Many-sorted first-order model theory as a conceptual framework for biological and other complex dynamical systems

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Abstract

When complex biological systems (among others) are conceived reductively, they are modeled in set-theoretical hierarchical terms from the bottom up. But the point of view of Systems Biology (SB) is to deal with such systems from the top down. So in this talk I will suggest the use of many-sorted first-order structures with downward nested sorts as an alternative conceptual framework for modeling them. In particular, the notion of a nested substructure allows one to study parts of a structure in isolation from the rest, while the notion of restriction allows one to study a structure relative to some of its parts treated as black boxes. The temporal dimension can be incorporated both as an additional sort and in the indexing of sorts, allowing for both static and dynamic views of a system. Furthermore, one may make use of a quite general theory of recursion on many-sorted first-order structures that includes both discrete and continuous computation. Some possible applications of this model-theoretic approach to SB include excision or substitution of a part as operations on structures, similarity of biological systems via similarity notions for structures, and homeostasis via least fixed point recursion.

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When I was invited by Jim Lynch and Leo Marcus to open this session I did not know what they thought I could contribute, since I have no background at all in biology. Off the top of my head, I threw out some ideas for the possible use of many-sorted models to describe structural aspects of biological systems. But at the same time, I told them that it seemed to me that those ideas could apply equally well to complex dynamical systems in general, including in addition to biological systems such things as mechanical, electronic and even social systems—for example, to cars, the internet, and the federal government. And so I expected that whatever I had to say would be rather superficial biologically; nevertheless, Jim and Leo accepted my proposal on that basis, so here we are. Since then I have spent a good deal of time reading about different parts of biology in order to see whether I could say anything more substantive. In the process I have only been able to

scratch the surface of the subject, but I am left in awe of what an extraordinary body of knowledge is offered to us by biology and how extraordinary biological systems are in and of themselves from the lowest to the highest levels. And I also see that my initial expectations were wrong; there are indeed special things to say about biology within the many-sorted model theoretic framework.

Before getting into the possible use of many-sorted systems as a logically based descriptive framework, let me mention an early attempt to apply logic to biology. That was a sustained effort carried out by the English biologist J. H. Woodger in his 1937 book, *The Axiomatic Method in Biology.* Woodger was very impressed with the logicist program for the foundation of mathematics and took Russell and Whitehead's *Principia Mathematica* as his model. His axiomatic system presumes the language of classes, relations and functions from type theory, and adds ten basic predicates and relations P, T, U, … that are interpreted as "part of", "before in time", "organized unity", "related by a succession of divisions and fusions", "cell", "male", "female", "whole organism", "environment", and "genetic property". Some of these notions apparently apply only to cells, others only to higher organisms. A defined relation R is that for which xRy is interpreted as "y is a descendant of x". All of that is then applied to a formalization of parts of Mendelian genetics. In a later book, *Biology and Language. An introduction to the methodology of the biological sciences including medicine* (1952), Woodger takes as a specific example, Harvey's analysis of the heart as an intermittent muscular blood pump, and shows how Harvey's hypotheses can be formalized in the first-order predicate calculus, and then how one can prove some theorems such as that if x is a heart and x is in action then x is a muscle and x is hard. But to be fair, Woodger's 1952 book contains more advanced formalization of parts of genetics as well as neurology. These efforts were supposed to encourage rigorous thinking in biology, but it appears that they had little impact because the payoff was negligible compared to the effort to master his symbolism. Still, I think that it might be worthwhile to have a fresh look at what Woodger did in modern terms that would allow a great deal of simplification given a moderate amount of sophistication. [Since writing this, I have learned from Barry Smith of his work with others that takes up once again the formal ontological idea underlying

Woodger's work and reformulates it in light of recent developments in biological science. Cf. the Postscript below.]

