mechanisms.

² There are other cases where equilibrium models have been used to explain the stability of biological associations [Baalen & Jansen (2001); Selosse *et al.* (2006)]. We have chosen to analyse Blaser & Kischner’s NEM for its generality, and because it is a case of equilibrium explanation generally accepted among biologists. Nonetheless, our conclusions also apply to these cases. Thanks to Philippe Huneman for pointing this fact to us.

³ Following Brigandt (2013), we consider that an element of an *explanans* is explanatory relevant if and only if removing it from the explanation entails that the *explanandum* does not follow, and it’s explanatory irrelevant otherwise [(2013), p. 480].

⁴ “Microbiota” refers to “[t]he assemblage of microorganisms present in a defined environment”, and “microbiome” is used to denote “the entire habitat, including the microorganisms (bacteria, archaea, lower and higher eukaryotes, and viruses), their genomes (i.e., genes), and the surrounding environmental conditions” in a given environment [Marchesi & Ravel (2015), p. 1]. For the purposes of this paper, we will not distinguish the two concepts, and they will be used to refer only to the community of microorganisms present in a given environment.

⁵ In biology, persistent infection refers to lifelong associations between a host and some species of microbes that do not necessarily harm the host, although they might do it in the long-term. The term should not be confused with its medical use, where “infection” is usually employed in reference to pathogens, or disease-causative agents.

⁶ Their model is in principle developed exclusively for pair associations, between one host and one microorganism.

⁷ Those different levels have both a temporal and a scale correlation: the macroscale refers to the evolutionary time, the mesoscale refers to organismal development and the microscale refers to the interactions among different cell types.

⁸ Since our purpose is only to illustrate the main features of the model and their relation to Blaser and Kirschner's explanation, for a matter of simplicity we only introduce two of the equations.

⁹ Information about the values that the variables must take for a concrete (empirically real) host-microbe association, if the association is known to be stable.

¹⁰ It exists, but if and only if the intruder changes the situation *in the three scales*. That is precisely the nature of the nested model.

¹¹ See Craver & Bechtel (2007) for a proposal.

REFERENCES

- BATTERMAN, R.W., and C. C. RICE (2014), "Minimal Model Explanations"; *Philosophy of Science* 81. 3, pp. 349-376.
- BECHTEL, W., and A. ABRAHAMSEN (2005), "Explanation: A Mechanist Alternative"; *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences* 36 (2), pp. 421-441.
- BLASER, M. J. (2006), "Who Are We? Indigenous Microbes and the Ecology of Human Diseases"; *EMBO Rep* 7, pp. 956-960.
- BLASER, M. J. and J. ATHERTON (2004), "*Helicobacter pylori* Persistence: Biology and Disease"; *J. Clin. Invest.* 113, pp. 321-333.
- BLASER M. J., and D. KIRSCHNER (1999), "Dynamics of *Helicobacter pylori* Colonization in Relation to the Host Response"; *Proc Nat Acad Sci* 96, pp- 8359-8364.
- (2007), "The Equilibria that Allow Bacterial Persistence in Human Hosts"; *Nature* 449, pp. 843-849.
- BRIGANDT, J. (2013), "Systems Biology and the Integration of Mechanistic Explanation and Mathematical Explanation"; *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences* 44, pp. 477-492.
- BRIGANDT, J., S. GREEN, and M. A. O'MALLEY (2017), "Systems Biology and Mechanistic Explanation"; in S. Glennan and P. Illari (eds.) *The Routledge Handbook of Mechanisms and Mechanical Philosophy*, London: Routledge (chapter 27).
- CHIU, L., and S. F. GILBERT (2015), "The Birth of the Holobiont: Multi-species Birthing Through Mutual Scaffolding and Niche Construction"; *Biosemiotics* 8 (2), pp. 191-210.
- CRAVER, C. F. (2007), *Explaining the Brain*, New York: Clarendon Press.
- (2014), "The Ontic Account of Scientific Explanation"; in Kaiser, M. I., Scholz, Plenge, R. D. Hüttemann, A. (eds.), *Explanation in the Special Sciences: The Case of Biology and History*, Springer Verlag. pp. 27-52.
- CRAVER, C. F., and W. BECHTEL (2007.), "Top-Down Causation Without Top-Down Causes"; *Biology & Philosophy* 22(4), pp. 547-563.

