Generalizations for Cell Biological Explanations:
Distinguishing between Principles and Laws

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Abstract

Laws have figured in the development of modern biology, but there is a tacit assumption particularly in cell biology that laws are only of the 'strict' kind, which cell biology appears to lack. The cell-biology-specific non-universal laws that do exist (e.g. scaling laws in cellular biochemical networks) are quite uncommon. This paper is motivated by the premise that mechanistic explanations, the dominant kind of explanation in cell biology, *and* laws can both be in the foreground of explanations and that a framework should be developed to facilitate the discovery of laws specific to and operative at the individual cell level. To that end, in the domain of scientifically-relevant non-universal generalizations, which some equate with *ceteris paribus* laws ('cp-laws'), I propose that a cp-law *might* have one or more corresponding 'principles'. I argue that while a cp-law and its *paired* principle(s) might explain the same phenomenon, a principle is *broader in scope* compared to its paired cp-law but *less expectable* or reliable in its predictions. This is because principles appear to be more qualitative and less numerically precise compared to cp-laws, reflective of our lack of precise understanding of the systems to which the generalizations apply. The principles–laws concept makes for a more lenient approach for what could count as a lawlike generalization and can encourage the discovery of novel generalizations in areas of cell biology where no specific generalizations typically figure in explanations. Newly posited principles could augment mechanistic explanations and also lead to the discovery of corresponding cp-laws.

Keywords

Biological Principles; *Ceteris Paribus* Laws; Mechanistic Explanation; Philosophy of Cell Biology; Scientific Explanation; Scientific Laws

Introduction

When it comes to studying single chemical reactions, organic chemists can usually provide a deep level of explanation. As a first step, they can draw out the reaction *mechanism*, which in organic chemistry entails mapping the movement of electrons between different atoms and the creation of new bonds. But the explanation does not stop there. A number of *why-this-and-not-that* type of questions can be asked: why does the reaction proceed to the 'right' and not to the 'left', or why is it endothermic rather than exothermic? To respond to such contrastive questions, appeals could be made to different laws applicable to organic chemistry, most notably the laws of thermodynamics in the form of Gibbs free energy, for example (Jung et al., 2023). Even though laws can provide resources toward prediction or manipulation/intervention when used solitarily in an explanation (Hüttemann, 2021), it is the combined mechanistic *and* nomological features of typical explanations in organic chemistry that provide descriptive *how*-answers along with *why-this-and-not-that* contrastive accounts.[1] One can refer to explanations combining mechanisms and laws as 'principled mechanistic' (PM) explanations.

The target domain of this paper is molecular and cellular biology ('cell biology' for short), where explanations are, one way or another, by far only mechanistic. Given the various problems in current cell biological explanations as introduced in other works, e.g. (Deulofeu & Suárez, 2018; Ehsani, 2020), a crucial theoretical question is how lawlike generalizations can augment mechanistic ones in cell biology to lead to a kind of 'generative complementarity'[2] seen in organic chemistry explanations. As I will argue later, generalizations *specific to* cell biology (i.e. specific to the individual cell level) are few and far between. I should also note that the framework developed here may additionally apply to other scientific disciplines. In fact, various examples from physics and chemistry are referenced in the paper. Moreover, by the term 'laws' I mean to include both strict laws and non-universal (i.e. non-exceptionless) generalizations, which some philosophers equate with the notion of *ceteris paribus* laws (henceforth, 'cp-laws'). Nevertheless, due to the vast complexity and scale of the unknowns in the field, it is unlikely that strict laws can be uncovered in cell biology and as such the paper is essentially concerned with cp-laws.

Within the context above, the main motivation for the paper is to develop a minimalistic philosophical framework to aid in the *discovery* of new generalizations in cell biology. Using an example from physics as a starting point, I will argue for the thesis that in the domain of scientifically-relevant generalizations, a law *might* have one or more corresponding 'principles'. These could be thought of as principle–law pairs. While related explananda could be explained in terms of a law and its paired principle, what appears to be a differentiating criterion is a principle's broader scope, in the sense that a principle might often have a wider range of applicable explananda compared to its (actual or hypothetical) paired cp-law. This multidomain nature of a principle may, as a consequence, afford it with less precise predictions than its paired law (see **Figure 1** for a schematic overview to be expanded on

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[1] See e.g. (Van Bouwel & Weber, 2002) for a discussion of contrastive cases in explanations in the field of psychology.

[2] Thanks to Phyllis Illari for suggesting this formulation of the added effect of mechanistic–nomological (i.e. 'PM' in my terminology) explanations.

throughout the paper). This is because by being applicable to a greater range of distinct systems, principles may be more qualitative and less numerically precise compared to laws, perhaps reflective of our lack of precise understanding of the systems to which the generalizations apply and/or because we are generalizing across many distinct systems.

Finally, I argue that the more lenient requirements for positing more qualitative generalizations in the form of principles than laws can facilitate the discovery of lawlike generalizations in areas of cell biology where specific generalizations do not typically figure in explanations. Newly posited principles could then enhance mechanistic explanations and also potentially lead to the discovery of new corresponding cp-laws.

In building the case for the above, I will begin with what could be considered a simple running example from physics (**Section 1**), abstract away from it to outline my framework (**Section 2**), and then reassess the framework against existing examples in biology that are not as clear-cut as the physics case (**Section 3**). This is the first part of this paper's arguments. In the latter half, I discuss ways in which the proposed framework could aid in the discovery process of cell biological generalizations (**Section 4**) and how these could work together with mechanistic explanations (**Section 5**). Next, I provide a proviso that I am not claiming that mechanisms and generalizations together would be the 'be-all and end-all' of cell biological explanations (**Section 6**). Finally, foreshadowing a possible avenue of further investigation, a brief context is provided in view of the broader literature on cp-laws (**Section 7**).

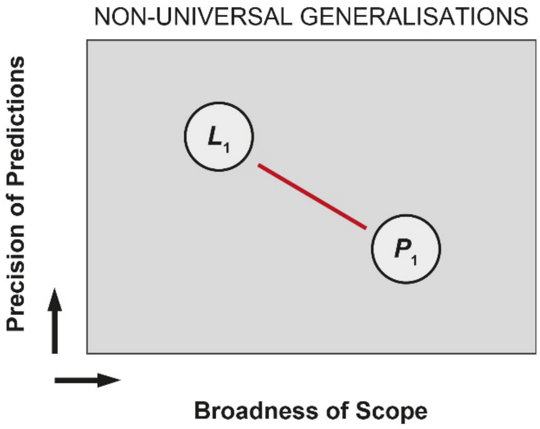

Figure 1. A schematic representation of a principle–law pair [P_1 and L_1] in the domain of non-universal generalizations viewed using a two-dimensional scale.

1. The pendulum example

Let us start with an arguably straightforward example from physics: the case of a pendulum. I begin with this, and not a cell biological example, for four reasons: (i) the notion of pendular motion is intimately associated with mechanistic and nomological explanations in the history of natural philosophy (Gabbey, 1985); (ii) very little contextual background is needed to imagine the mode of a pendulum's movement;

(iii) the conclusions I draw from this example are potentially applicable to all domains of natural science, not just cell biology; and (iv) the terminological notions of a 'law' and a 'principle' are generally uncontroversial, and fixed, in this particular case.