By the way, J. H. Woodger had a significant connection with Alfred Tarski. They first met at the 1935 Unity of Science congress in Paris, where among other things, Woodger presented his ideas for the axiomatization of biology. The Unity of Science organization was an offshoot of the Vienna Circle and was dominated by logical positivists like Rudolf Carnap and Otto Neurath, for which the Russell and Whitehead *Principia* was a kind of bible, the *ne plus ultra* of logicism. As testimony to that, it was Bertrand Russell who was invited to give the opening lecture to the congress. At any rate, after Tarski heard Woodger's lecture there he strongly encouraged him in his project to axiomatize biology on the basis of the theory of types. And a few years later he contributed an appendix to Woodger's book with a simplification of the logic of the relations "part of" and "before in time". They became close friends and great boosters of each other. Some time in the early 1950s, Woodger proposed to gather and translate a number of Tarski's articles from the 1930s, especially the *Wahrheitsbegriff*; the collection was eventually published in 1956 under the title, *Logic, Semantics, Metamathematics* with Woodger as editor. And thereby hangs an interesting side story about why Dana Scott left Tarski and Berkeley to work with Alonzo Church in Princeton; you can find that in our biography of Tarski (Feferman and Ferman 2004).

Now, in thinking about the logicist approach vs. a model-theoretic approach I was reminded of a couple of essays by Jean van Heijenoort that received a certain amount of attention. The first of these was "Logic as Calculus and Logic as Language" (1985, [52]) and the second was "Absolutism and Relativism in Logic" (1985, [60]). They contrast the role of logic and the interpretation of associated formal languages in the work of Frege and Russell on the one hand and that in the work of the early model theorists like Löwenheim and Skolem on the other. The essential difference is that in the Frege–Russell work, the individual variables are supposed to range over *everything*, including both concrete and abstract objects, while in that of the model-theoretic (or set-theoretic) approach, individual variables are taken to range over some specified domain of things, and the main notions are those of a formula being satisfied in the given domain and of

being valid in some or all domains. The puzzling thing for Tarski is that his work especially in the *Wahrheitsbegriff* allies him with the *Principia* crowd, but other work in the 30s also makes him an early adopter of the model-theoretic approach. However, from the 1950s on, Tarski became a leader in espousing the model-theoretic approach.

So now let's return to biological systems: taken as individuals, these are organized combinations of one or more cells that are spatially bounded and genetically programmed to sustain themselves by drawing food, energy and other resources from the environment either in isolation or in combination with related systems. All biological systems whether singly or multiply celled consist of heterogeneous interacting materials, and it is the heterogeneity that suggests the use of many-sorted model theory for the description of their structure. There are two common perspectives on them, *bottom-up* or *top-down*. When they are considered reductively, the viewpoint is bottom-up, i.e. it starts from the level of cells or even more basic genetic and biochemical entities and processes. But the talk in terms of systems suggests a top-down approach instead, regarding them as consisting of interacting subsystems that may in turn consist of interacting subsystems, and so on.[1] The view from many-sorted logics that I will propose starts with a top-down approach but admits a bottom-up approach as well as a *side-by-side* approach. This last is in accord with the view of biological organisms as comprising a number of distinct systems that carry on concurrent processes.

Let's start with the biological system of *Homo sapiens* as both a familiar and paradigmatic example, at least for higher organisms in the animal kingdom. We begin with the gross anatomy of this system and only later take up its physiology, i.e. how it varies with time. The human body consists of a number of systems: the musculoskeletal, nervous, respiratory, digestive, cardiovascular, endocrine, etc., that are interrelated in certain ways. Each of these in turn consists of a number of subsystems, some of which we think of as objects or organs but shall also be called systems; for example the musculoskeletal system consists of the skeleton, ligaments, tendons, cartilage, and muscles, connected in various ways.   The skeleton in turn consists of various subsystems,

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[1] The article Fisher, Piterman and Vardi (2008) compares levels of abstractions in biology and in computer science. Its title suggests a bottom up approach but I read the article itself as espousing a bottom-down approach.

