RESEARCH STATEMENT – Maciej Swat

Past Research

Even though my current research focuses on computational biology, I spent a significant portion of my earlier career researching nuclear/particle physics. My Ph.D. and postdoctoral training exposed me to a variety of complex modeling problems in particle physics. I learned how to approach difficult modeling problems systematically and not to be intimidated by their apparent complexity. I also learned multiple programming techniques (including parallel programming) and studied topics such as data structures, algorithms, algorithm analysis and operating systems, which are typically taught in doctoral Computer Science programs. Since the data-analysis techniques, approach to developing theoretical models of elementary-particle interactions, and software development I learnt during this period have proved surprisingly relevant to solving problems commonly encountered in computational biology, I begin with a brief description of my particle physics research.

After an undergraduate degree in Electrical and Mechanical Engineering, my career as a physicist began in 1998 when I was accepted as a graduate student in Physics at Indiana University, Bloomington. For most of my studentship I worked under the supervision of Prof. Adam Szczepaniak. My early research focused on theoretical calculations of the mass spectra of light-quark gluonic excitations. I soon realized that my real interests were in applied sciences rather than in pure theory. In the summer of 2000, I began working with the experimental group led by Prof. Alex Dzierba. My theoretical background and desire to do applied work overlapped nicely with Prof. Dzierba's scientific program. Together with Prof. Szczepaniak, I provided theoretical support and led data-analysis efforts for Prof. Dzierba's group.

Search for Exotic Meson in the $\eta\,\pi$ and $\eta'\,\pi$ systems. The main motivation behind my Ph.D. work was to search for low-mass exotic mesons with $J^{PC}=1^{-+}$. We knew of several publications claiming the discovery of such mesons decaying into $\eta\pi$ or $\eta'\pi$ particles. However, the evidence presented in those publications seemed incomplete and their data analyses assumed that the mesons existed, introducing significant bias. Following the intuition of Prof. Dzierba and Prof. Szczepaniak, I investigated experimental data from the E852 experiment conducted at Brookhaven National Laboratory for reactions which were claimed to show evidence of exotic particles, specifically: $\pi^-+p\rightarrow\eta\pi^0 n$, $\pi^-+p\rightarrow\eta\,\pi^- p$ and $\pi^-+p\rightarrow\eta'\pi^- p$

I used Partial Wave Analysis (*PWA*) to effectively separate production amplitudes based on the relative angular momenta of the decay products ($\eta\pi$ or $\eta'\pi$). The result was the mass spectrum of the $\eta\pi$ ($\eta'\pi$) system, which I then examined for the presence of exotic particles in the P-wave (the so-called $\pi_1(1400)$). The main difficulty in interpreting the PWA results was that for two scalar particles in the final state ($\eta\pi$ or $\eta'\pi$), each mass bin of the $\eta\pi$ ($\eta'\pi$) had up to 8 degenerate sets of production amplitudes which perfectly satisfied the extended-likelihood fit criteria. Only one of set of amplitudes could be physical. I developed a minimal set of criteria sufficient to resolve the PWA ambiguities by requiring: (1) continuity of amplitudes as a function of mass, (2) continuity of relative phases and (3) Breit-Wigner shapes around known resonances ($a_0(980)$, $a_2(1320)$). In contrast to previous analyses, where selection of the physical solutions assumed an exotic meson present in the P-wave, unbiased data analysis of the three studied reactions found no evidence of low-mass exotic mesons. Previous analyses cited the relative phase motion of the P-wave as evidence for the existence of an exotic meson. However, I showed (by fitting theoretical models) that such phase motion should be attributed to the final-state interactions and not to the presence of exotic mesons. I published this research in peer reviewed journals [**14-16**] and in my Ph.D. thesis.

Search for Exotic Meson in the $\pi^-\pi^-\pi^+$ and $\pi^0\pi^0\pi^-$ systems. After defending my PhD thesis in 2003, I worked in Prof. Dzierba's group as a postdoctoral researcher searching E852 data for exotic mesons in 3-pion final states. As with the $\eta\pi$, another exotic meson, the so-called π_1 (1600) had been reported in the 3-pion final state. The evidence for the π_1 (1600) seemed more robust than for the π_1 (1400). Unlike the $\eta\pi$ final states, the 3-pion PWA was unambiguous, so signals reported there apparently could be taken at face value. However, the reported signals were quite noisy. I suspected that part of this noise might result from the limited statistics of the π_1 (1600) analyses. The full data samples were one of the largest light-meson spectroscopy data sets then available and, for a variety of reasons, they remained unanalyzed. During the summer of 2003, I wrote a general-purpose parallel PWA software suite capable of handling very large data samples within a reasonable time. With generous help from UITS personnel, in 2004, I was able to present full PWA analyses of the 3-pion final state which showed no sign of any 1^{-+} signal [**11**]. This unambiguous result had an order of magnitude better statistics than the earlier analysis, showing that previously claimed low-mass exotic mesons were data-analysis artifacts, not actual particles. These results also agreed with theoretical predictions described in [**17**], where, together with Prof. Szczepaniak, I showed that a pion beam probe is suboptimal for producing light-quark exotics, while a photon beam should favor them. This paper was one of the motivations behind recent upgrades at Jefferson Lab, where the new GlueX experiment will probe gluonic excitation spectra.