One way to explain a 'simple' swinging pendulum's harmonic motion is to rely on Newton's second law of motion ($F = ma$), make certain assumptions such as the lack of friction or a massless cord, and derive a differential equation:

$$\frac{d^2\theta}{dt^2} + \frac{g}{l}\sin\theta = 0$$

Here, *g* represents the magnitude of the gravitational field, *l* is the cord's length and *θ* is the angle from the vertical to the pendulum.[3] For simplicity, let's call this **Newton's pendulum law** (henceforth, '**NPL**'). As such, to help explain a pendulum's swinging motion, a specific derivation from the second law of motion can help predict the changing angle from the vertical to the pendulum over time.

But a physicist might ask *why* the pendulum moves the way it does, i.e. in a curved line through space and not, for example, in a zigzag manner (recall the earlier-mentioned contrastive mode of explanation). The pendulum's non-zigzag motion can perhaps be said to be assumed in NPL (and is predicted by it), but it is in no way obvious how NPL can explain the non-zigzag mode of motion. Is there a way of getting at this 'why' question? Writing in 1989, Wesley Salmon emphasized that "virtually all philosophers of science of widely diverse persuasions agree that science can teach us, not only *that*, but also *why*" (Salmon, 1989, p. 181). To that end, physicists may appeal to the **principle of least action** (henceforth, '**PLA**').[4] The PLA is not new; indeed, it traces its origins to the 18th century in the works of Pierre Louis Maupertuis, Leonhard Euler and Gottfried Leibniz. In one sentence, the PLA states that a "physical system seeks out the 'flattest' region of 'space'" (Coopersmith, 2017, p. 4). What does this mean, exactly? Jennifer Coopersmith explains as follows: "The Principle of Least Action postulates that when a physical system goes from a prescribed initial state to a nearby prescribed later state, the path connecting these states is a path of tiny incremental changes in action,[5] and, of all possible paths, the path actually followed is the one for which the total change in action has exactly the same value as

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[3] The simple and accessible wording and equation are from the *Wikipedia* article on "Pendulum (mechanics)" (https://en.wikipedia.org/wiki/Pendulum_(mechanics)). For more in-depth perspectives on equations representing the motion of a pendulum, see (Antman, 1998; G. L. Baker & Blackburn, 2005).

[4] The PLA has a related principle called the principle of stationary action, but the technical nuances between them are not germane to my arguments. The PLA is a member of a broad class of so-called variational principles (not further expanded on here). For a discussion on the history of the reception of the PLA in the philosophy of science of the past century, see (Stöltzner, 2003).

[5] 'Action' is a postulated scalar quantity, having "dimensions of *energy* × *time*, or *linear momentum* × *distance* or *angular momentum* × *angle*, and so on" (Coopersmith, 2017, p. 5). Where do these requirements come from? Coopersmith explains: "In one of its first incarnations, 'action' was given as '$m \times v \times ds$', where m is the mass of a 'free' particle, v is its speed, and ds is a small distance along the particle's path. As we have to do with a postulate, we cannot justify the choice by deduction from even more elemental principles. Nevertheless, 'action' does seem like a worthy candidate for a telling physical quantity - it is a scalar (a pure magnitude, having no direction - therefore more likely to be an invariant), it 'spans the physical space' (nothing crucial is missed out), and it does so in the simplest way possible ($mvds$ is postulated rather than, say, $m^2v^3d^4s/dt^4$)" (p. 5).

it does for all infinitesimally close-by paths – in other words, the actual path occurs in a ‘flat’ region of the ‘space-of-paths’” (p. 192).

This principle not only concerns motion in the strict sense, but also such things as fields, given the PLA’s applicability to Maxwell's equations of electromagnetism (Landau & Lifshitz, 1975, pp. 66–88; Moore, 2004). Indeed, the PLA apparently underlies many things in physics, from Newton’s laws to relativistic laws, laws of thermodynamics and so on. Going back to the case of the pendulum, thinking of it as a particle, it might be said that it “feel[s] out the entire path before deciding which way to go [and] at each stage along the trajectory, the particle has only to minimize the action between a point in time and a neighboring point in time” (Susskind & Hrabovsky, 2013, p. 114). Hence, the PLA “just becomes a differential equation at each instant that determines the immediate future” (p. 114).

Going in-depth into the details of the PLA is too technical, but an analysis provided by Benjamin Smart and Karim Thébault is helpful in envisioning one way in which the PLA can relate to things such as Newton’s laws (Smart & Thébault, 2015). The authors propose thinking about generalizations in physics in terms of two categories, namely “instantaneous laws” and “atemporal” principles. In the case of instantaneous laws, which Smart and Thébault say include “Newton’s law of gravitation, Maxwell’s laws of electromagnetism and the Schrödinger equation in quantum mechanics[,] if one knows the state of the system at a given time *t*, one can apply the instantaneous laws and predict the state of the system at *t* + 1” (p. 387). On the other hand, the PLA is an example of “the fundamental meta-laws underlying an atemporal nomology; they state that for any given physical system, and any specified initial and final conditions, that system will evolve through the sequence of states that minimize, or more accurately, extremize, a quantity called ‘action’” (pp. 387–388).

For now, let us think of the PLA as simply being more general than Newton’s laws and yet related in interesting ways, and leave it at that. The PLA–NPL pair will be this paper’s running example. In the next section, I will suggest some conclusions that could potentially be made from these generalizations.

2. Outlines of a principles–laws framework

Two preliminary topics can be raised using the PLA–NPL example. The first is the issue of nomenclature, and, the second, the question of the criteria that may set the two generalizations apart.

2.1. Nomenclature

Notice that it just so happens that, historically, NPL (in view of the second law of motion) can be called a ‘law’ and the PLA a ‘principle’. There is no systematic terminology historically as to what generalization to call a law and what to call a principle. There are some precedents in the literature where attempts have been made to distinguish between laws and principles, e.g. (Clay, 1946; McDonald, 2009), but no systematic framework has taken hold. Relatedly, Nancy Cartwright and colleagues, for instance, note in a recent paper that “we shall use ‘laws’ and ‘principles’ interchangeably, depending on what is common usage for the ones under discussion” (Cartwright, Pemberton, & Wieten, 2020, p. 3). In scientific practice, the use of these terms is also not systematized. For example, biologists can sometimes refer to “laws” of evolution (Koonin, 2011) but also “principles” of evolution (Prud'homme, Gompel, & Carroll, 2007). In other areas of biology, one encounters different nomic terms: laws (e.g. Mendelian laws of inheritance), theorems (e.g. the Price theorem on allelic frequency), rules (e.g. Foster’s rule in ecology), and principles (e.g. Lack’s principle in evolutionary biology).

Given the mostly mixed use of these terms in the literature, what is the historical context when thinking of a law and a principle as distinguishable entities, as hinted at by NPL and the PLA? The development of the concept of ‘laws of nature’, especially since Descartes, suggests a strong connection with the societal notions of law (and the lawgiver) and the implantation of those concepts to the study of the natural sciences (Ott, 2009). Indeed, while beyond the scope of the discussion here, there is an interesting lineage from the ‘laws of the city’ to ‘natural laws’ and ‘laws of nature’ (see e.g. (Degnan, 1982; McNulty, 2021; Watkins, 2019)). There are also semantic demarcations between laws and principles in legal theory. Consider, for instance, that there exists the *principle* of the universality of human rights which has then given rise to (and has been used as a basis for) international human rights *law* and various national human rights *laws*. In the same vein, national legislative bodies do not enact principles; they enact specific laws. These I think suggest that there is a worthwhile context, to be explored elsewhere, of clear and distinct uses of the two words.