the cranial, neck, thoracic, spinal, etc. So I suggest we consider systems as consisting of subsystems which in turn may consist of subsystems and so on, and at each level, the subsystems are interrelated or interconnected in different ways. How can such systems be viewed in terms of many-sorted models? The latter are usually described as structures $M = (M_1,\ldots,M_n, R_1,\ldots,R_m, f_1,..,f_j, a_1,\ldots,a_k)$ consisting of a number of basic domains or *sorts of objects*, together with relations, functions, and designated individuals of specified *arities*. Geometry provides a paradigmatic example; we have three sorts of objects, points, lines and planes and three incidence relations (point on a line, point in a plane, line in a plane) and the equality relations in each sort. The signature of a many-sorted relational structure $M = (M_1,\ldots,M_n, \ldots)$ is given by a list $s_1,\ldots,s_n$ of the basic sorts, and for each relation a specification of the sorts that it relates, for each function a specification of the sorts on which it operates and in which its values lie, and for each individual the sorts to which it belongs. Evidently, if we are to apply this to systems as described above, we need to refine this so that in addition to the sorts we have a *subsort* relation, that serves to classify sorts at different levels. And at each level we will say *what that sort consists of*; these will not necessarily be objects in the usual sense of the word, but rather *substructures*, though when we come to the bottom level "sort-wise," we may finally speak of those constituents as objects. For example, pursuing the human body down to the bones of the hand, say, we would say that that consists of the carpal bones, the metacarpal bones, the phalanges (finger bones), etc.

Coming back to logical and mathematical many-sorted structures, among further examples we have typed hierarchies, either of sets or of functions or both. Those are what one would take from a bottom-up point of view, but we can also "flatten" them out, i.e. with the types conceived side-by-side. Ramified typed hierarchies provide an example of many-sorted structures with a natural subsort relation. An algebraic example is provided by vector spaces, where we have two basic sorts, vectors and scalars. As a special case for Galois theory, we can consider fields as vector spaces over subfields, thus scalars become a subsort of vectors. And in various work that I have done on forms of constructive and semi-constructive mathematics, it has been convenient to consider universes of objects that include (possibly partial) operations and classes as two basic

subsorts, while allowing operations to apply to individuals at large, including operations and classes among others.

Note that there are two notions of *model* going on in the present discussion. The one coming from model theory in logic and mathematics is that of a *specific structure* consisting of specific objects with specific relations, e.g. the points, lines and planes in Euclidean space together with the standard incidence relations. The other is the general idea of a *theoretical model* of some part of reality. The important difference is that the latter is necessarily abstract and limited in scope, but always subject to refinement. *There is no such thing as a complete model*; rather, what the scope of a theoretical model is taken to be is determined by a variety of aims, be they scientific, pedagogical or practical. Each such determines a collection of sorts and subsort relation.

For biological systems, let's return to the example of the human body and expand the gross anatomical model indicated above. And let's now take as top sorts: cells, tissues, organs, systems and non-organic constituents. The reason for including cells as a top sort is that cells may be of many sorts: bone marrow cells, muscle cells, blood cells, neurons, etc. and when we come to describing the constituents of organs and organ systems, we soon come to specifying one sort or another of them. Similarly, tissues are taken as a top sort because they have many sorts that figure in the descriptions of organs and organ systems: epithelial (further subdivided as simple or stratified), connective (further stratified as skin, cartilage, tendons, adipose, etc.), etc. Among various sorts of organs we have the brain, the heart, the lungs, the stomach, the kidney, etc. Some of the organs constitute a separate sort such as glands, including the thyroid gland, the pituitary gland, the hypothalamus, the pancreas, etc. Note that some sorts may fall under several higher sorts, for example muscle cells both fall under cells and under muscle tissue; muscle tissue in turn is part of various organs such as the heart and the stomach, while those are part of different major systems, the circulatory and digestive system, respectively. The non-organic components include water, oxygen and other gases, and minerals such as bone calcium, etc. (I'm ignoring organisms such as bacteria that take the human body and higher organisms in general as a host). There is no complete enumeration of the sorts,

subsorts, subsubsorts, etc. Instead, as already stated, any collection of these may be isolated to concentrate on for an explanation or study of their structure and function.

Given a nested many-sorted structure M with a specified signature σ—including the subsort relation—by a *restriction* of M is simply meant the same structure considered just with respect to a signature σ′, a subset of σ with the subsort relation restricted to it. This corresponds to a shift in perspective or choice of concentration to explain structure and function as far as possible independently of other sorts. One way this is done is to consider a specific organ as a black box, i.e. to suppress all the sorts of objects that are specific to its constitution. That then gets conceived as a simple object given only with certain input and output relations. If we replace that organ by another with the same use of inputs and production of outputs, the structure *over it* hasn't changed. This is illustrated for example by transplantation of a kidney in place of a failing one, or replacement of a defective heart by an artificial heart. In the latter case, none of the constituents of the new organ are as before, but their organization may be largely similar. One's appendix may be considered as a black box with no functioning inputs or outputs, so removing it does not change the organism in any significant way.

