In: IEEE Fourth International Symposium on Plant Growth Modeling, Visualization and Applications. Shanghai China, October 2012. IEEE Press.

Topological object types for morphodynamic modeling languages

Eric Mjolsness Department of Computer Science University of California Irvine, California, USA Email: emj@uci.edu

Abstract-We survey useful ingredients for a new class of mathematical process-modeling languages aimed at spatial and developmental biology. Existing modeling languages for computational systems biology do not fully address the problems of spatial modeling that arise in morphodynamics (the local dynamics of form) and its applications to biological development. We seek to extend the operator algebra semantics approach from our previous "Dynamical Grammars" modeling language, whose most spatial object type is the labelled graph, to encompass more flexible topological objects. Taking clues from current developments in 3D meshing and from topological modeling for biology, illustrated by a plant tissue example, we seek language support for the approximation of lowdimensional CW complexes (which are nontrivial topological spaces, with cardinality of the continuum) and dynamic fields thereon, by finite labelled abstract complexes. Some of the proposed types would be computationally demanding, without further restriction. Restrictions and control of these approximations can be specified by use of "metricated" types. Minimally, such approximations should permit the accurate simulation of spatial diffusion processes.

Keywords-biocomputation, modeling languages, topological object types, process calculi, morphodynamics

I. INTRODUCTION

The operator algebra (OA) approach to process semantics can rationalize modeling languages that support models in developmental biological and more generally morphodynamics, the local dynamics of form. A missing ingredient so far has been the continuum limit of spatial models, an idealization that while not essential [26, 27] is convenient for bridging large gaps in spatial scale. Continuum limits tend to increase the cardinality of all mathematical objects involved, making their analysis a more advanced subject that we can only sketch here. The present work builds on our previous paper [22] where "metricated" object types were defined, and an approach to integrating OA process semantics and object type semantics was initiated. That study uses very different mathematics (borrowed from physics) from most work in foundations of programming languages. To bridge the gap we will try to use natural language in the present exploration. Readers who would like a more formalized context for the present discussion are referred to the previous paper.

Alexandre Cunha Center for Advanced Computing Research California Institute of Technology Pasadena, California, USA Email: cunha@cacr.caltech.edu

II. KEY TYPES FOR MORPHODYNAMICS

The object types essential for morphodynamics fall into two classes: spatially discrete, graph-like types, and spatially continuous types built from topological spaces. (Topological spaces on finite sets are trivial in the sense that T_1 or Hausdorff = T_2 separation axioms imply the discrete topology.) Each class can be given process semantics in terms of an operator algebra; the discrete types and their processes should "approximate" the continuous ones in some norm. Dynamics on discrete types can be computed (approximately) with a hybrid discrete/stochastic/differential equation system solver such as that in Plenum [21]. Often dynamics on continuous types can be approximated by dynamics on discrete types. On the other hand, spatial continua can also pose non-Turing-computable situations such as fields (functions of space) encoding infinite information density or flux.

As an example, it is possible to define a diffusion process on a spatially discrete undirected graph such as a d-dimensional square lattice of dimension N^d , using the graph Laplacian. The result is a coupled set of ordinary differential equations representing the diffusion of a particle or substance on the graph. We may then take a limit of smaller lattice spacing and larger N, keeping the density of points constant, and approach a continuum diffusion process represented by a partial differential equation. Unlike the lattice, the results of the continuum model are rotationally invariant for salient convergent observable quantities such as particle density. In this way, a graph type with real-valued vertex labels may approximate a space that is locally Euclidean, eg. any compact differential manifold, for diffusion processes. Furthermore, the graph-limiting process itself can be defined by local subdivision rules in a graph grammar.

The concept of "salient observable quantities" can be formalized by a sigma-algebra of indicator functions, out of which other observables can be constructed. In Dynamical Grammars and again here for morphodynamic modeling we assume there is a sigma-algebra and a measure for each of our object and parameter types. Furthermore, from level sets of the solutions of a diffusion process (Figure 1) we can define distance metrics on both graph and manifold that agree in the small lattice spacing limit (converging to a



Figure 1. Contours of equal density in steady state solution of diffusion equation from a central point source with global decay, on a 61 square lattice. Countours approach circularity on an intermediate spatial scale, farthest from the lattice spacing and the global boundary conditions.