During my work on the PWA software I had the pleasure to work with two students from Bloomington South High School (David Collins and Zach Dwiel) who contributed significantly to early versions of the PWA suite.

The Biocomplexity Institute and CompuCell3D. While successful, my work in nuclear/particle physics lacked the real-life applications I sought in my career. In March 2005 I joined the group of Prof. James Glazier, which focused on understanding the biophysical mechanisms of development and developmental diseases. Although such research might appear more appropriate to a Biology Department, building mechanistic, physics-based, predictive models of tissues, organs, and organisms requires a good grasp of how cells interact physically with each other. Because their heterogeneity makes most analytical techniques useless, most mathematical models in biology which treat cells individually are implemented as computer algorithms. The field of computational biophysics/biology allowed me to apply my physics background and understanding of programming to solve important biomedical problems, exactly the type of career I was looking for.

In the Glazier group I began developing and improving the open-source software package CompuCell3D (*CC3D*), originally developed by Prof. Glazier and collaborators at the University of Notre Dame to allow biologists and non-programmers to develop simulations of developmental phenomena and diseases. CC3D uses the Glazier-Granner-Hogeweg (*GGH*) model, also known as the Cellular Potts Model (*CPM*), as its underlying computational methodology. This model is an extension of the classical statistical mechanics Ising and Potts models. Just as the Potts model provides insights into the behaviors of ferromagnets and phase transitions, GGH models allow us to better understand the dynamics of soft tissues. For correct model parameters, the GGH agrees quantitatively with experiments on soft tissues where cell motion can be described as visco-elastic. We have recently extended the GGH approach [**9**] to include interactions which also model the elastic properties of tissues, making GGH one of the most versatile approaches for studying development.

The version of CC3D I received was inadequate to its goals and not much more usable or flexible than typical research code, though it did have some features that facilitated code reuse when building new simulations. However, each new CC3D-based model required recompilation of a large C++ code-base, which was not acceptable to users. Between 2005 and 2007, I developed a completely new CC3D which, featured Python scripting language support (similar to Matlab or Mathematica), a new graphical user interface and a much richer set of modules for modeling specific cell behaviors. The scripting language

support and improved CC3D modeling capabilities, computational performance and visualization tools redefined researchers' perceptions of CC3D, making it the tool of choice for multi-cell simulation development. We began receiving enquiries and invitations to collaborate from researchers worldwide who were adopting CC3D for their biological simulations. The wave of interest in CC3D led the NIH to decide to fund CC3D development in 2007. As lead developer, I co-wrote the NIH grant proposal with Prof. Glazier as lead PI. NIH funding allowed us to hire Mr. Randy Heiland (developer), Mr. Benjamin Zaitlen (web-developer), Dr. Alex Dementsov (developer), Mr. Andy Somogyi (developer) and Dr. Mitja Hmeljak (developer). I became responsible for management of the development team. As team leader, I distribute programming assignments, strategize overall development of CC3D, set goals and priorities, write progress reports to the NIH, promote CC3D at conferences, *etc*. I also screen and interview software-developer job-candidates.

In 2007 Prof. Glazier and I began organizing week-long CC3D training workshops (held in Bloomington). Virtually all of those workshops are oversubscribed and since we admit only people who are serious about multi-cell, multi-scale modeling, they have expanded our collaboration network substantially. We have also presented extended tutorials on CC3D during summer schools in Beijing, Paris, Santa-Fe, Los Alamos and Dundee. During organization of the training workshops I prepare the workshop program, documentation and tutorial assignments. I then teach multi-scale modeling using CC3D. In the absence of textbooks or established syllabi for multi-cell biomedical/biophysical modeling courses, I have developed all training materials. Each workshop consists of 20 hours of lectures and 20 hours of hands-on tutorials. In August 2010, I expanded the annual workshop into a joint CompuCell3D and Systems Biology Workbench Training Workshop, which gathered almost 30 participants from around the world. The growing interest in our workshops indicates that the field of multi-cell and multi-scale modeling is entering a phase of rapid growth and that the CompuCell3D project that I lead is a driving factor in this growth.