So far, we have only illustrated the use of sorts and subsorts. But for many-sorted structures, we need also to say what the relations, functions and constants are, so I turn to relations next. Among these, to begin with, one would include the relations of input and output just indicated. To expand on that, in general we have for each constituent a specification of what part admits input such as information or fuel from the environment, and what part serves as output. And then the relation has to tell us what serves as input and what happens to the output. For the human body as a whole, the inputs are provided by the eyes, ears, nose, mouth, etc. and the outputs again the nose and mouth, and of course the urinary tract and the rectum. For the heart, grossly speaking, the inputs are the veins and the outputs are the arteries, and for the stomach the input is the esophagus and the output is the small intestine. Then for each of these we would say what comes into the input and what goes out, for example for the heart it is oxygenated blood that goes out and "used" blood that returns as input. Finally, we need to have a specification of the genitalia and their inputs and outputs according to gender.

Besides the input/output relations, other relations to consider could be those of connectedness—for example as specified in the song "Dem bones"—and of contiguity, such as that of the liver and pancreas to the stomach. In addition we have constituent relations of a three dimensional topological character such as that of having a boundary and being interior to something else. Boundaries are in general "thick", as for example the concentric layers of skin: the epidermis, the dermis and the subcutaneous layer, in turn consisting of fatty tissue, blood vessels and nerves. In addition to these, we might further add relations of number and shape, for example, number of teeth and which kind of each, and shape of the jaw, as well as relations of orientation, such as right side-left side, and anterior-posterior. [See the Postscript for systematic work on the one hand by Smith and Varzi on applicable topological relations, and on anatomical relations in human beings under the FMA project on the other hand.]

By a *sortal-relational signature* σ I mean a specification of sorts, subsorts, their constituents and the arity of the relations between them. So far, schematically, relative to such a σ the anatomy of each spatio-temporally located human being is treated as an individual many-sorted structure M of signature σ. But when we speak of the anatomy of the human body, male or female, we have in mind some sort of *generic* structure of that kind. How could that be explained in terms of structures? One option seems to me to consider the class **H** of all adult human beings M of a given gender currently living (or living since a time when it had emerged as a clearly separate species), and then take *the theory of* **H**, i.e. the set of all first-order properties that hold of each M in **H**. This presumes that we have an idea in advance of what counts as a human being and what doesn't, and that sets aside anomalous cases such as those of conjoined twins or six-fingered people. As an alternative, it is conceivable one could apply the idea of model-theoretic forcing (due to Robinson 1971) in order to explain which are the generic structures, and then consider only the theory of such.

More generally, in principle we could talk in many-sorted model theoretic terms about the anatomy of any given species, and we could compare different species as long as they have a non-trivial sortal-relational sub signature in common. Presumably, that could be done for species such as *Homo erectus* from which *Homo sapiens* has descended, as well

as species more generally in the *Hominidae* family such as chimpanzees, gorillas, and so on, or even all mammals. A basic distinction made in evolutionary theory is between traits of a pair of species that are *homologous*, i.e. occur in a common ancestor and those that are simply *analogous*, i.e. are similar but not homologous, such as the usual example of the wings of birds and the wings of bats. I presume that evolutionary biologists start with sets of analogous traits in order to propose lines of descent and once those are firmed up one can speak of which of those traits are homologous along different sub-lines. In any case, the language of many-sorted structures can be used to explain which traits of two different species, S_1 and S_2, of signatures σ_1 and σ_2, resp. are held in common in one of several possible ways. Given structures M_1 and M_2 of these signatures, resp., we can compare M_1 and M_2 along their common signature σ, the intersection of σ_1 and σ_2 by considering the restrictions of both to σ. The strongest similarity relation is simply that of *isomorphism* of the restrictions $M_1|\sigma$ with $M_2|\sigma$. But all we are concerned with is the question of *which properties* are shared in common, and for that the strongest relation is that of *elementary equivalence* of $M_1|\sigma$ and $M_2|\sigma$. One way to establish that in part for properties of relatively low complexity would be to make use of the relations of bisimilarity up to, say, level 2 or 3. Of course, all of this is merely by way of suggestion since I don't have any specific illustrations to offer.