Euclidean rather than a Manhattan metric). Possession of a sigma-algebra, measure, and generalized distance are the essential features of a "metricated type" [22]. Metric spaces, undirected graphs and differential manifolds are metricated types. Metricated types permit certain quotient types to be formed.

Undirected graphs and manifolds thus in principle form a (discrete, continuous) pair of topological types, which in some cases are related by approximation in the limit as a single real-valued parameter tends towards zero. Every finitedimensional compact manifold can be so approximated; but some graph limits (such as the Sierpinski gasket) have convergent Laplacians but are not manifolds [15, 24]. Also, function spaces on graphs and manifolds can form such approximation pairs. Low-order partial differential equations such as the diffusion equation can be formulated covariantly on a manifold, reformulated as partial differential equations (PDEs) in local patches of Euclidean space, and finally approximated by a system of ODEs on a lattice. Processes that actually change the manifold itself, such as nonuniform growth of various two-dimensional animal tissues [14], the sepals of Antirrhinum (snapdragon) plants [34], or the abstract geometrical Ricci flow, can also be formulated as systems of PDEs and their boundary conditions in the continuum spatial limit. So it suffices to provide the OA semantics for partial differential operators in \mathbb{R}^n .

The OA semantics for partial differential operators in \mathbb{R}^n is provided simply by the *derivative escalation* of Equations 1 and 2 below. A common form for such PDE's is second-order nonlinear PDEs. In that case (all quantities are vectors,

with indices suppressed here)

pa

$$\frac{\partial\varphi(x)}{\partial t} = F[\varphi](x) = F(\varphi(x), \frac{\partial\varphi(x)}{\partial x}, \frac{\partial^2\varphi(x)}{\partial x^2}) \quad (1)$$

receives an operator algebraic expression derived from the Fokker-Planck equation [22], which is a form of the Master Equation for the evolution of probabilities by time-evolution operators in OA semantics:

$$O_{\rm drift} = -\int \int \mathcal{D}\varphi \mathcal{D}\varphi' \ \hat{a}(\varphi)a(\varphi') \\ \left\{ \int dx \ F[\varphi](x) \frac{\delta}{\delta\varphi(x)} \Delta_{\rm Dirac}(\varphi - \varphi') \right\}$$

In this way, partial derivatives are "escalated" to functional derivatives:

$$\underbrace{\partial_x}_{\text{trial derivative}} \longrightarrow \underbrace{\delta/\delta(\partial\varphi/\partial x)}_{\text{functional derivative}}$$
(2)

which occurs also in the variational calculus. For example, x and ∂_x may be monomial basis elements in a Weyl algebra. Thus, PDE's expressible in a Weyl algebra are all given OA semantics compatible with and extending that of Dynamical Grammars. In this way we obtain a probabilistic representation of deterministic PDE dynamics, which can be integrated with stochastic dynamics of pointlike particles in the same topological spaces. To allow for stochastic partial differential equations (SPDEs) takes another kind of OA term [22]. A quantum mechanical interpretation of Weyl algebras is conventional but the Master Equation for p(f(x)) is missing a crucial factor of i in the Schrodinger equation, and hence governs classical probability densities p(...) rather than quantum amplitudes.

For actual morphodynamic modeling we also need the concept of *cell complexes* to explicitly model compartmental structure in biology, to guide the formulation of invariant PDEs, and to eliminate nongeometrical graph limits. Cell compexes also come in discrete and continuous versions. The discrete cell complex will be an abstract cell complex, defined as an "abstract polytope" [19] which is somewhat more general than the usual "abstract simplicial complex" [11, 25] and allows discrete analogs of polyhedral cells other than simplexes. The natural "fields" on such complexes are cochains that map their cells to an abelian group, eg. positions in \mathbb{R}^n under vector addition. The continuous cell complex will be a CW complex, with fields as cochains. The simplest connection between these takes the form of polyhedral cell complexes such as Voronoi diagrams and Delaunay triangulations, along with useful generalizations such as power diagrams, all of which can be considered either as \mathbb{R}^n -valued fields on abstract cell complexes or as particular CW cell complexes. These objects are generally referred to as "meshes" in numerical analysis. Questions of approximation of a continuous cell complex by a discrete one thus become questions of approximation within the class of CW complexes i.e. of a general CW complex by a series of restricted CW complexes, namely meshes. Finite Element Methods (FEM) [13] allow functions to be approximated on such meshes by low order polynomials within each cell, satisfying specified degrees of continuity.