2.2. Two criteria: first scope, then precision

Moving on from the choice of terminology, what can be said of our example generalizations’ features? While both the PLA and NPL can apply to the same phenomenon (i.e. a pendulum’s harmonic motion), the PLA appears to be more qualitative and less numerically precise. These conditions may allow it to be more general: “Newton’s laws cannot be extrapolated to things that are very small or very fast or very large […] From a principle of least action we can derive Maxwell’s equations, and can use this principle in relativity if we find the correct form for the action” (Hanc, Tuleja, & Hancova, 2003, p. 391). Thus, the PLA can still be applicable when, for example, deriving Maxwell's equations of electromagnetism, which concern phenomena that are obviously distinct from the movement of a pendulum.

Note that the concern is not with a lack of formalism, for the PLA can surely be stated in formal terms. The heart of the issue of qualitative-ness here has to do with the informational content and specificity thereof in the generalization, whether it is expressed formally or in natural language terms. In a recent study of physical laws, Michael Wong and colleagues write that “while most of […] natural laws can be quantified in the form of an equation, such a formulation is not an essential feature”, further observing that “the second law of thermodynamics, for example, is often presented as an inequality: The entropy of a closed system remains constant or increases (a statement that subsumes the observed asymmetry that ‘heat will not flow spontaneously from a colder to a warmer body’)” (Wong et al., 2023, p. 1). They continue that what unites these laws is that they each possess “measurable parameters—

mass, force, acceleration, distance, energy, or charge" (p. 1). In agreement with this contention, what appears to set the NPL and the PLA apart *formalism-wise* is the former's clear stipulation of its relevant parameters/variables.

Now, it seems that we can encapsulate the multidomain nature of the PLA as having a *broader scope*. Many more physical phenomena could be explained in terms of the PLA (albeit with some work) than NPL. NPL, by definition, is concerned only with motion, and simple harmonic motion for that matter. I propose a simple account of scope here, limited to our current discussion and not implying applicability to all uses of the term 'scope': a broader scope can imply that compared to an actual or hypothetical corresponding law,[6] a principle might apply to a broader range of phenomena to be explained (i.e. more *domains* of explanations). This can result from the more qualitative and general formulation of the principle. Also notice that in our example, NPL might be 'derivable' from the PLA (Hanc et al., 2003),[7] but I am *not* claiming that laws should somehow always be mathematically or conceptually derivable from or explainable by their corresponding principles. Their minimum connection, I am claiming, is their related explananda. In the case of the PLA, NPL is not contained within it; much contextual information has to be brought into any derivation work to get to the latter from the former.

Analogous takes on scope have also been put forward by others. To name one example, Michael Morreau analyzes models of the solar system and compares their scope as follows:

> "Suppose we count Copernican and Ptolemaic models as having the same scope, meaning that they are both about the same thing: where the celestial bodies are, and when. Newtonian astronomy, which additionally addresses the physical causes of their motion, we count as having greater scope than they have. […] Surely the Copernican and Ptolemaic models could not have been about something other than the positions of celestial bodies. Newtonian astronomy could not have lacked the theory of gravitation, and yet still have been the theory that it is. The scope of these theories, in this sense of 'scope' […] is just a matter of which theories they are" (Morreau, 2015, pp. 249–250).

Morreau equates scope with being "about the same thing", or *domains of explanation* in my account. Staying on the topic of scientific models, the notion of model 'imperialism' might also be relevant here, whereby "imperialism, unlike migration, relies upon extension of the original model via an expansion of the domain of phenomena it is taken to adequately describe" (Bradley & Thébault, 2019, p. 81). But the characterization of the PLA and NPL cannot stop here, for we still haven't said much about a principle's greater qualitative-ness and lower numerical precision.

If the PLA has a broader scope than NPL, if may follow as a *consequence* that it also has lower *precision of predictions*: NPL affords numerically precise predictions, whereas the PLA requires some

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[6] A principle's corresponding law might either already exist (i.e. an actual law) or its possible existence might have been envisaged (i.e. a hypothetical law).

[7] In their analysis, Jozef Hanc and colleagues state that the PLA can lead to Newton's second law "and only ordinary calculus is needed to derive almost all of classical mechanics" (Hanc et al., 2003, p. 386).

elaboration using natural language or other means to determine what exactly it is predicting and what the exact parameters/variables and their relationships are in a particular circumstance. More broadly, we can posit that relative to their paired laws, principles might afford less precise predictions due to their less formal and greater contextual-input-requiring formulations. The connection between the criterion of broadness of scope and this secondary criterion of precision of prediction might have to do with the degree of vagueness or uncertainty in a generalization, but this requires a fuller analysis elsewhere.

Do analogous takes on the precision of predictions criterion exist in the literature on scientific laws? In fact, this criterion can be thought of as being related to the notion of 'expectability', one of the criteria proposed by Sandra Mitchell to differentiate among scientific laws, the other two being 'stability' and 'abstraction' (Mitchell, 2000). Expectability, or specifically 'nomic expectability', is a hallmark of generalizations, particularly from the perspective of Carl Hempel's accounts of explanation (Strevens, 2000; Weslake, 2010). Hempel wrote that a deductive-nomological explanation "explains the explanandum phenomenon by showing that it was to be expected in view of the general laws adduced, given the particular circumstances specified" (Hempel, 1968, p. 116), whereas an inductive-statistical explanation explains "*i*'s being *G* by showing that this is to be expected, with probability *r*, in view of the general statistical law and the statement of particular fact included in the explanans" (p. 117).[8] These ideas have been revived in recent years, for example in the work of Roger Deulofeu and Javier Suárez who advocate that "the use of scientific laws is supposed to be a minimal requirement of all scientific explanations, since the purpose of a scientific explanation is to make phenomena expectable" (Deulofeu & Suárez, 2018, p. 95) (see also (Díez, 2014)). In the case of our example, one could ask of the PLA "what exactly is to be expected?", or "what exactly is a 'flat' space in a particular situation?". If the relationship among variables stipulated in a generalization is imprecise (or no variables are stipulated at all), then it is less clear what exactly is to be expected based on the generalization in each context.

The framework and criteria discussed here have thus far been demonstrated using our example from physics. Next, I will turn to the question of whether other examples, particularly in biology, support these claims.

3. Applicability to biological examples

The pendulum example was chosen as a starting point because it is immediately relatable. However, given that our target domain is cell biology, we also need to look at examples from biology. It would have been ideal if well-established generalizations analogous to the PLA and NPL could be found in cell biology concerning a related explanandum. But such paired generalizations are very difficult to find in current cell biology, *and hence the motivation of this paper to encourage their discovery*. Having said that, isolated cases can indeed be found. For example, the **rate–length law of protein folding** is one of the very few cell-biology-specific laws that has been postulated in the literature. It describes how the

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[8] Incidentally, Hempel looked at the explanation afforded by another variational principle, namely Fermat's principle of least time (Hempel, 1965, p. 353). See also (Reutlinger, 2018, p. 82).

time it takes a protein to fold scales with the length of the protein's chain of amino acids (Chan & Dill, 1991; Lane & Pande, 2013; Nassar, Dignon, Razban, & Dill, 2021). It has a mathematical (Gaussian) formulation with a number of stipulated parameters. Its scope is restricted to explaining protein folding, and it makes specific predictions about protein folding. In a sense, it can be thought of as analogous to NPL; however, an established cell-biology-relevant principle analogous to the PLA is currently lacking. This is an interesting area for further investigation.