Let's turn now to the expansion of sortal signatures to include functions and constants, beginning with the latter. I think gender, suitably construed, e.g. by specification of the genitalia, should be taken as a basic constant. Otherwise, the choice of constants seems to me to be more or less arbitrary: one speaks of *the* heart, *the* lungs, *the* right kidney, etc. But there are other constants that one naturally thinks of such as age, height, weight, blood pressure, temperature, heart rate, white blood cell count, red blood cell count, pH, etc. However, those require that we add the real numbers as a basic sort and also consider each structure as a time-dependent entity.

In biology there is another use of the notion of *constant*, and that is the essential aim of the physiology of living organisms to maintain relatively stable values of such things as temperature and pH that have some sort of ideal value; the process of maintenance of that is called *homeostasis*. And that is usually described in terms of a negative feedback

mechanism such as for a thermostat, i.e. there is supposed to be a built-in means of sensing the biological constant to be regulated, and a mechanism for diminishing the difference between its actual value and its ideal value at any given time. As a mathematician, it is natural in this respect to think of finding fixed points of a given function, namely of the biological constant as a function of time, while as a logician, one thinks of things like the recursion-theoretic fixed point theorems. So it may be rather far fetched, but one could think of applying the theory of recursion on arbitrary structures to the description of homeostasis in living organisms (cf. Moschovakis 1984, Feferman 2015).

I have left functions in many-sorted structures for the last. And here we again have a double use of terminology, the mathematical notion of function and the biological notion of physiological function. They are of course related. For example, we're told that the function of the kidneys is, among other things, to remove waste products of metabolism from the blood. As a function on the structure that can be described as an operation from inputs to outputs—of blood in to urine out—and that can then be refined to a composition of concurrent operations on localized units. Or to come back to Harvey and the heart, its function is to pump blood, and one of the corresponding mathematical functions would be a description of the contraction/relaxation alternation as a wave function of time. Many more examples come to mind but the real interest would be in the details, and as usual, it's the devil that's in them.

To conclude, one may well ask whether there is any genuine use of the model theory of many-sorted structures here. Clearly not. What has been offered is only a suggested use of the language of such structures as a conceptual framework within which to describe various facets of anatomy and physiology. What more could it provide? First of all, in almost all of the main respects, many-sorted model theory has the same results as single-sorted model theory, and can be obtained from the latter by the standard process of unification of domains, replacing each sort by a unary relation and taking their union as the single domain of objects. In particular, one has the completeness of many-sorted logic just as well as for single-sorted logic. In principle, then, that could be used to pursue Woodger's ideal of rigorous reasoning about biological processes. There is one

place in my own work that I found that the standard reduction of many-sorted logic to single-sorted logic could not help is in obtaining certain many-sorted interpolation theorems (cf. Feferman 2008). And that conceivably could be useful in pursuing the question of homology between different species touched on above.

Finally, one possible aspect of modeling the anatomy of biological systems as mathematical structures of one kind or another that has not been touched on here is their in principle finiteness relative, say, to their underlying cellular composition. And that suggests looking for example at the work on complexity classifications over finite structures (cf., e.g., Libkin 2004). Reexamination of that in terms of concurrent computations on many sorts might be a way of explaining the miracle of real-time feasible computation by biological systems.

Postscript. I circulated essentially the preceding as a draft to three people I thought could have useful comments, namely Tom Henzinger, Barry Smith, and Rasmus Winther, and, indeed, to my great appreciation, they brought to my attention a rich body of relevant work that was previously unknown to me. The following gives brief summaries of and references to some of these sources. As I circulate this piece more widely, I would appreciate any further comments and pointers to the literature.