As a reminder, in a CW Complex an open *p*-cell is a topological space, homeomorphic to an open ball of dimension $p \leq n$; it is also called an open cell or in context just a "cell". A CW complex is then a Hausdorff topological space X which is partitioned into a set of open cells, such that each *p*-cell *c* has a continuous function from the closed ball of dimension *p* to X, equal to *c* on the image of the open ball, and equal to a union of lower-dimensional cells of X on the image of the (spherical) boundary of the closed ball [8, 7]. A CW complex can be given a differential structure by embedding in a differentiable manifold [23], in which case the component cells become manifolds with corners [6].

Likewise an abstract polytope is a graded poset (partially ordered set with an integer-valued rank function) whose maximal chains can be interconverted by changing one node at a time, and so that for a rank i - 1 node and a rank i+1 node there are exactly two intermediate rank i nodes [19]. The poset relationship is interpreted as the boundary relationship between cells of neighboring dimensionality in a polyhedron. Brisson [5] observed the navigation property, that maximal cell chains may be interconverted one cell at a time, in computational geometry. This representation was generalized by Cardoze et al. [8] to "cell chains". Giavitto's MGS modeling language [10] adopts an even looser definition of an abstract complex and similarly emphasises the role of cochains in modeling fields on discrete geometric complexes for use in morphogenesis; MGS provides quite a forward-looking formulation of discrete topological modeling for biological applications.

The foregoing construction of CW complexes by partitioning a topological space can be repeated for each cell in the complex, creating a refinement of a coarse complex into a finer one if compatibility is maintained at the boundaries of the coarse cells. This can be done by partitioning coarse cells in the order from lowest dimension to highest, with each *p*-cell partition constrained to be compatible with the (p-1)-cell partitions on its boundary (an essentially elliptic or boundary value problem). Alternatively the partitions of two CW complexes embedded into the same differential manifold can be intersected, provided that they satisfy the transversality constraints of [Munkres 1967]. If the CW complex has a differential structure eg. by embedding into a manifold, then we also need to know where to draw map the new boundaries that partition coarse cells. This is naturally specified by means of level sets of scalar fields that evolve within each cell according to PDE dynamics. A biological application would be the biophysical sepatation process that precedes plant cell division. Computationally, mesh refinement is the subject of much literature eg. [28] on refinment

of Delauney tetrahedral meshes in three dimensions.

As an example, consider the growth equation that governs 1-dimensional displacements of position between times t_1 and t_2 , starting from position x_1 and ending up at position $\Phi(t_2, t_1, x_1)$. Using covariant derivatives ∇_x ,

$$\lim_{t_2 \to t_1} \frac{\partial}{\partial t_2} \nabla_{x_1} \cdot \Phi(t_2, t_1, x_1) = \gamma(t, x_1)$$
(3)

In one dimension, if the history of the growth function $\gamma(v(x_1))$ is known then the solution is:

$$\Phi(t, t_1, x_0) = \int_0^{x_0} \exp[\int_{t_0}^t \gamma(t, x_0) dt] dx$$
(4)

But generally the growth function depaends on the current state of some biophysical fields v(x), so

$$\gamma(t, x_0) = \gamma(v(x_1(t, x_0)))$$

Some components of these fields v may diffuse:

$$\Delta_a^{\text{diffusion}} = \nabla_x \cdot \left[D_a(v(x)) \cdot \nabla_x v_a(x) \right]$$

and some of them might participate in a gene regulation network at each point:

$$\frac{dv_a(x)}{dt} = R_a g(h_a + \sum_b T_{ab} v_b(x)) + \Delta_a^{\text{ext}}(x) - \lambda_a v_a(x)$$
(5)

The result is a general reaction-diffusion-growth model which is Turing-universal at least, since every point has a circuit and local memory attached, and perhaps much more powerful for many initial conditions since more space can be grown arbitrarily and real-valued variables can thereby rise above any noise-induced floor. Biological applications of similar 1D growth and cell division models have been developed for auxin patterning in *Arabidopsis* root [35].