Even though there may not currently be a principle that could definitively be paired to the rate–length law of protein folding, an instance of a cell-biology-specific principle does exist that is at least in the same explanatory ballpark: the **goldilocks principle of protein function**. It is exemplified by chaperones (a type of protein), and states that such proteins "can exist in many different shapes and forms that need to be 'just right' for efficient function" (Radford & Karamanos, 2021, p. 397). Even though perhaps not obviously pairable with the rate–length law, for the sake of argument, we can see that it is much broader in the domains it could potentially apply to than the law: it might as well also apply to other macromolecules, not just proteins. Furthermore, compared to the law, it does not make specific numerical predictions.

Staying with cell biology and proteins, recent experiments with a type of proton pump enzyme ('V-ATPase') have revealed a working principle of these proteins, i.e. a **principle of ultraslow mode-switching** (Kosmidis et al., 2022), whereby they "randomly switch between proton-pumping, rest and leaking modes" (Stamou & Kosmidis, 2022, p. 1). Moving beyond the level of individual proteins, the **Hayflick principle** or the "Hayflick limit" is another example among the small repertoire of such generalizations in cell biology. Named after the anatomist Leonard Hayflick, the principle postulated that "there was a limit for the propagation of primary epithelial cells while retaining normal ploidy" (Huch, 2023, p. 348). Although the principle has been challenged with the advent of stem-cell-derived 3D cellular models, violation of an empirically-verified generalization can itself open new avenues of investigation.[9]

Finding biological examples of a paired principle and law is somewhat easier if we move beyond cell biology, for example to the domain of evolutionary biology. A recent growth law, called the **biophysical law for beak morphogenesis**, has been proposed that applies specifically to the beak properties of Darwin's finches (Al-Mosleh, Choi, Abzhanov, & Mahadevan, 2021).[10] This was derived based on the evolutionary **principle of adaptive radiation**, generally defined as "the rapid (sometimes 'explosive') origin of taxonomic, ecological and morphological diversity as a consequence of adaptation

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[9] Indeed, it is generally taken that in fields such as physics, "new physics often arises when important symmetries or conservation laws are broken" (Hallatschek et al., 2023, p. 408), and exceptions (at least to extant physical laws) are also beginning to be unmasked in cell biology (Ishimoto, Moreau, & Yasuda, 2023).

[10] The authors found that "in addition to beak size, beak shape is determined using its orientation relative to the skull, aspect ratios, and curvatures" (Al-Mosleh et al., 2021, p. 5). Also, the biophysical law for beak morphogenesis is a cp-law. For example, the authors note that in their cellular and tissue model, they "assume that each cell produces the morphogen χ at a constant rate P, which subsequently diffuses with diffusion constant D_c and degrades at a rate given by Γ" (p. 6).

to novel or hitherto underutilized ecological niches" (Salzburger, 2018, p. 705). The principle of adaptive radiation applies to the diversity of all organisms in various environments, whereas its paired biophysical law for beak morphogenesis applies only to the properties of the beaks of Darwin's finches. The biophysical law is also expressed mathematically as a paraboloidal function precisely linking beak properties such as length, width and depth. Therefore, the principles–laws framework appears to hold here as well (see **Figure 2** for a visual depiction of some of the described principles and laws).

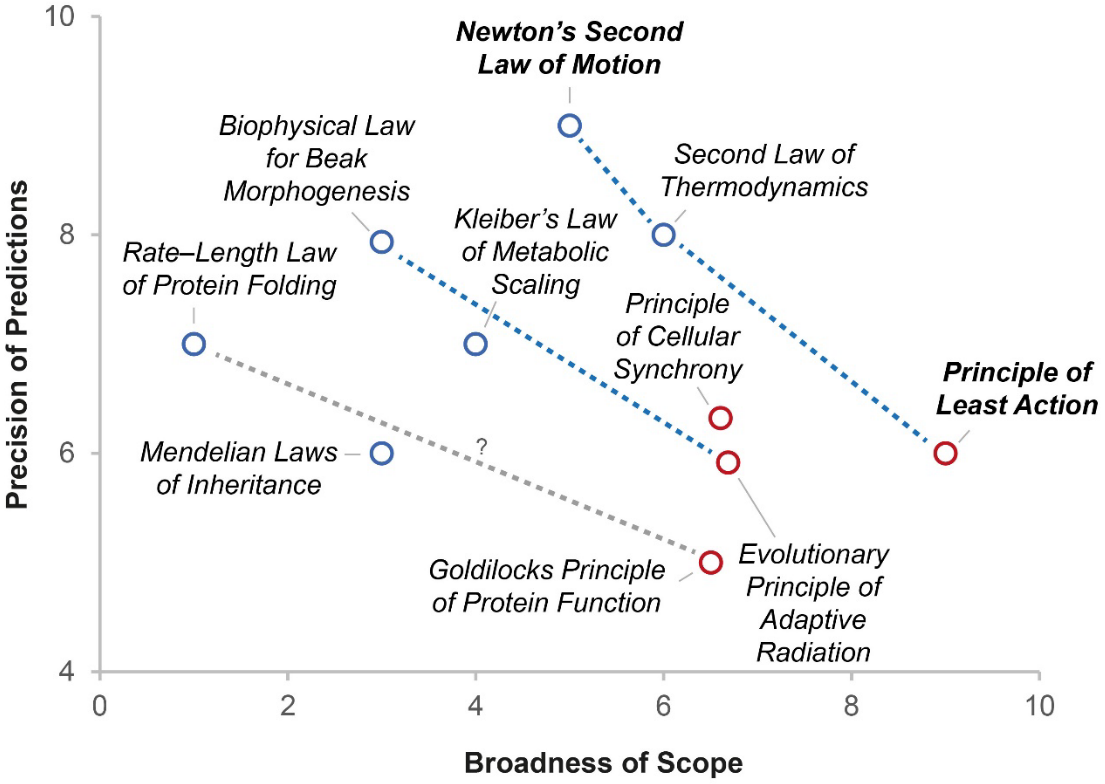

Figure 2. Two-dimensional illustrative plot of a number of generalizations based on best-guess-assigned values for the criteria of broadness of scope and precision of predictions. I acknowledge that others may assign different values and/or disagree with quantifications of this sort to begin with. (The generalizations in this group that have an established 'law' or 'principle' label in their name probably acquired their label according to convention and their historical development.) As is apparent, the generalizations called 'principles' occupy the imaginary bottom right 'quadrant', whereas the laws are closer to the top left quadrant. Interestingly, a generalization such as the second law of thermodynamics seems to lie somewhere in the middle of this space, indicating that based on the proposed framework here, it is a generalization that could arguably also be called a principle. Moreover, various corresponding pairs of generalizations have been indicated with dotted lines. The running example generalizations of **NPL** (derived from Newton's second law of motion) and the **PLA** are indicated in bold. Of note, the PLA, the second law of thermodynamics and Newton's second law of motion have been proposed to be linked together in intriguing ways: not only are the two laws derivable from the PLA, but the three generalizations may all be facets of the same law (Annila, 2021; Kaila & Annila, 2008). The unconfirmed connection between the rate–length law of protein folding and the goldilocks principle of protein function is indicated with a question mark. The principle of cellular synchrony (for which no corresponding law has been postulated) is also plotted (see Ehsani, 2022 for a discussion of this principle). Lastly, Kleiber's law of metabolic scaling, as a specific case of allometric laws in physiology

that concern the scaling of various biological processes relative to body size (Spence, 2009), is also shown.