Formal ontology. By *mereology* is meant the theory of the part-whole relation or more precisely the relations of part to whole and part to part within a whole. The ideas go back to early philosophy but its formal study was initiated by Bolzano, Brentano, Husserl and especially Lesniewski (cf. Varzi 2015).[2] Woodger (1937) incorporated mereological concepts in his axiomatic approach to biology in order to give formal specifications of the notions of gamete, zygote, allele, and so on. Smith and Varzi (1999) criticize Woodger's project, saying that it rests on an outdated version of genetic theory, and that it involves a confusion between formal notions (such as *part*) and biological notions (such as *cell*). What they provide in its place is a domain independent rigorous formal theory of the part-whole relation conceived of as holding at some given time, expanded by topological notions and axioms based on the primitive notion of *boundary*. To account for

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[2] Lesniewski was Tarski's doctoral advisor, and among Tarski's works are a few contributions to mereology; cf. Feferman and Feferman (2004).

environments, that is then expanded by a primitive notion of *niche*, and the project as a whole is called *mereotopology*.   The article Smith and Brogaard (2002) then proposes a way to expand this in order to incorporate aspects of time and change.

Part-whole Science. The paper Winther (2011) proposes a kind of *part-whole science*, that introduces the idea of *partitioning frames* that are "multiple cross-cutting manners of abstracting a system into kinds of parts", including mechanistic, structuralist, and historical part-whole explanations in various sciences, including biology as a leading example (for which, cf. also Winther 2006). Two overlapping frames for that are the morphological partitioning frame and the physiological frame. From the point of view of many-sorted model theory as presented here, the former deals with structures having only a sortal-relational structure, while the latter adds time and functions. In biology, the historical frame would be that involving phylogenetic trees. Viewed in many-sorted terms, this would fall under certain comparisons of structures.

Systematic biological and biomedical ontologies. The Foundational Model of Anatomy ontology (FMA) as described in Rosse and Mejino (2008) is a general theory of anatomy that "provides a unifying framework for grasping the nature of the diverse entities that make up the bodily structure of biological organisms [primarily vertebrates] together with the relations that exist among these entities." Associated with the theory is a remarkable computer implementation of FMA for human anatomy with an associated browser that can be found at http://xiphoid.biostr.washington.edu/fma/index.html. This was developed by the Structural Informatics Group at the University of Washington. According to http://sig.biostr.washington.edu/projects/fm/AboutFM.html, "The Foundational Model of Anatomy ontology contains approximately 75,000 classes and over 120,000 terms; over 2.1 million relationship instances from over 168 relationship types link the FMA's classes into a coherent symbolic model. The FMA is one of the largest computer-based knowledge sources in the biomedical sciences." Inspection of the tables in the Appendices of Rosse and Mejino (2008) or of the browser shows that the various entities and relations employed in FMA are tailor-made to fit into the many-sorted relational picture that I propose in the text above.

The aim of the Gene Ontology project (GO), as described in the Gene Ontology Consortium (2001) is " to provide a set of structured vocabularies for specific biological domains that can be used to describe gene products in any organism. This work includes building three extensive ontologies to describe molecular function, biological process, and cellular component, and providing a community database resource that supports the use of these ontologies." I have not looked into this work but apparently GO incorporates functional and temporal elements as well as static structural sorts and relations. Smith (2005) aims to provide a formal axiomatic basis for GO and similar biomedical ontologies; FMA is briefly addressed there too. Smith et al. (2007) describes an ambitious project (the OBO Foundry) that aims to provide a framework for intercommunication of some 60 biomedical ontologies, including GO and FMA.

Some generalities. Henzinger wrote me the following three valuable comments (despite their being "off the cuff") that are worth quoting directly:

"First: many folks have proposed formal languages for (aspects of) systems biology, from Petri nets to process algebras, so your proposal should certainly be taken seriously, and is more foundational than most.

Second: the main issue I have found in interacting with biologists is that they have a very narrow view of what a model or theory or formalism is, mostly limited to approaches from theoretical physics (statistical mechanics). Several prominent systems biologists are former physicists. I have a hard time trying to explain to them even basic notions from our world such as the difference between a language (syntax) and a model (semantics). Injecting more "logic" can only help with this and personally I welcome every contribution by "nonphysicists" to the field.