- CRAVER, C. F., and L. DARDEN (2013), *In search for Mechanisms: Discovery Across the Life sciences*; Chicago: University of Chicago Press.
- DEULOFEU, R. and J. SUÁREZ (2018), “When Mechanisms Are Not Enough: The Origin of Eukaryotes and Scientific Explanation”; in Christian A., Hommen D., Retzlaff N., Schurz G. (eds) *Philosophy of Science*. European Studies in Philosophy of Science, vol 9. Springer, Cham.
- DEULOFEU, R, J. SUÁREZ and A. PÉREZ-CERVERA (2019), “Explaining the Behaviour of Random Ecological Networks: The Stability of the Microbiome as a Case of Integrative Pluralism”; *Synthese*. <https://doi.org/10.1007/s11229-019-02187-9>.
- DÍAZ, J. S. (2015), “El Mecanismo Evolutivo de Margulis y los Niveles de Selección”; *Contrastes* XX (1), pp. 7-26.
- DOUGLAS A. E. and J. H. WERREN (2016), “Holes in the Hologenome: Why Host-Microbe Symbioses Are Not Holobionts”; *mBio* 7 (2), e02099-15.
- EASLEY, D. and KLEINBERG, J. (2010), *Networks, Crowds, and Markets: Reasoning about a Highly Connected World*; Cambridge University Press.
- EBERL, G. (2016), “Immunity by Equilibrium”; *Nat. Rev. Immunol.* 16, pp. 524-532.
- GINTIS, H. (2000), *Game Theory Evolving: A Problem-Centered Introduction to Modeling Strategic Behavior*; Princeton University Press.
- GLENNAN, S. (2002), Rethinking Mechanistic Explanation; *Philosophy of Science* 69 (S3), pp. S342–S353.
- GLENNAN, S. and ILLARI, P. (Eds.) (2017), *The Routledge Handbook of Mechanisms and Mechanical Philosophy*, Taylor and Francis.
- GREEN, S. (2016), *Philosophy of System Biology*; Dordrecht: Springer.
- (2017), “Philosophy of Systems and Synthetic Biology”; *The Stanford Encyclopedia of Philosophy* (Edition Spring 2019), Edward N. Zalta (ed.), URL = <<https://plato.stanford.edu/archives/spr2019/entries/systems-synthetic-biology/>>.
- GREEN, S. and JONES, N. (2016), “Constraint-Based Reasoning for Search and Explanation Strategies for Understanding Variation and Patterns in biology”; *Dialectica* (70)3, pp. 343-374.
- HUNEMAN, P. (2010), “Topological Explanations and Robustness in Biological Sciences”; *Synthese* 177, pp. 213–245.
- (2018a), “Outlines of a Theory of Structural Explanation”; *Philosophical Studies* 175 (3), pp. 665–702.
- (2018b), “Diversifying the Picture of Explanations in Biological Sciences: Ways of Combining Topology with Mechanisms”; *Synthese* 195, pp. 115–146.
- (2018c), “Realizability and the Varieties of Explanation”; *Studies in History and Philosophy of Science*. <<https://doi.org/10.1016/j.shpsa.2018.01.004>>
- HUTTENHOWER C, GEVERS D, KNIGHT R, CREAS HH, et al. (2012) “Structure, Function and Diversity of the Healthy Human Microbiome”; *Nature* 486, pp. 207–214.
- ISSAD, T., and C. MALATERRE (2015.), “Are Dynamic Mechanistic Explanations Still Mechanistic?”; in P. A. Braillard and C. Malaterre (eds.) *Explanation in*

