Processes and Problems That May Define the New BioMathematics Field

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Abstract. Historically, mathematics developed hand-in-hand with the physical sciences. While biological processes must obey the laws of physics, biology is not reducible to physics (otherwise we would not be able to distinguish one set of phenomena from the other!), and therefore mathematics that have been adequate for describing physical processes are often inadequate to describe biological ones. In consequence, I argue that the a new phase of scientific development is required in which mathematicians turn to biological processes for inspiration in creating novel forms of mathematics appropriate to describe biological functions in a more useful manner than has been done so far. Many the kinds of problems that seem to remain unaddressable at present involve forms of mathematics that currently have competing assumptions. For example, biologists need to describe phenomena that involve discrete and continuous functions simultaneously (control of metabolism through binding of single molecules to unique gene promoters; the statistical description of continuously varying molecular complexes); they need to handle spatial descriptors (geometry?) at the same time as kinetic data (calculus?) to explain developmental processes; they need to explain how scalar processes (random diffusion) gave rise to vectorial ones (facilitated transport). These, and other hybrid problems described in this paper, suggest that a fertile field of enquiry exists for mathematicians interested in developing new forms of biologically-inspired mathematics. I predict the result of the development of this new field of biologically-inspired mathematics will be as fundamentally revolutionary as physics-inspired mathematics was during the original Scientific Revolution.

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I once took a graduate course on the history of physics that focused on the work of Laplace. The professor teaching the course pointed out a phenomenon that he found very surprising. Laplace, he noted, had a very checkered career. He seemed to work on physics or astronomy for several years and then drop whatever he was working on and switch to studies of pure mathematics for a few years; then suddenly, he would switch back to physics or astronomy, and so forth for decades (Gillispie, 2000).

The professor could think of no good reason for such erratic behavior. I, however, suggested a very simple explanation. I believe that Laplace was such a productive scientist *and* mathematician because the two fields were completely integrated in his mind. He derived his mathematical problems from his astronomical and physical researches and his astronomical and physical problems from the regions in which existing mathematical methods failed. So in practice, what Laplace did was to study a physical process, develop a model for the behavior of the system that would, in turn, yield a set of equations describing the model. More often than not, because Laplace focused on processes that had no adequate physical explanation, he would find that it was impossible to solve the equations needed to model the system. Being a first-rate mathematician, he would therefore refocus his efforts on deriving from first principles the new methods necessary to solve the sets of equations he had invented. This effort often took him several years. Once he had satisfactorily set that new area of mathematics to rights, he would go back to his astronomical or physical studies, apply his new mathematical insights to his models, and see what kinds of new problems these revealed.

I recount this story about understanding Laplace's methods because it is important in devising a new field of biomathematics that those undertaking the work understand that, historically, both science and mathematics have provided *each other* with fruitful problems and methods. Laplace was not a mathematical physicist or a physical mathematician – he was both, simultaneously. I understand full well that this integral (or back-and-forth) view of the relations between science and mathematics is quite at odds with the dominant (and long-outmoded) Comteian positivistic philosophy of science that still predominates among scientist and mathematicians today. Positivism explicitly posits the notion that mathematics drives progress in the rest of science so that it is possible to rank-order the scientific reliability of a field on the degree to which it has become mathematized. The increase in "positive knowledge" is always from mathematics through physics to the "softer" sciences.

There are two errors in this positivistic philosophy. One is that even pseudoscience can be expressed in equations, this process making the pseudoscience no more "true" than it was when expressed only in words. The other error is to mistake the purpose of mathematization as being primarily a means of validating scientific research. To the contrary, I believe that mathematics can provide novel tools for exploring scientific problems. But that said, I also believe that existing mathematics does not contain all the possible tools that scientists may need. Like Laplace, present-day mathematicians are likely to find fascinating and valuable mathematical problems by learning enough biology to understand where existing mathematical tools fail. From this perspective, mathematics is useful to any given science only to the extent to which it is appropriate to addressing the problems posed by that science. Simply mathematizing biology using existing methods does not, in fact, add anything to our understanding of biology unless the mathematics illuminates points that non-mathematical statements of the same models or theories cannot address. Unfortunately, many scientists make their models conform to existing mathematical methods rather than doing what Laplace did, which is to devise an appropriate model and then invent the mathematics to describe it. Thus, historically, "mathematical biology" has not yielded many deep insights.