Progress in meshing for n = 3 dimensions is now bringing the approximation of both geometry and dynamics into the realm of practicality, even for challenging models. For example, "Tetgen" [29] is a program that can input a 2D mesh on the surface of a polyhedral object and refine it into a 3D mesh on the interior. (Note that this is the minimal functionality required in the lower-dimension to higher dimension iterative refinement of a CW complex described above.) "Stellar" [16] can improve the numerical quality of a mesh, measured ultimately by the condition number of linear algebra problems required for approximate PDE solution; this capability together with its interpolation capability allows Stellar to dynamically remesh so as to maintain mesh quality as a dynamical system deforms FEM meshed models such as elastic solid or fluid continuous media [32]. "Sundance" [18] and "DOLFIN" [17] explicitly represent function spaces (Banach spaces), meshes containing various polyhedra, and FEM models specified indirectly as variational problems rather than PDEs. These topological types and their dynamics are represented in Sundance and Dolfin by a C++ class library and a Python language interface. Further computational geometry support software that may be useful includes CGAL [33]. Of course, all of these programs are limited to low-dimensional meshes and to CW complexes that can be approximated by such means.

Another way to leverage cell complexes for the formulation of dynamical systems is through the Discrete Exterior Calculus (DEC) [9]. In DEC, PDE-like differential operators are translated into the language of differential forms of degree 1, 2, ... n, and then given meaning on discrete meshes which in the continuum limit of small mesh size agrees with their meaning on differential manifolds. Differential operators are translated into three operators of exterior calculus: d (exterior derivative) for which $d^2 = 0, *$ (Hodge star), and $\delta = \pm * d*$ (codifferential). The Laplacian is expressed as $\Delta = \delta d + d\delta$. Assuming a field φ vanishes quickly enough at infinity, the Hodge decomposition theorem permits φ to be decomposed as $\varphi = d\psi + \delta\theta + \omega$, where $\Delta \omega = 0$. This generalizes the Helmholtz decomposition from 1-form vectors to *p*-forms of any dimension *p*. Advantages of the exterior calculus approach include: automatic restriction to coordinate-invariant dynamics (shared with covariant derivatives); explicit conservation laws for use in symplectic numerical integrators; correct relation of dynamics in compartments and in their boundaries; and natural mapping to discrete cell complexes. Unfortunately we are not aware of 3D DEC software that permits dynamic topology or geometry for the base space on which dynamic fields are defined.

The operations supported by cell complexes go beyond those of manifolds. For example there is "refinement", which requires a level set as input, and "coarsening" which is combinatorial. But all topological types can engender "embedding" function types, so that embedding is a type constructor. Yet more general non-manifold geometries, that may be useful in modeling plant development and/or biomechanics of cytoskeleton during cell division, include *stratified spaces*, in which a topological space is decomposed into manifold "strata" of varying dimensions whose boundary relationships to one another are topologically invariant within each stratum.

Normed function spaces can be used to prove the existence of solutions to complicated PDEs, eg. [31] where diffusion provides the necessary convergence power, and also to prove the convergence of FEM approximations [1] including the advantage of nonuniform meshes for elliptic PDEs.

In summary the key topological types needed for morphodynamics are shown in Table 1. These are to be augmented by function spaces, function type constructors, and a dynamics-defining calculus of differential operators defined on each of the types in Table 1, as indicated (in parentheses). OA semantics for the resulting process expressions can be provided by means of the "derivative escalation" illustrated



Figure 2. Cell complexes are natural computational representations for many biological cells. (a) A horizontal slice of a three dimensional confocal microscope image of live plant cells (in a shoot apical meristem) which form a tightly packed connected network. These epidermal plant cells are naturally approximately convex-polyhedral; cells in other tissues can be decomposed into such shapes. Fluorescent green cell membrane marker highlights the cell walls; cell nuclei are marked with red. (Image courtesy of Marcus Heisler). (b) Automatic image segmentation followed by hand marking of a subset of 13 cells. (c) The marked cells are given a uniform thickness and then meshed with nonuniform sized tetrahedra useful for finite element simulations. The cutaway visualization displays an output mesh created using Tetgen [29]. (d) Closeup of (c), with color coding of the quality of tetrahedra according to a minimum dihedral angle criterion. Mesh quality can be further improved by Stellar [16] while preserving the mesh local feature size. Note that we are able to specify distinct levels of spatial refinement as shown in regions of (c) and (d), where tetrahedra are directed to be much smaller along the walls and particularly the edges of a central cell, than elsewhere.