Before closing this section's discussion, two questions should be clarified. First, having surveyed a few cell biological and biological generalizations and what sets them apart, what *commonalities* do they share together and also with the PLA and NPL? These principles and laws can all share four characteristics by virtue of being non-universal generalizations, albeit to varying degrees: they can figure in explanations and predictions, support counterfactuals, be inductively confirmed, and they "may be used for purposes of manipulation" in an experimental system (Reutlinger, Schurz, Hüttemann, & Jaag, 2021 § 1.1). In the case of NPL, it can provide a very specific explanation and prediction for a swinging pendulum's motion but is limited to such systems and cannot apply to other kinds of motion (such as circular motion) and perhaps lead to some kind of explanatory unity of disparate systems; this is something that the PLA could potentially do across many physical systems. The mathematical formulation of NPL can facilitate a straightforward counterfactual test of its statement, and also allow for precise variables to be selected for testing and manipulation. This also allows a direct pathway towards the confirmation of the mathematical relationship posited in this particular law (bearing in mind its idealized assumptions).

Second, when we say that the PLA has a broad scope, why can it not be applicable to cell biology? To be sure, laws and principles of physics should conceivably figure at some fundamental level in cell biological processes. But such physical principles, and the PLA in particular, should be adapted to the larger scale of cellular phenomena if they are to be relevant in cell biological explanations. Consider, for example, that in chemistry, moving from explaining an atom to explaining a molecule has entailed the development of molecular orbital theory, since atomic orbital theory alone is not sufficient. We also need generalizations specific to the scale of cell biological phenomena. Furthermore, there are already precedents for this: Hyunju Kim, Harrison Smith and colleagues have discovered that "comparing real biochemical reaction networks to random reaction networks reveals that the observed biological scaling is not a product of chemistry alone but instead emerges due to the particular structure of selected reactions commonly participating in living processes" (Kim, Smith, Mathis, Raymond, & Walker, 2019, p. 1) (see also (Gagler et al., 2022)). We can thus search for bona fide cellular network scaling laws.

Having considered the above examples, why is it difficult to find more cases of generalizations and their use in cell biological explanations in the first place?

4. Discovering cell biological principles and laws

Let us first start with biology as a whole. Generalizations have indeed figured in the development of modern biology, and they continue to play important explanatory roles in developmental biology, ecology, systems biology and so on. To name a few examples, one could point to laws in ecology

(Linquist et al., 2016), laws in biogeography (Simberloff, 1974), laws in embryology (Abzhanov, 2013), network ‘principles’ in systems biology (Barberis & Verbruggen, 2017) and ‘principles’ in behavioral neuroscience (Herzfeld, Hall, Tringides, & Lisberger, 2020; Perez Velazquez, Mateos, & Guevara Erra, 2019). I should note that the preceding law/principle designations are as per the original usages in the cited literature.

In many of these fields, there is reliance on explanations that feature both mechanisms and laws. Focusing on ecology, for example, an explanation can contain the mechanism of predator search behavior coupled with the Lotka–Volterra equations, a pair of nonlinear differential equations that model the dynamical interactions of two species (Hein et al., 2020; Hein & Martin, 2020; O'Dwyer, 2020). This is a field that deals with higher-scale phenomena compared to cell biology. But the situation is the same when we consider organic chemistry, a field that concerns lower-scale phenomena compared to cell biology. There, too, laws and mechanisms figure in explanations: for example, reaction mechanisms and laws of thermodynamics are present in organic synthesis explanations (Norman & Coxon, 1993). In fact, the degree to which an organic chemistry explanation invokes thermodynamic laws can be crucial. For example, on studying the reaction mechanism of urea decomposition, one group of authors notes that “previous models did not pay much attention to the thermodynamics of the system” (Tischer, Bornhorst, Amsler, Schoch, & Deutschmann, 2019, p. 16788), whereas their proposed reaction scheme (i.e. their explanation) “is stringently based on thermodynamics” and “closer to the real processes than the previously published mechanisms” (p. 16788).

My argument here is that we should not suspect that cell biology is somehow in a unique position where few or no generalizations could be discovered and used in its explanations. To be sure, mechanistic explanations have been quite successful in cell biology and are relatively easy to grasp and comprehend. This may be because understanding structures or dependencies requires seeing or grasping them (Grimm, 2015), something that mechanistic explanations facilitate. But as argued elsewhere, e.g. (Deulofeu & Suárez, 2018; Ehsani, 2019, 2020; Nicholson, 2019), mechanistic explanations face challenges in cell biology and their utility has been checkered in different biomedical areas. A parallel focus on discovering cell-biology-specific generalizations is thus called for;[11] however, a big impediment is that our understanding of many cellular phenomena is still quite qualitative and imprecise. And this is exactly where the principles–laws framework could be of use. A biologist would not need to look for laws in the first instance; they could look for principles: e.g. natural-language descriptions of patterns or regularities that seem pertinent to the phenomenon being studied. As such, discoveries of generalizations could be simplified by allowing for a greater range of generalizations to be considered for their explanatory utility and also potentially connecting a newly proposed generalization with related principles and laws on the scope–prediction dimensions (**Figure 2**, and **Figure 3** below).

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[11] The cell biologist Richard Strohman has also emphasized that “the rich history of twentieth century molecular biology has included a failure to find […] laws” (Strohman, 2003).

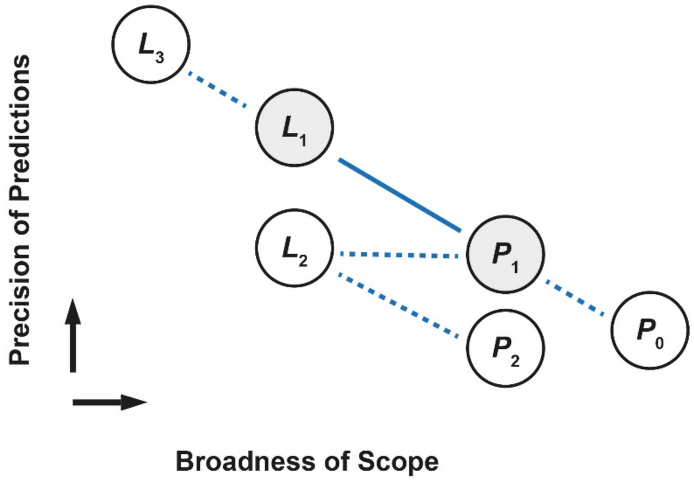

Figure 3. A schematic representation of a principle–law pair [P_1 and L_1] on a two-dimensional scale that adds more detail to the concept presented in **Figure 1**. The main intention of this paper is to propose this dyadic connection [P_1 and L_1]; however, in theory, other connections are also possible: (i) a more 'general' principle [P_0] paired with a given principle (P_1), (ii) pairwise connections between laws themselves [L_1–L_3], and more than one principle [P_1 and P_2] being paired with a law [L_3].