My studies of the history of science suggest a second reason that mathematics has not been as useful in the biological sciences as in the physical sciences. Scientists tend to ascribe the power of physical sciences to their mathematization, but I would argue that the real power has come from the ability of astronomers and physicists to define their problems accurately and precisely enough for mathematical methods to be valuable. My emphasis here is on problem finding and defining. Historically, chemists, biochemists, biologists, and social scientists have rarely been able to define their problems with the precision and accuracy of the physicist or astronomer, making the mathematical investigation of their relatively "fuzzy" problems difficult. Thus, one reason for the lack of mathematics in biology is that the lack of well-defined problems has made the field less amenable to mathematization than, say, physics. Recognizing that categories in non-physical systems are often "fuzzy" is, in fact, what led Zadeh to invent his theory of "fuzzy sets", a major advance for both mathematics and modeling in biological and social sciences (Zadeh, 1996). I would therefore argue that the degree to which we can define our biological problems accurately and precisely enough to intrigue mathematicians will determine whether we make progress in developing biomathematics.

The third reason that biology has so far failed to benefit from mathematization to the degree that physics and astronomy have, is that the mathematics that is used to describe physics and astronomy developed hand-in-hand with those sciences but has not developed hand in hand with biological problems. Laplace is hardly unique in having had hands in both mathematics and physics simultaneously – think Descartes, Leibnitz, Lagrange, Fourier, Poincare, etc. Unfortunately, the mathematical methods developed to model physical processes do not (in general) illuminate biological problems. Biology is not chemistry which is not physics. Simple hierarchical reasoning states that we can recognize a new level of organization when the principles, properties and models that worked for the previous level of organization can be ignored (Weiss, 1971). Chemistry becomes chemistry and not physics at the point where we can ignore the physical properties of the components carrying out the chemistry. We don't need an understanding of nuclear physics to describe the kinetics of a chemical reaction; we don't need to know the movements of every molecule in a gas to measure its temperature or volume; we don't need an understanding of electron shells to explain how DNA encodes genetic information. Similarly, biology becomes biology and not chemistry when we can ignore the chemical properties of the components carrying out the biology. For example, Mendelian genetics was invented without any concept of the structure of a gene, let alone what macromolecular structure encoded genetic information. Darwinian evolution by survival of the fittest does not rely upon any chemistry at all! This is not to say that biological systems are not comprised of chemicals or to deny that they obey the laws of physics, but rather to make the point that biological systems are recognizably biological because they have organizational properties that allow them to carry out processes that cannot be accounted for purely on the basis of the physics and chemistry of their individual components. So what we need is a new mathematics and a new form of computing that permits us to model the emergence of new properties resulting in the carrying out of novel processes as a result of innovative forms of organization within complex systems. Or, put more

simply, a mathematics appropriate to biology must be motivated by problems that are biological in their origins and nature, just as a mathematics appropriate to physics was physical in its origin and nature.

In order, therefore, to develop a new field of biomathematics, I would therefore hope that we will behave as a community as Laplace and his colleagues did, by going back and forth between the science and the mathematics, letting each inform the other. Biology has much to contribute to mathematics, especially to the development of new forms of mathematics appropriate to solving the kinds of problems that make biology different than physics or astronomy. And biologically-inspired mathematics can be expected to return to biology the same kinds of gifts that physics-inspired mathematics returned to physics. Indeed, not until we abandon the Comteian idea that mathematics should *drive* science will biology benefit as it should from mathematics. I maintain that reversing the equation and permitting biology to *drive* the mathematics (at least half of the time!) may yield us new insights as important as those generated by Laplace and the other physicist-mathematicians who founded their fields. Moreover, it may revolutionize mathematics itself, just as the focus on physical problems motivated many of the great mathematicians of the past.

So what kinds of well-defined biological problems exist that seem not to be amenable to current mathematical approaches, or have simply been overlooked by mathematicians who already have the kinds of novel approaches that would open up these biological areas to formal analysis? I and my collaborators and colleagues have been struggling with five such areas, all of which are general enough to have broad implications both in and beyond biology and are therefore potentially worth the effort of a mathematician to explore. All of them, in one way or another, share the common feature that the systems that need to be described combine some type of continuous function with some type of discontinuous function and some add the fillips of vectorial and geometrical aspects as well. The mathematical challenge is how to analyze biological problems that currently exist in two or more of these (as far as I know) essentially unrelated domains of mathematics.