Table I KEY TOPOLOGICAL TYPES

Discrete	Continuous
(differential operators)	
Lattice	\mathbb{R}^{n}
(finite differences)	(differential operators)
Undirected graph	Differential manifold
(finite differences)	(covariant derivatives;
	exterior calculus)
Abstract complex	CW complex
(discrete exterior	(cell manifold operators;
calculus)	covariant derivatives;
	exterior calculus)

in Equation 2.

The continuing challenge to mathematical analysis raised by Table 1 is to define restrictions on all the continuous topological types, including their differential operator languages (eg. bounding the degree of derivatives, and the information content of fields), that guarantee their reduction to or computable approximation in terms of the corresponding discrete topological types. A potential dividend is the definition of novel dynamical systems *outside* the bounds of practical computation (at least for some initial condition data, as for partial recursive functions) which can nevertheless be explored by mathematical proof and may help to further define the limits of computability, and of what can be proven about it.

III. LANGUAGE FEATURES

We have previously considered *sum*, *product*, and *quotient* type constructors for metricated types [22]. In the topological context, "gluing" operations quotients that identify points in different objects. This is a way to construct CW complexes.

Another important type constructor generates "functions" from one type to another, possibly iteratively (as in a Cartesian Closed Category or CCC); this is the basic idea in functional programming and the lambda calculus. The first level of such a hierarchy was defined for metricated types in [22]. For topological types, several routes to function types are open. If a CCC is essential, then Steenrod pointed out [30] that topological spaces with continuous functions don't qualify but compactly generated Hausdorff topological spaces do. Booth and Tillotson [4] removed the Hausdorff separation restriction from this statement, and showed that many "convenient topological categories" that are cartesian closed are also closed under quotients. All topological spaces we have considered so far qualify as compactly generated - along with a lot of superfluous ones. Somewhat more specific than compactly generated spaces, CW complexes are not closed under the "exponential" but their homotopy equivalence classes are [20]. These equivalence classes may also suffice for our purposes, since an n-dimensional manifold has the homotopy type of a CW complex of dimension $\leq n$ ([12], p. 166, Theorem 4.3). Steenrod also suggested taking the intersection: the category of compactly generated CW complex homotopy classes. Yet another relevant kind of "function" is an *embedding* between differentiable manifolds. Differentiable manifolds don't form a CCC but various other, more general definitions of "smooth spaces" do [2].

Using the concept of manifold embeddings one can impose constraints f(x) = 0 to define new submanifolds ([12], pp. 21-22, Theorems 3.1 and 3.2). Thus constraints can also act as a type constructor for objects that live on manifolds. As an example, one can construct the "type" consisting of points on the surface of a sphere, given vectors in \mathbb{R}^n , either as an equivalence class modulo nonnegative scaling (a quotient type) or by imposing the unit-norm constraint.

As in [3], each type has a type-specific logical language of functions and relations involving objects of that type and others, along with a set of axioms. Often the axioms can be specified in terms of algebraic structures: groups, rings, sum and product types, and so on. The types of Dynamical Grammars were sufficiently elementary – products, normed function spaces, and labelled graphs built out of basic algebraic types such as real vectors – that formalized specification of new types wasn't needed. However the requirement for approximation by limiting processes creates a new situation. Now a "limit type" with its own algebra of convergent observable quantities can emerge from a much larger set of measurable functions before the limit is attained; nonconvergent information must be "hidden" from the logical language of the limit type.

What is happening fundamentally is that a limit type (such as a manifold or CW complex obeying implementability constraints) is a special case of a reduction or implementation of one type in terms of others - similar to a "model" of the first type's logical language, in model theory. The tenets of object-oriented programming provide ample precedent for types that are defined by their computational reductions to other types. The results of mixing type definition with reduction include public and private accessor functions, inheritance relations, and so on. Rather than tackle the whole problem of representing such reductions algebraically eg. using category theory, we propose here to treat just the special case of limit types by dividing up the processes associated with a limit type (and their OA semantic expressions) into those that do depend on a real-valued parameter that tends towards zero or infinity, and those that don't. Those that do are "private" and stereotyped for all instances of a type; they are always added into the set of operative processes in a model involving the given type. An example would be automatic mesh refinement implemented by "fast" rules that respond to high gradients of any designated fields.