- Biology: An Enquiry into the Diversity of Explanatory Patterns in the Life Sciences*. Dordrecht: Springer, pp. 265–292.
- JONES, N. (2014), “Bowtie Structures, Pathway Diagrams, and Topological Explanations”; *Erkenntnis* 79 (5), pp. 1135–1155.
- KAPLAN, D. M. and C. F. CRAVER (2011), “The Explanatory Force of Dynamical and Mathematical Models in Neuroscience. A Mechanistic Perspective”; *Philosophy of Science* 78.4, pp. 601–627.
- KITANO, H., and K. ODA (2006), “Robustness Trade-Offs and Host-Microbial Symbiosis in the Immune System”; *Molecular Systems Biology* 2, pp. 1–10.
- KOSTIĆ, D. (2018), “The Topological Realization”; *Synthese*, 195(1), pp. 79–98.
- (2019), “Minimal Structure Explanations, Scientific Understanding and Explanatory Depth”; *Perspectives on Science*, 27 (1), pp. 48–67.
- KRICKEL, B. (2018), *The Mechanical World: The Metaphysical Commitments of the New Mechanistic Approach*; (Vol. 13). Springer.
- KUORIKOSKI, J. (2007), “Explaining with Equilibria”; in Persson, J., and Ylikoski, P. (Eds.), *Rethinking explanation*; Springer, Dordrecht, pp. 149–162.
- LOZUPONE, C. J. I. STOMBAUGH, J. I. GORDON, J. K. JANSSON, and R. KNIGHT (2012), “Diversity, Stability and Resilience of The Human Gut Microbiota”; *Nature* 489 (7415), pp. 220–230.
- MACHAMER, P., DARDEN, L., and C.F. CRAVER (2000), “Thinking About Mechanisms”; *Philosophy of science*, 67(1), pp. 1–25.
- MARCHESI, J. R., and J. RAVEL. (2015), “The Vocabulary of the Microbiome Research: A Proposal”; *Microbiome* 3, p. 31.
- MORAN, N., and D. B. SLOAN (2015), “The Hologenome Concept: Helpful or Hollow?”; *PLoS Biol* 13 (12), e1002311.
- MORENO A., and J. SUÁREZ (submitted), “Plurality of Explanatory Strategies in Biology: Mechanisms and Networks”.
- NASH, J. F. (1950a), “The Bargaining Problem”; *Econometrica: Journal of the Econometric Society* 18 (2), pp. 155–162.
- (1950b), “Equilibrium Points in N-Person Games”; *Proceedings of the National Academy of Sciences* 36 (1), pp. 48–49.
- NICHOLSON, D.J. (2012), “The Concept of Mechanism in Biology”; *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences* 43 (1), pp. 152–163.
- POTOCHNIK, A. (2015) “Causal Patterns and Adequate Explanations”; *Philosophical Studies*, 172(5), pp. 1163–1182.
- PRADEU, T., JAEGER, S., and E. VIVIER (2013), “The Speed of Change: Towards a Discontinuity Theory of Immunity?”; *Nature Reviews Immunology*, 13(10), p. 764.
- PRADEU, T., and E. VIVIER (2016), “The Discontinuity Theory of Immunity”; *Sci. Immunol.* 1 (1): aag0479.
- RICE, C. (2015), “Moving Beyond Causes: Optimality Models and Scientific Explanation”; *Noûs* 49.3 pp. 589–615.

- ROSENBERG E and I ZILBER-ROSENBERG (2014), *The Hologenome Concept*. London, Springer.
- (2016) “Microbes Drive Evolution of Animals and Plants: The Hologenome Concept”; *mBio* 7 (2): e01395-15.
- SALMON W. (1984), *Scientific Explanation and the Causal Structure of The World*; Princeton: Princeton University Press.
- SELOSSE, M. A., RICHARD, F., HE, X., and S.W. SIMARD (2006), “Mycorrhizal Networks: des Liaisons Dangereuses?”; *Trends in Ecology and Evolution* 21 (11), pp. 621-628.
- SMITH, J. M. (1974), “The Theory of Games and the Evolution of Animal Conflicts”; *Journal of Theoretical Biology*, 47(1), pp. 209-221.
- SMITH, J. M., and G. R. PRICE (1973), “The Logic of Animal Conflict”; *Nature*, 246(5427), p. 15.
- SOBER, E. (1983), “Equilibrium Explanation”; *Philosophical Studies* 43.2, pp. 201-210.
- SUÁREZ, J. (2018). “The Importance of Symbiosis in Philosophy of Biology: An Analysis of the Current Debate on Biological Individuality and its Historical Roots”; *Symbiosis* 76(2) pp. 77-96.
- SUÁREZ, J. and V. TRIVIÑO (2019), “A Metaphysical Approach to Holobiont individuality: Holobionts as Emergent Individuals”; *Quaderns de Filosofia* 6(1), pp. 59-76.
- VAN BAALEN, M. and V.A. JANSEN (2001), “Dangerous Liaisons: The Ecology of Private Interest and Common Good”; *Oikos*, 95(2), 211-224.
- WOODWARD, J. (2003), *Making Things Happen: A Theory of Causal Explanation*; New York: Oxford University Press.
- (2013), “Mechanistic Explanation: Its Scope and Limits”; *Aristotelian Society Supplementary Volume* 87 (1), pp. 39–65.