My first problem concerns the modeling of a cell as a dynamic process. The cell itself is a discrete object yet the flow of materials in, out, and through a cell is continuous. Moreover, if one asks what defines the cell at any given time, the details of this description will differ at any other time point. For example, when a cell replicates, it breaks down its Golgi apparatus, its actin fibers, and various other cell organelles, into the molecular constituents from which they are assembled. These molecular constituents are randomly distributed into the two daughter cells. Both of the resulting cells are still cells of the same species as the parent cell, yet neither has exactly the same number or even exactly the same proportion of cellular constituents as the parent cell or as each other. So clearly there is variance in the absolute numbers and in the proportions of the constituents of a cell within which the cell can still function as a cell. Moreover, the rates at which these constituents turn over, are replenished and excreted also vary from cell to cell and from time point to time point. Now, this variance is clearly open to experimental manipulation. One can dehydrate cells and find out how little or how much water they require or can sustain and continue to live. One can destroy particular cellular constituents, or block particular

receptors or transporters, and see how these modifications affect the proportions of other cellular constituents in relation to whether, and how, the cell continues to function. So we can obtain plenty of quantitative data. But what do these data mean in terms of what the interactive variances in constituents can be within a living system? The problem becomes even more complicated when we start playing with cellular structures and macromolecules. While there are so many molecules of water or glucose or ATP in a cell that it might be acceptable to model cellular dehydration as a continuous function, one cannot vary the numbers of actin fibrils, Golgi apparatus, mitochondria, chloroplast, ribosomes, nucleoli, centrosomes, chromosomes, etc. as continuous functions. These are very discrete variables, with variances that are measured in discrete units. The mathematical problem therefore becomes one of finding means to utilize all of this information – both continuous and discrete – in an integrated model that lets us understand what are the limits of variance, and therefore the limits of life, for a functioning cell.

The posing of the question of what constitutes a cell in this way has caused me to become interested in set theory as a possible basis of a new biological mathematics. But the current state of set theory (at least as available to a novice such as myself) seems inadequate in two fundamental ways. First, cells are autopoetic – they form themselves. Indeed, evolutionary theory asserts that cells evolved from primordial aggregates of self-organizing compounds built from even simpler interactive modules, back to the primordial soup. Sets, at least as they exist in mathematical forms, are not autopoetic. There is always a "god" – the mathematician – who defines the criteria for what is a set and what is not. What would happen if one did not have the mathematician "god" to define sets, but created a system of definitions that would permit sets to form autopoetically? This is, in a sense, what complexity theory is about (e.g., Kauffmann, 1993), but complexity theory does not incorporate most of the useful features of set theory. Could a mathematics that described autopoetic sets through complexity-like theory exist? Might it shed light on the evolution of the "sets" we call "cellular life" by permitting us to describe continuous functions that produce rules that then limit the entry and exit of possible components of the set and that can undergo transformations (metabolism) within the set? After all, this *is* what cells do, so why cannot there be a mathematics that describes what nature can already do?

The second way in which modern set theory (again in my limited experience) seems to fail to inform biological problems is because biological sets have the variance property I described above. Any given cell must have chromosomes, but their number can vary (as they do in cancers and parthenogenotes) and still be viable; they can have many ribosomes and mitochondria or few and still live; they can accumulate certain amounts of toxins or lose a certain amount of key ions and still function; etc. So in addition to inventing autopoetic sets, is it possible to invent sets that are not defined by specific numbers of constituents, but by variances within which all of these constituents must exist. A bacterial cell that becomes dehydrated may die, or it may sporulate. How can some form of set theory be devised that models the process of switching between stable states when certain variances are exceeded? What, in general, does such a state-sensitive, mathematical set look like? How does it behave? What properties does it have that sets, as currently defined in mathematics, do not?

How might these new set properties inform living systems and perhaps even our understanding of social processes, supply chains, and other useful functions?

So one thing that is needed in our new biomathematics are ways to model self-emergent sets (origins of first cells; self-assembly of viruses, etc.) But these self-emergent sets would seem to need the ability to carry out functions (selecting/rejecting among possible components; minimizing what a physicist thinks of as free energy; etc). So one possible focus of a new biomathematics would be to invent an appropriate theory of self-emergent sets that can carry out functions within variances. Such a set theory would preferably incorporate the work that has been done on understanding hierarchical systems, emergent properties, complexity theory and so forth. Such a mathematics would therefore be extrordinarily integrative, a point to which I shall return below.