It might be informative in this context to mention briefly two historical precedents in biological theory that I argue followed along the principles–laws path. The first is **metabolic scaling laws**, also known as Kleiber's law. The starting point was perhaps from broad-scope and less-precise 'principles': "as early as in 1839, Sarrus and Rameaux proposed that metabolic rates might depend on heat dissipation […] and therefore increase with surface area, something originally checked in dogs by Rubner in 1883" (Ballesteros et al., 2018, p. 1). There was then a gradual movement toward a more specified generalization in the form of a law: in the 1930s, "Kleiber found that basal metabolic rate of animals seemed to vary as a power law of their body mass with exponent 3/4, instead of 2/3, as a surface-to-volume argument predicts" (p. 1). There is more to say, but let's move to the second example, namely that of the **square–cube law**. Galileo posited a 'principle' (in this paper's terminology), whereby "geometry teaches us that, in the case of similar solids, the ratio of two volumes is greater than the ratio of their surfaces" (Allen, 2023, p. 172). In the 19th century, some specification took place: "[Rudolf] Leuckart and later Herbert Spencer […] pointed out that the absorbing surface of an animal only increases as the square of its length, while its size increases as the cube" (Weismann, 1891, p. 7). On this trajectory, the application of what we now term the square–cube law to the cellular level, for example in conjunction with other generalizations such as Fick's laws of diffusion, can be used to explain and investigate the emergence of multicellularity (Niklas & Newman, 2013).

Moving now to the present, the principles–laws framework and the lenient requirements of discovering generalizations can be seen at work concerning a newly-posited principle called the **principle of cellular synchrony** (Ehsani, 2022). Discussed in the context of a case study on Alzheimer's disease, the principle posits that "all processes within a cell (e.g. the activity of proteins, intracellular transport, DNA transcription, etc.) happen in a synchronised manner and are cyclically coordinated based on a subsecond [picosecond] vibrational frequency", entailing that "unsynchronised processes may lead to cell death" and "answer[ing] to the fact that cellular processes have a mind-boggling level of coordination and interdependence" (pp. 73–74). While it remains to be seen how such a principle might perhaps lead to the discovery of a specific law, the mere fact of the principle being formulated can connect it with previously-underappreciated modes of inquiry and testing. For instance, the principle's picosecond timing regime may overlap with efforts in the field of bioelectricity to investigate "the effects of picosecond pulsed electric fields on protein[s]" wherein "results observed upon application of longer pulses and from picosecond pulses simulations suggest that the latter may affect protein aggregation [a hallmark of Alzheimer's disease] and warrant an extended research effort" (Zamponi, Petrella, & Mollica, 2021, p. 178).

For the sake of completeness, one should bear in mind that sometimes a discovery may not even immediately begin with a principle, but with practical 'rules of thumb'. Aromaticity 'rules' in organic chemistry are a good case in point. A variety of such rules have been posited, each with its own limitations. One of the more widely-known aromaticity rules, Hückel's rule, states that "annulenes with $4n + 2$ π-electrons (where n is an integer) are aromatic" (Solà, 2022, p. 585). Why have discovering these 'rules' been useful? As Miquel Solà points out, these "allow chemists to better understand molecules and their behaviour, as well as identify the formation or elimination of (anti)aromatic species in a reaction, which helps understand and predict possible outcomes" (p. 585). But the ultimate goal is to arrive at a unified generalization: "perhaps more important than drawing up different rules for different situations or classes of compounds is the idea to generalize the existing rules and connect them to each other" (p. 589). Indeed, the discovery process can even be aided using automatic means, such as using recently-developed machine-learning-based symbolic regression to arrive at mathematical equations describing patterns within a dataset (Neumann, Cao, Russo, Vassiliadis, & Lapkin, 2020). In all, how and in what order a discovery of a principle or law is made cannot be formulated. Once awareness of the potential for biological principles exists, the creative process that brings a scientist from observation and experimentation to discovery is an arguably mysterious path.[12] Charles Sanders Peirce termed this process 'abduction', suggesting that it "occurred when on the presentation of some, perhaps unexpected, facts we adopt a hypothesis to explain these facts [and] He regarded this as the reasoning typical of scientific discovery" (White, 1971, p. 294).

An important question, one that I will only acknowledge here but not delve into further, is what evidence might be required to empirically assess a proposed principle. If a newly-posited principle or law could in theory be empirically testable (preferably in different settings), it will have a much greater chance of gaining traction in cell biological practice and explanations. For instance, "the theory of evolution is accepted not because each experiment and observation from Charles Darwin's 1859 book *On the Origin of Species* was independently replicated, but because the principles derived from them

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[12] Some aspects of the discovery process can indeed be amenable to investigation when one considers the cognitive roles of analogies and metaphors, for example.

were verified across widely different settings” (Costa & Schoenbaum, 2021, p. 201). Recall that for many areas in cell biology where a principle might be posited, no other form of generalization has been specifically proposed because known cell biological laws are few and far between; therefore, it is not the case that one is positing a principle in a space of generalizations that already has various corresponding laws. Furthermore, in positing new principles, it is vital to be mindful of the pitfalls of ‘overgeneralization’ if the evidence is too thin (Guttinger & Love, 2019).

Now, assuming that new principles and laws do begin to be discovered, how exactly can they work in the context of existing mechanistic explanations in cell biology, and how can the overall explanation be enhanced?

5. Putting principles and laws together with mechanisms

To answer the above question, first a brief clarification: there has been a continuing debate about the primacy of mechanisms and laws in special science explanations. Among the views, one concerns the dependence of mechanisms on laws, e.g. “while some laws and counterfactuals must be taken as primitive (non-mechanistic) facts of the world, all mechanisms depend on laws/counterfactuals” (Ioannidis & Psillos, 2017, p. 154). Another links mechanisms and laws through the notion of regularities: “regularities are what laws describe and what mechanisms explain” (Andersen, 2011, p. 325). But here I subscribe to what might arguably be called a consensus view expressed by Carl Craver and Marie Kaiser: “no mechanist denies that there are pragmatically useful regularities [that afford prediction, explanation, and control of biological phenomena]. And nobody who thinks there are pragmatically useful regularities should feel any pressure to deny that the search for mechanisms is central to the practice of biology and many other sciences” (Craver & Kaiser, 2013, p. 143). In the ‘principled mechanistic’ (PM) framework motivating this work, the point is that both mechanisms and laws can be in the foreground of explanations in cell biology. And that, moreover, the paucity of cell-biology-relevant generalizations can begin to be addressed by the discovery potential afforded by the simple-to-implement principles–laws framework.