In most programming languages there is a strong distinction between types that are built-in to the language, those that are implemented in a standard library, and those that are user-defined. One may ask where these boundaries should be drawn for a morphodynamic modeling language. Clearly the type constructors are intended for extensibility: creating library and user-defined object types. Beyond the basic measurable types of Dynamical Grammars, the bare minimum for built-in topological types is to support labelled graphs explicitly (rather than through integer-valued Object ID parameters as in Dynamical Grammars) and also to add compactly generated topological spaces, of which manifolds and CW complexes are special cases. However, with the type constructors we have considered so far, quite a bit of construction would be required to move from compactly generated spaces to differential manifolds and CW complexes. This observation argues for providing the key topological types of Table 1 as built-in types.

It is possible that a more abstract point of view, such as sheaf theory, may simplify the construction of the key topological types and thereby make it possible to refactor the foregoing design sketch and move some of the key topological types for mophodynamics out of the set of basic or built-in types and into a library. Indeed many topological object types, including differentiable functions, differential manifolds, differential operators, differential forms, and probability distributions, can be formalized as sheaves. So these or other object type abstractions may be useful for future progress in formal modeling languages for morphodynamic processes.

IV. ACKNOWLEDGEMENTS

Pawel Discussions with Krupinski, Przemek Prusinkiewicz, Brendan Lane, and Petros Koumoutsakos were helpful in this work. Equation 4 is the result of joint work with Przemek Prusinkiewicz. Research by EM was supported by NIH R01 GM086883, and by a Moore Distinguished Scholar visiting appointment at the California Institute of Technology during academic year 2010-2011. Research by AC was supported by a gift grant from the Gordon and Betty Moore Foundation to Caltech's Cell Center. We also acknowledge the Kavli Institute for Theoretical Physics' NSF-funded Miniprogram in Morphodynamics, August 2009, for support of collaborative work.

REFERENCES

- Ivo Babuška, The Rate of Convergence for the Finite Element Method SIAM Journal on Numerical Analysis, Vol. 8, No. 2 pp. 304-315, June 1971.
- [2] John C. Baez, Alexander E. Hoffnung, Convenient Categories of Smooth Spaces. UC RIverside preprint, arXiv:0807.1704v4, 8 October 2009.
- [3] J. S. Bell, *Toposes and local set theories*, Chapter 3, Oxford U. Press 1988. Dover reprint 2008.