A biological problem related to their set-like properties is that their organization strictly limits their variance through the formation of modules in a manner that requires novel approaches to probability theory. Imagine a clueless, blind "watchmaker" of the sort that Richard Dawkins likes to put in charge of evolutionary processes. But let this watchmaker carry out a process first investigated by Herb Simon in one of his little-known and under-appreciated essays on evolutionary processes (Simon, 1981). Combining Dawkins's and Simon's watchmakers produces the following scenario that I believe exemplifies one of the critical problems that needs to be addressed in the origins and evolution of life. I imagine two watchmakers, the first of which must randomly assemble 25 parts in order to put together a "watch". This completely ignorant watchmaker must explore every possible combination of the 25 parts he has in front of him, which is to say 25!, or about 1.55×10^{25} possibilities! If it took a single minute for each of these possibilities to be explored, our watchmaker would not succeed in making even a single watch within the lifetime of the universe! Moreover, because he's just a random assembler and cannot learn from experience, he has to explore all these possibilities each and every time he tries to build a watch! Clearly, such an entity working by such a process would, for all intents and purposes, never succeed, making *de novo* evolution of life virtually impossible.

But what Simon first recognized, and I have developed (Root-Bernstein and Dillon 1997; Hunding, et al., 2006), is that an equally dumb, blind and random watchmaker who uses stable modules built on the principle of molecular complementarity would succeed, and astoundingly quickly! Simon's model assumed that the watchmakers knew how to make a watch (a clearly un-biological assumption), from which he derived the following equation: The time required for the evolution of a complex form from simple elements depends critically on the number and distribution of potential intermediate stable forms. In particular, if there exists a hierarchy of potentially stable 'sub-assemblies', with about the same span, s, [i.e., the number of parts or components required to form each stable subunit] at each level of the hierarchy, then the probability that a subassembly process will be completed within any given time, T, can be expected to be about $1/(1 - p)^s$, where p is the probability that the assembly process will be interrupted during time T. Clearly the less stable each step is in the assembly (i.e., the greater p is) and the larger the number of components that must be assembled to achieve a complete assembly (s), the less probable any particular

assemblage is to evolve. Conversely, the more stable each step in assembly is (i.e., the smaller p gets) and the smaller the number of components required to produce a completed assembly (s), the greater the probability an assemblage is to evolve, (Simon, 1981, p. 203). The implication of Simon's model is that we should therefore expect evolution to be characterized by the selection of semi-stable modules arranged in a hierarchical fashion that minimizes wasted time, effort and resources. This is precisely what we do see. But Simon's model is not an accurate portrayal of the biological problem.

The problem with Simon's model is that evolutionary watchmakers do not know how to make a watch and must search randomly for stable modules. Fortunately, molecular complementarity between compounds naturally forms such stable modules, so these come into existence in just the kind of random fashion that needs to be assumed. So once again assume our modular watchmaker needs to make a watch from 25 pieces, but also assume that she makes her watches in stable sets of five parts. Assume also that all other combinations of the five parts are unstable. Stable five-element modules could be built by exploring only 5! possibilities, or just 120 combinations. Then our modular watchmaker would need to explore randomly the 5! possible combinations of these five modules, or another 120 possibilities. Altogether, the modular watchmaker explores only 720 possible combinations, which, if they could be explored at one possibility per minute, would yield a watch every two hours. Quite a difference from 1.55×10^{25} minutes to explore the original 25! Combinations! The impossible becomes highly likely (Root-Bernstein, 2011)!

Now obviously, the advantage of modularity is not as great as I have just stated for a real, molecularly complementary system. In the first place, stable modules might not result from any given set of five components so that our modular watchmaker may have to explore more sets than I have assumed. Secondly, the specificity of module building is not perfect and some non-functional modules will also likely be stable, confusing final assembly. We can also assume that the proper modules will outcompete the improper ones in producing complete watches, but this may not be the case if improper modules, inefficient at assembly as they may be, so out-number the proper ones as to swamp them. Finally, there is no biological reason to assume that stable modules have five components – the number could vary from two or three to two or three dozen per module. And this is exactly the point at which current probability theory fails. How do I model the kind of system I have just propounded in which modular sets are formed in a chemically reversible manner (describable as a continuous function), may contain variable numbers of components, and compete with each other in a probabilistic scenario? To solve this problem requires a mathematics that can simultaneously deal with continuous variations in chemical kinetics yet yields information about modular probabilities. Again, such a mathematics must exist since Nature already performs these functions, but what does that mathematics look like?