A traditional view of explanations, which I am stating here not necessarily as an endorsement, is that “to explain an event is simply to bring it under a law [understood as any uniformity of nature]; and to explain a law is to bring it under another law” (Hospers, 1956, pp. 98–99).[13] While discovered principles or laws could be put forward to independently explain a particular cellular phenomenon, they could additionally enhance an existing mechanistic explanation by allowing different aspects of the mechanism to be explained in terms of them, helping, for instance, to answer a variety of *why-this-and-not-that* type of questions. As noted earlier, these dynamics can be seen in organic chemistry explanations. Laws of thermodynamics can help (i) predict something about the reaction being studied

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[13] Commenting on nomic generalizations in explanations, David-Hillel Ruben notes that “citation of an appropriate regularity can show that the phenomenon about which I may be perplexed or puzzled is, in any case, not atypical or extraordinary or irregular in any way” (Ruben, 2012, p. 185).

and (ii) provide some sort of quantification for the yield of the reaction. These could arguably be achieved without necessarily appealing to the mechanistic details of the reaction. However, the thermodynamic notion of Δ*G* (the change in Gibbs free energy) can also (iii) be applied to the details of the reaction mechanism itself to reveal new insights. As an example, chemists have used thermodynamic notions of molecules' lowest free-energy states to study the immensely complex mechanism of hydrogen bond formation among clusters of water molecules (Richardson et al., 2016), allowing them to reveal how the bond formation mechanism itself might be operating (see also (Llored, 2011)).

Analogously, in cell biology, a generalization could provide independent explanation of a phenomenon, such as the rate–length law of protein folding or the goldilocks principle of protein function explaining the form or function of a protein independently of and without reference to other cellular mechanisms. Nevertheless, a principle or law could also help explain the 'activity' of a 'part' within a broader *mechanistic* explanation (e.g. a protein's specific enzymatic function), or the interaction of some parts (e.g. a principle explaining protein–protein interactions), and so on up to a mechanism's overall function (e.g. a principle explaining the outcome of the cellular mechanism of action potential propagation along a neuronal axon). This outlined strategy seems to be thematically in line with stances argued for by Cartwright and William Bechtel regarding mechanisms and laws: "typically in mechanistic explanations, the account of what the parts are expected to do in context uses already established principles, typically ceteris paribus laws" (Cartwright & Pemberton, 2021, p. 2) and "laws may be invoked to characterize the overall functioning of the mechanism or some of its operations" (Bechtel, 2011, p. 537).

Of note, an analogy to computer programs may be apt here: as Frank Jackson and Philip Pettit point out, a computer program can ensure "that certain things will happen – things satisfying certain descriptions – though all the work of producing those things goes on at a lower, mechanical level" (Jackson & Pettit, 1990, p. 114). Generalizations could act as such programs. The analogy could be extended further: high-level programming languages can be compared to principles (higher generality and abstraction from the hardware details) vs. laws which might be akin to low-level programming languages that are 'machine-readable' (see (Frampton et al., 2009)). In addition to generalizations acting to 'program' the mechanistic part of a PM explanation, the explanation may become more 'complete' in that the addition of principles/laws could heuristically lead to the discovery of missing parts, interactions and activities in the mechanistic explanation.

Back to the running example, suppose that a Martian encounters a mechanical clock and its pendulum but doesn't know what they do (assuming nonetheless that the Martian has some concept of time). Now, the PLA may in an abstract way explain the overall behavior of the pendulum. But NPL can have a more specific enhancing behavior. It can, for instance, shed light on the interaction of the pendulum and the immediate mechanical parts connected to it: how does the length of the pendulum's cord contribute to how fast a connected cogwheel rotates. Moreover, the law can lead to new puzzles for the mechanistic explanation of the clock. For instance, the law assumes the bob (the mass on the end of the pendulum) is a point mass. If, however, the Martian sees two identical clocks but with two different bob *sizes* (same mass) keeping time differently, this hints that the law's proviso concerning point masses is a critical omission, and that the overall mechanistic explanation should make reference to both the bob's mass and size. Puzzles of this nature are potentially numerous even in simple cases like this. Lastly, circling back to the debates in the literature about the relationship between mechanisms and laws, these examples are compatible with how a given generalization "contributes to the search for mechanisms" (Craver & Kaiser, 2013, p. 127). Indeed, when a number of equally likely mechanisms have been proposed to explain a given phenomenon, the addition of a particular generalization in the form of a principle or law to the explanation could restrict the choice of likely mechanisms. For example, in explanations in evolutionary biology, when a few equally likely mechanisms for the emergence of a particular gene or trait are proposed, the mechanism that most closely adheres to a principle of parsimony or Ockham's razor (i.e. with the fewest possible steps and modifications) is usually the preferred explanation (Ehsani et al., 2011; Gross, 2019; Steel & Penny, 2000).[14]

I have discussed some of the many ways in which generalizations and mechanisms can interact in a cell biology explanation. However, on a more basic level, could a newly-proposed generalization in fact really be a mechanism in disguise? This could lead to an extensive metaphysical analysis, but I will summarize my thinking on this using an example. Consider that in protein biology, a current puzzle pertains to why certain sequence-identical proteins twist in a left-handed direction whereas others take a right-handed twist (Kollmer et al., 2019). Now, finding a principle or law that might underlie this difference of behavior can perhaps not appeal to any protein-level mechanistic details, because the proteins have an identical sequence. Having said that, the explanation could additionally appeal to the *chemical* mechanisms of the proteins' amino acid residues, but one has then moved to the domain of chemical explanations where chemical laws and principles would be at play, not cell biological ones. This is only a single example and there may be many possible counterarguments in other cases. However, although determining what might undergird laws and principles is a crucial question, I would be more partial toward the pragmatic approach suggested by the chemist Joseph Black (1728–1799) to, in essence, defer such questions until such time as the generalizations have been understood more fully in various explanatory contexts: "let chemical affinity be received as a first principle, which we cannot explain any more than Newton could explain gravitation, and let us defer accounting for the laws of affinity, till we have established such a body of doctrine as he has established concerning the laws of gravitation" (Schofield, 1970, p. 226).

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[14] This scenario can be observed in other areas of science as well: in linguistics, for example, Noam Chomsky writes that the Strong Minimalist Thesis (SMT) "serves a disciplinary function: it restricts the mechanisms that are available for description of language, a necessity if we are to approach the goal of genuine explanation. [However,] less recognized is the fact that SMT also serves an enabling function. It provides options and systems for language that would have no reason to exist if language did not abide by SMT" (Chomsky, 2021, p. 14). Chomsky further notes that in a sense, "SMT is somewhat analogous to the laws of form and structure that determine the space of possible organisms, very narrowly it seems" (p. 14).

6. A pluralistic caveat

It is important to complement the discussion so far with an important caveat. Although discovering principles and applying them in the context of PM explanations would conceivably enrich our understanding of the target phenomena, the PM framework alone cannot be expected to have the capacity to explain the totality of cellular phenomena in a 'holistic' manner. This is because in addition to being explainable in terms of mechanisms and (potentially many) operating biological generalizations, the cell is a 'computer' and also constrained by its very physics. The cell is a computer because it computes on a pre-determined genetic program whereby, for example, a caterpillar can only turn into a butterfly and not any other invertebrate. It is constrained in a simpler sense as well: its physicochemical properties. For example, cells are constrained by their physical size (D'Ario et al., 2021), they have no sharp edges,[15] or the fluid inside the cell is part of an 'osmotic system' which is "not related to any specific activities of the cell" (Konrad, Schott, & Roth-Nebelsick, 2019, p. 161). Similarly, the cell's cytoplasmic space is so crowded that the movement of proteins and cargo is often influenced by macromolecular 'crowding' effects (Dey & Bhattacherjee, 2018). It is not immediately clear how even a combined mechanistic and nomological explanation could account for these features of the cell.