- [4] P. Booth and J. Tillotson, Monoidal closed, Cartesian closed and convenient categories of topological spaces. Pacific J. Math. Volume 88, Number 1 (1980), 35-53.
- [5] D. Burghelea, A short course on Witten Hellfer Sjöstrand Theory (lectures given at the summer school on Groups and Geometry, Goettingen, June 2000). Available at http://www.math.osu.edu/~burghele/preprints/index.html, last accessed February 2011.
- [6] Glen E. Bredon, *Topology and Geometry*, Springer GTM 139, 1993.
- [7] Brisson E. (1993) "Representing structures in d dimensions: Topology and order". Discrete and Computational Geometry 9: 387- 426.
- [8] Cardoze, David E.; Miller, Gary L.; and Phillips, Todd, "Representing Topological Structures Using Cell-Chains" (2006). Computer Science Department. Paper 1124. http://repository.cmu.edu/compsci/1124.
- [9] Mathieu Desbrun, Eva Kanso, and Yiying Tong, "Discrete Differential Forms for Computational Modeling". Chapter 5, pp 39-55, in Discrete Differential Geometry: An Applied Introduction, ACM SIGGRAPH 2006 Courses, http://doi.acm.org/10.1145/1185657.1185665.
- [10] Giavitto JL (2003), "Topological Collections, Transformations and Their Application to the Modeling and the Simulation of Dynamical Systems". In Rewriting Techniques and Applications, Springer Lecture Notes in Computer Science 2706/2003: 208-233.
- [11] Allen Hatcher, *Algebraic Topology*. Cambridge University Press, 2002.
- [12] Morris Hirsch, Differential Topology, Springer GTM 33, 1976, Sixth edition (corrected) printed 1997.
- [13] Thomas J. R. Hughes. *The Finite Element Method: Linear Static and Dynamic Finite Element Analysis*. Dover Publications, 2000.
- [14] J. Jaeger, D. Irons, N. Monk. Regulative feedback in pattern formation: Towards a general relativistic theory of positional information. Development 135, 3175–3183, 2008.
- [15] Jun Kigami, "Measurable Riemannian geometry on the Sierpinski gasket: the Kusuoka measure and the Gaussian heat kernel estimate". Math. Ann. 340:781–804, 2008.
- [16] Bryan Matthew Klingner and and Jonathan Richard Shewchuk, "Aggressive Tetrahedral Mesh Improvement". Proceedings of the 16th International Meshing Roundtable 2008.
- [17] Anders Logg and Garth N. Wells, "DOLFIN: Automated Finite Element Computing". ACM Transactions on Mathematical Software, Vol. 37, No. 2, Article 20, April 2010.
- [18] K. Long, "Sundance, a rapid prototyping tool for parallel PDE-constrained optimization". In Large-Scale PDE-Constrained Optimization. Lecture Notes in Computational Science and Engineering. Springer Verlag 2003.
- [19] Peter McMullen and Egon Schulte, Abstract Regular Polytopes, Cambridge University Press 2002.
- [20] J. Milnor, On spaces having the homotopy type of a CW complex, Trans. A.M.S. 90 (1959), 272–280.
- [21] E. Mjolsness, G. Yosiphon. Stochastic process semantics for dynamical grammars. Annals of Mathematics and Artificial Intelligence 2006, 47:329-395.
- [22] Eric Mjolsness, "Towards Measurable Types for Dynamical Process Modeling Languages". Electronic Notes in Theoretical Computer Science (ENTCS), vol. 265, pp. 123-144, 6 Sept. 2010, Elsevier.

- [23] James R. Munkres, Compatibility of imposed differentiable structures. Illinois J. Math. 12:4, pp. 610-615. 1968.
- [24] Kasso A. Okoudjou, Luke G. Rogers, and Robert S. Strichartz, Generalized eigenfunctions and a Borel theorem on the Sierpinski Gasket, Canad. Math. Bull. 52, p. 105, 2009.
- [25] L. S. Pontryagin, Foundations of Combinatorial Topology. Dover 1999; Graylock Press, 1952.
- [26] Sebastian A Sandersius and Timothy J Newman, Modeling cell rheology with the Subcellular Element Model. Phys. Biol. 5:015002, 2008.
- [27] B. E. Shapiro, E. Mjolsness, "Developmental Simulations with Cellerator", Paper presented at the Second International Conference on Systems Biology, Pasadena, CA, November 2001.
- [28] Tetrahedral mesh generation by Delaunay refinement. Proceedings of the Fourteenth Annual Symposium on Computational Geometry, pp 86-95, Association for Computing Machinery, June 1998.
- [29] Si H. and Gartner K., Meshing Piecewise Linear Complexes by Constrained Delaunay Tetrahedralizations, Proceeding of the 14th International Meshing Roundtable, September 2005.
- [30] N. E. Steenrod, "A convenient category of topological spaces". Michigan Mathematical Journal, Volume 14, Issue 2, 133-152, 1967.
- [31] Christoph Walker and Glenn F. Webb, "Global existence of classical solutions for a haptotaxis model", SIAM J. Math. Anal 38:5, pp. 1694-1713, 2007.
- [32] M. Wicke, D. Ritchie, G. M. Klingner, S. Burke, J. R. Shewchuk, J. F. O'Brien. Dynamic local remeshing for elastoplastic simulation. ACM SIGGRAPH Computer Graphics Proceedings, 2010.
- [33] CGAL: Computational Geometry Algorithms Library, http://www.cgal.org/ .
- [34] E. Coen, A. Rolland-Lagan, M. Matthews, J. Bangham, P. Prusinkiewicz: The genetics of geometry. Proceedings of the National Academy of Sciences 101 (14), pp. 4728-4735.
- [35] Mironova VV, Nadya A Omelyanchuk, Guy Yosiphon, Stanislav I Fadeev, Nikolai A Kolchanov, Eric Mjolsness and Vitaly A Likhoshvai, A plausible mechanism for auxin patterning along the developing root. BMC Systems Biology 4:98, 2010.