The importance of being able to address this modularity-probability problem can be seen by the fact that the formation of complementary module building within complex systems can prune out huge numbers of possibilities at each step of hierarchical assembly. In general, the greater the number of pieces, and the more modular steps

involved in the process, the more efficient the process becomes. Given the mathematics of these probabilities, there must be some optimal number of pieces per module, and an optimal number of modules per functional unit, and an optimal stability that must be attained. All of these variables must be optimized so as to maximize the rate at which functional modules are generated while minimizing the number of possibilities that must be explored. My guess is that nature has already solved this problem, and that the answer is about 3 to 6 elements per module. Analyzing naturally occurring modular hierarchies for rules of optimization might therefore have vast implications for not only understanding the evolution of life, but also, as Simon (1981) notes in his original essay, for the most efficient design of chemical, technological, and even human systems of organization.

Now, I have already alluded above to various biological problems that require working at the interfaces between continuous and what might be called "grainy" functions (e.g., continuous flow of elements through discrete sets; modular probabilities determined by continuous chemical kinetics). One might posit that most of biology consists of sets of problems that exist at this continuous-grainy interface. For example, chemical neurotransmitters (describable as continuous functions) release a single electrical discharge (a discrete function); individual organisms such as bacteria (discrete) can potentially interact more or less strongly with other individuals by means of chemical messages (continuously variable) that determine whether they develop as many individuals or transform themselves into a single super-organism (a biofilm). How can we mathematically handle interactions that may vary continuously but act on a small set of definable individuals? These are not amenable to modeling solely using mathematics that assume continuous or infinitely small functions.

I am particularly interested in these continuous-grainy problems from the perspective of complementarity. Any given species of molecule may interact more or less with any other type of molecule, so that in a very diverse mixture of molecules, a large number of weak interactions may overwhelm a small number of strong ones. The same can be true among sets of cells or in species or social interactions that involve what Csermely has called "weak links" (Csermely, 2006) and I call "complementarity" (Root-Bernstein and Dillon, 1997; Root-Bernstein, 2011). There appears to be no good way to model such systems mathematically at present, yet such systems occur at every level of biological complexity. Again, since biological systems are able to integrate units with continuous functions, surely there is a mathematics that is appropriate for modeling how biological systems do so.

A fourth set of problems are also very intriguing and currently resistant to mathematical analysis. One of the characteristic features of biological systems is that some of their properties involve transformations from scalar to vector quantities. Now we know from tensor calculus that multiplying a scalar and a scalar gives a scalar; and multiplying a scalar times a vector gives a vector; and multiplying a vector times a vector gives a scalar; but how does one get from purely scalar quantities to a vectorial one? How do racemic mixtures of chemicals give rise to chiral handedness in living systems? How does a chemical neurotransmitter signal (scalar diffusion) become a directional electrical signal? How does one evolve from random diffusion (scalar) to facilitated transport systems (vectorial)? How does one evolve from all possible

reactions occurring (primordial soup, laboratory bench) to reaction pathways (vectorial)? In all these cases (and many more) scalar processes result in vectorial ones, yet mathematics generally treats either scalar quantities or vectorial quantities, but not the transformation of scalar to vector. Do we need a new mathematical formalism to do so?

If I might speculate, what we may need is a mathematics in which one assumes that every scalar quantity is actually a pair of inverse vectors that normally cancel each other out, but which, under the appropriate circumstances can be disentangled. For example, in all vectorial systems in biology of which I am aware, an inflow of one kind of molecule is always balanced by an outflow of another; selection for right-handed sugars occurs only where there is concomitant selection for left-handed amino acids. So is it possible that in fact the overall balance of vectors in a biological system is always conserved and that the local manifestation of one half of an inverse vector pair (e.g., inflow) is always balanced by the expression of the opposite vector pair (outflow) in the opposing process? Is there a mathematics that can help us investigate the rules that might govern such processes by integrating vectorial reasoning into the kinds of set thinking postulated above so we can understand how molecules move directionally through cells as a result of metabolic processes, etc.?