This aspect of cellular life can perhaps best be captured by an explanatory framework termed 'constraint-based' explanation. Expounding this approach, Sara Green and Nicholaos Jones note that constraint-based explanations essentially try to bring out the "boundaries of the possible biological variation" (Green & Jones, 2016, p. 370).[16] This type of explanation is concerned primarily with the role of mathematical abstractions in biological explanations, a prime example being *topological* explanations of gene/protein networks (Ma, Trusina, El-Samad, Lim, & Tang, 2009). Alan Baker, in exploring the role of mathematics in scientific explanations, has pursued similar directions, but from an ecological constraints standpoint: e.g. "cicadas in ecosystem-type E are limited by biological constraints to periods from 14 to 18 years" (A. Baker, 2009, p. 614).

How exactly constraint-based approaches could be integrated with PM should be the subject of future investigations, but we can at least speculate that pure mathematical generalizations can complement cell biological laws and principles in fruitful ways. Circling back to the running example, consider that an implicit constraint placed on NPL is the very fact that there is a constant downward force of gravity on the pendulum. If the direction or strength of the force of gravity changed every once in a while in a haphazard way, the simple harmonic motion of the pendulum might not have happened at all, or at least looked very different. Moreover, NPL needed to be modified in a fundamental way to still explain the pendulum's motion.

In summary, a framework that distinguishes principles from laws has been proposed based on an example in physics, and the framework further tested against other generalizations in biology.

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[15] While some cells like certain plant cells have sharp edges and corners at a microscopic level (Gorelova, Sprakel, & Weijers, 2021), at a deeper structural level individual cells essentially assume various elliptical shapes (at least at the corners if compressed) due to the biophysics of the plasma membrane.

[16] See also (Ross, 2023) for a proposed taxonomy of these constraints.

Following this, I have discussed ways in which the framework could aid in discovering new generalizations in cell biology and how these could be used together with mechanistic explanations. In the final section, I focus on some similarities and points of divergence between my account and existing frameworks within the scientific laws literature.

7. Contextualizing the principles–laws account

As I began with in the introduction, the immense complexity and sheer scale of the unknowns in cell biology make it quite unlikely that *strict* laws can be uncovered in this domain of inquiry and as such all my references to laws have concerned cp-laws. Generalizations in the form of cp-laws are held by some philosophers to represent extant laws in all the special sciences, not just cell biology (Cartwright, 1999; Elgin, 2017), a view that I subscribe to here. In the running example, NPL can also be thought of as a cp-law because of a number of provisos (e.g. having a massless cord, not losing energy due to friction, having the pendulum move in only two dimensions, and a number of other assumptions; see also (Cartwright, 2002)),[17] but it is not clear without further argument if the PLA should count as a cp-law too. Nevertheless, the question in this final section is whether a template within the cp-laws literature could be found to specifically aid in the *discovery* of new generalizations in cell biology, arguing that it cannot. This may in part be because a main focus of philosophers of scientific laws has been on how the 'space' of non-universal generalizations could be carved up into (usually) non-mutually exclusive categories.

To take a few examples, Gerhard Schurz has proposed to divide cp-laws into 'comparative' vs. 'exclusive' categories (Schurz, 2002). Briefly, "comparative cp-laws require that factors not mentioned in the antecedent or the consequent of the law remain unchanged" whereas "exclusive cp-laws assert the connection between antecedent and consequent only under the condition that certain factors are excluded" (Reutlinger et al., 2021 § 3.1): cf. "ceteris paribus, an increase of gas temperature leads to a (proportional) increase of gas volume (Gay-Lussac's gas law)" (Schurz, 2002, p. 352) vs. "ceteris paribus, planets have elliptical orbits" (p. 352). Exclusive cp-laws are themselves then divided into definite, indefinite and normic subcategories. A definite exclusive cp-law "specifies the disturbing factors which are excluded (or the validity conditions which are required) in the antecedent of the law" (Reutlinger et al., 2021 § 3.2). Schurz later proposed to distinguish all cp-laws from '*ceteris rectis*' laws (other things being *right*) (Schurz, 2014): "the difference concerns the degree of invariance of the causal relation" set out in the law and our knowledge about it (p. 1815). Alternatively, Luke Fenton-Glynn has proposed to distinguish between cp and '*minutis rectis*' laws (the *details* being right) (Fenton-Glynn, 2016), where the latter "admits of exceptions that aren't explained by the non-satisfaction of a cp clause" (p. 275). By these accounts, NPL could be considered a *ceteris rectis* law, but it is not immediately clear which category would best fit the PLA.

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[17] In a different take, Barry Ward, writing about a version of the Newtonian pendulum law, held that "the law is derived on the assumption that the only forces operative on the bob are the tension of the string and the Earth's surface gravitational force, mg, and this is well known […] The CP clause is trivialized, since the content is secured by these implicit but strict background conditions" (Ward, 2007, p. 361).

In all, the cp-laws literature has shed light on the various ways that a generalization can be non-universal: “due to idealizations, by expressing statistical regularities and probability distributions over initial conditions, by drawing on the notion of normality, by being sensitive to changes in initial and background conditions, and so on” (Reutlinger et al., 2021 § 10). To be sure, mapping how non-universal generalizations could be carved out into different categories is important to understanding how these generalizations could figure in explanations. However, I think more amenable to this paper’s goal of encouraging the discovery of laws in cell biology was to step away from looking at *all possible* non-universal generalizations and to focus on some specific non-universal generalizations individually (i.e. NPL and the PLA): How specific or general were they? Could they be expressed in formal terms? Were they more speculative or deduced from known/tested facts? These questions I believe allowed this paper to provide a simpler way of carving out the space of non-universal generalizations—a system more in line with the goal of generalization discovery—compared to the existing granular ontology that focuses mainly on cp-laws alone.

8. Conclusions

Starting off the discussion with two generalizations in physics that could explain aspects of a pendulum’s movement, i.e. a derivation of Newton’s second law of motion (that I referred to as Newton’s pendulum law) and the principle of least action, a framework for non-universal generalizations was then outlined in which a given cp-law could potentially be paired with one or more less-constrained ‘principles’. Paired principles and cp-laws (where one form of generalization *could* be derived or inspired from the other, but not necessarily) can be linked on a two-dimensional space formed by two criteria: the first is the broadness of scope, and the second, a corollary of the first, is the precision of predictions, both relative to an actual or hypothetical corresponding generalization. Compared to cp-laws, principles can be characterized as typically applying to a wider range of phenomena and distinct systems to be explained (and hence can be said to be ‘multidomain’ generalizations). As a consequence, principles may afford less precise predictions across the cases where they could potentially apply because they may be stated in more general, qualitative and imprecise terms. The principles–laws concept makes for a more lenient approach for what could count as a lawlike generalization and can encourage the discovery of novel generalizations in cell biology and their inclusion in PM explanations. But the concept also does something more: it brings into dialogue different forms of scientifically-relevant generalizations in a simple framework, and can be a stepping stone toward cell biological explanations that not only provide descriptive accounts, but can also help to answer *why* things may be the way they are.

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