Third: I believe a key to the debate is to define the scope of applicability of what one is talking about. Many sorted hierarchies will likely be important almost anywhere in biology, but so are time (especially continuous change), space, stochasticity, and possibly more abstract notions such as causality. In particular, hierarchical classifications must cope with dynamic change, e.g., during development, a "generic" cell becomes a cell of "type A" or "type B"." [Indeed.]

For Henzinger's own contributions to computational methods in biology, see http://pub.ist.ac.at/~tah/Publications/bytopic.html#bio, including Fisher and Henzinger (2007) and Fisher, Henzinger, Mateescu, and Piterman (2008).

References

A. Burger et al., eds. (2008), *Anatomy Ontologies for Bioinformatics*, Springer-Verlag, Berlin.

A. B. Feferman and S. Feferman (2004), *Alfred Tarski. Life and Logic*, Cambridge Univ. Press, New York.

S. Feferman (2008), Harmonious logic: Craig's interpolation theorem and its descendants, *Synthese* 164, no.3, 341-357.

S. Feferman (2015), Theses for computation and recursion on concrete and abstract structures, in *Turing's Revolution* (G. Sommaruga and T. Strahm, eds.), Birkhäuser Publishing Co., Basel.

J. Fisher and T. A. Henzinger (2007) Executable cell biology, *Nature Biotechnology* 25, 1239-1249.

J. Fisher, T. A. Henzinger, M. Mateescu and N. Piterman (2008), Bounded asynchrony. Concurrency for modeling cell-cell interactions. *Proc. First International Workshop on Formal Methods in Systems Biology (FMSB)*, Lecture Notes in Computer Science 5054, 17-32.

J. Fisher, N. Piterman, and M. Y. Vardi (2011), The only way is up. On a tower of abstractions for biology, in *17th International Symposium on Formal Methods,* LNCS 6664, 3-11.

Gene Ontology Consortium (2001), Creating the gene ontology resource: design and implementation, *Genome Research*, Aug, 11(8), 1425-1433 (also http://www.ncbi.nlm.nih.gov/pmc/articles/PMC311077/).

L. Libkin (2004), *Elements of Finite Model Theory,* Springer, Berlin.

Y. N. Moschovakis (1984), Abstract recursion as a foundation for the theory of recursive algorithms, in *Computation and Proof Theory* (M. M. Richter, ed.), LNCS 1104, 289-364.

A. Robinson (1971), Forcing in model theory, *Proc. International Congress of Mathematicians, Nice 1970*, vol. 1, 245-250.

C. Rosse and J. L. V. Mejino, Jr. (2008), The foundational model of anatomy ontology, in Burger (2008), 59-117.

B. Smith (2005), The logic of biological classification and the foundations of biomedical ontology, in *Invited Papers from the 10th International Conference in Logic,*

Methodology and Philosophy of Science (Oviedo, 2003), D. Westerstahl, ed., King's College Publications, London, 505-520.

B. Smith, et al. (2007), The OBO Foundry: coordinated evolution of ontologies to support biomedical data integration, *Nature Biotechnology* 25 (11), Nov. 2007, 1251-1255.

B. Smith and B. Brogaard (2002), Quantum mereotopology, *Annals of Mathematics and Artificial Intelligence* 35, 1-9.

B. Smith and A. C. Varzi (1999), The niche, *Nous* 33, no. 2, 198–222.

A.Tarski (1983), *Logic, Semantics, Metamathematics*, J. Corcoran, ed., Hackett Publishing Co., Indianapolis. (1st edn. 1956, translated and edited by J. H. Woodger, Oxford Univ. Press)

J. van Heijenoort (1985), *Selected Essays*, Bibliopolis, Naples.

A. Varzi (2015), Mereology, *The Stanford Encyclopedia of Philosophy*, E. N. Zalta (ed.), http://plato.stanford.edu/archives/fall2015/entries/mereology/>.

R. Winther (2006), Parts and theories in compositional biology, *Biology and Philosophy* 21, 471-499.

R. Winther (2011), Part-whole science, *Synthese* 178, 397-427.

J. H. Woodger (1937), *The Axiomatic Method in Biology*, Cambridge Univ. Press, Cambridge.

J. H. Woodger (1952), *Biology and Language. An introduction to the methodology of the biological sciences including medicine*, Cambridge Univ. Press, Cambridge.