My fifth and final type of problem involves the linkage of form and function. Biologists who deal with almost any level of biological organization recognized that natural selection attempts to optimize forms to carry out particular functions, but since novel functions evolve from existing forms, these attempts may be seriously limited. The mathematical challenges involved in attempting to model these form-function interactions are far from trivial. On the one hand, we do not have geometrical tools that can easily model processes such as the complex folding of proteins or chromosomes let alone embryological development. Fractals and other forms of mathematics that generate lovely images that look like the final products of some of these processes (e.g., the branching structure of the bronchioles in the lungs) share nothing of the actual biological processes that give rise to these structures. Thus, our mathematical geometries generally do not illuminate the processes that give rise to biological geometries, but only their outward forms. More importantly, the interesting things about biological forms is not their geometries per se, but the ways in which these forms are reifications of the biochemical processes they carry out or make possible. For example, it has become evident that the folding of chromosomes is a prerequisite to bringing together genes that would otherwise be spatially separated; and that spatial proximity permits the rapid diffusion and control of interactive gene products that would otherwise be unable to interact in a reasonable biological time frame across an unfolded genome (Junier, et al., 2011). But what kind of mathematics would make it possible to model simultaneously the effects of geometry (spatial structure) on continuous functions such as diffusion that in turn regulate on-off gene regulatory switches that act discontinuously or digitally?

Similarly, in developmental biology, we now have excellent data concerning the sets of genes that must be turned on and when they must be activated or inactivated in order to produce proper embryological development (e.g., Carroll, 2005), yet the discrete information generated from combinations of individual genes is expressed as

continuous flow of proteins and hormones that produce gradients which must be reified as organized groupings of cells that have a specific form. So once again, embryology is stymied by the lack of mathematical approaches that can link discrete, continuous and geometrical information simultaneously. Current approaches to these sorts of problems rely on modeling one aspect of the problem with one form of mathematics, switching to another sort of mathematics to address the next aspect, and to a third to describe yet another. All this switching is an indication of how inadequate our mathematical tools are for addressing these problems. Biological systems function at all of these levels simultaneously, so why cannot our mathematics?

I maintain that it is not the biology that is too messy to be modeled in these cases, but the mathematics that is inadequate (because inappropriate) to addressing these sorts of biological problems. This is why we need a new biomathematics! Indeed, I speculate that complementarity might be the solution to both the biological and the mathematical problems here. What we seem to need are the means to describe all of the biological problems listed above as manifestations of a single problem that can be examined using a single, new type of math – a mathematics that treats continuous functions, sets, vectors and geometries within a single formalism or through complementary formalisms that are integratable.

To summarize, my contention is that the reason that biology has failed to develop a viable set of mathematical methods appropriate to solving its problems is that we have relied too long on mathematics developed to model physical problems that are intrinsically different. The assumption has been that biology can be reduced to chemistry and eventually to physics and therefore that a physics-derived mathematics should be sufficient. But hierarchy theory suggests that reductionism can never explain how novel properties and processes emerge. Biological entities have properties that are different from chemical and physical ones and which require novel mathematics to describe. What we need is not, therefore, more detailed physical models of biological systems that can handle greater and greater amounts of detailed data from increasingly find-grained studies of the components of systems, but ways of identifying the biological properties that are as unique to such complex conglomerations as temperature is to a set of molecules. What we lack, in short, is a uniquely evolutionary mathematics that deals with the emergence of organization from non-random selection among replicating variations within complex populations of things. The challenge of a biological mathematics, or biomathematics, is to invent what a mathematics of such emergent properties and organization look like. This new biomathematics will have to integrate at a minimum concepts of continuous mathematics with discrete mathematics, vector formalisms, and geometrical principles. Such a biologically relevant mathematics does not currently exists.

In conclusion, if I may be permitted one final speculation, I feel compelled to ask whether biomathematics may revolutionize mathematics itself by finding novel links between set theory, probability theory, hierarchy theory, network theory, vectorial mathematics etc. leading to a new type of super-mathematics that integrates (hopefully through fundamentally simple insights) disparate areas of both mathematics and the sciences. Since I have to think about biological systems in all of these ways in order to model them, and since biological processes are intrinsically carried out in these

integrated ways by Nature itself, it seems to me logical that real and useful connections must exist within the mathematical formulations of these natural processes as well. Indeed, as I have indicated in passing several times above, I believe that biology is just one of many such sets of emergent properties resulting from spontaneous organization within complex systems. In consequence, the principles that are derived from our studies of biomathematics should apply to an understanding of how novel properties can emerge in complex systems of any kind, whether ecological, social, behavioral, technological or economic. Thus, just as the Scientific Revolution provided us with physics-based mathematics that made possible the investigation of whole new realms of science, so can we expect the development of a biology-based mathematics to have equally far-reaching and revolutionary results.

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