In addition to developing CC3D, I am an active member of the NIH *IMAG* (Interagency Modeling and Analysis Group) working groups that target model sharing, model validation and curation. In April 2007, together with Prof. Glazier and Dr. Grace Peng (NIH), I organized a Model Sharing Workshop at the NIH campus in Bethesda, MD, which led me to assume leadership of an NIH-supported push for model specification standards and model shareability. Two years later, in May 2009, we organized the first NIH-sponsored Cell Behavior Ontology Workshop, again at the NIH campus. The audience of both workshops consisted of researchers from all over the world (most of them NIH-grantees) as well as NIH Program Directors. These events helped strengthen the image of Indiana University, Bloomington as an institution where novel research is done successfully. Improving the profile of IUB (from the NIH standpoint) should increase "Institutional Support" grant scores for all applications originating from IUB.

In October 2009, with Prof. Glazier and Mr. Benjamin Zaitlen, I organized the Biocomplexity X Workshop in Bloomington, IN, which attracted many international presenters and participants and also helped continue development of the Cell Behavior Ontology which we started 5 months earlier in Bethesda. In October 2010, with Prof. Glazier, I will run a Cell Behavior Ontology and Multi-Scale Modeling Standards Workshop in Edinburgh, Scotland. At the conclusion of Edinburgh meeting I will draft a white paper proposing Multi-Scale Modeling Standards which I will implement in subsequent versions of CompuCell3D and which should also be adopted by other multi-cell modeling environments.

Prof. Glazier's group develops multi-scale simulations to explore the role of fundamental cell-level processes in development (*e.g.,* segmentation, gastrulation, limb bud formation, *etc*…) and developmental diseases such as cancer and Age-Related Macular Degeneration (*AMD*). In all of these, CompuCell3D is a key enabling technology that allows rapid model development and analysis of dependencies on model parameters. Because CompuCell3D is used by researchers worldwide, I often share my expertise in CompuCell3D model development with other research teams to make sure that they can focus on the science of their projects and are not slowed down by the technical aspects of

model implementation. These numerous collaborations allow me to investigate many scientific problems at the same time, since most mundane modeling work is done at my collaborators' sites.

Publications [**1-10**] represent my research between 2005 and 2010. Articles [**2,5,8**] discuss computer-science aspects of aspects of CC3D, multi-scale approaches to biological modeling and why Problem Solving Environments are essential tools for computational biology. [**5**] is an invited paper presenting a comprehensive overview of CC3D modeling capabilities in the context of physics and computational biology. [**2**] discusses how graphical model configuration capabilities improve accessibility and usability of modeling frameworks such as CC3D. We are currently submitting multiple collaborative proposals to the NIH, EPA, NSF to further explore this topic and to develop the first model exchange format for multi-cell, multi-scale computational biological models. Other biomodeling communities (*e.g.* Systems Biology) have such standards, which greatly improve the quality of models and ensure that models can be shared, cross-validated and curated. Model exchange standards also improve the quality of modeling software, make modeling more accessible to non-programmers and increase acceptance of modeling among experimentalists. The current lack of multi-cell, multi-scale modeling standards presents a big opportunity to make a significant impact in this branch of biophysics .

[**9**] reviewed the applicability of CC3D to biological problems and outlined future directions for CC3D development - especially features that CC3D needed to become a better platform for biomedical modeling. These priorities largely guided my preparation of successful NIH grant applications for CC3D software development and somitogenesis research.

One unique feature of CC3D is that it allows for quite faithful modeling of large numbers of cells while permitting modification of the properties of individual cells. [**3**] presents a CC3D-based model of vascularized tumor growth, which demonstrates that suppressing vascular growth and remodeling paradoxically increases the likelihood of metastasis. While our cancer model makes many simplifying assumptions and lacks subcellular models to control cell properties, it has been downloaded 2000 times since October 2009, encouraging us to model cancer in more detail and explore NIH and NSF funding opportunities.

[**7**] investigates patterning of biofilms under variable availability of nutrients. Starvation of biofilms produces patterns similar to those of simulated starved tumors (discussed in [**4**]). This analogy suggests that nutrient supply has a strong impact on the efficacy of, *e.g.,* tumor-suppressing therapies, especially if the goal of the therapy is to not only to destroy the primary tumor but to avoid metastasis.

[**1**] and [**10**] both showed that the simple physical phenomenon of cell-cell adhesion is a key cell-level interaction during biological patterning. We reached the same conclusion in [**6**], where we modeled normal somite segmentation and segmentation for different gene knockouts. Somites are segmental precursors to ribs, vertebrae and other structures in developing vertebrate embryos. Improper somitogenesis may lead to serious birth defects. Our model correctly predicts the shapes of intersomitic boundaries and shows that error correction during somitic cell differentiation is largely based on differential adhesion between cells, demonstrating the importance of physical cell-cell interactions in development.

Coupling cell-cell adhesion to transport of growth factors in the developing limb bud allowed us to predict the shape of the growing limb in early development [**8**]. Our collaborators at the EPA are continuing this research to model later stages of limb-bud and digit formation. Since most prior research on limb growth used continuum models, a cell-based model of limb growth will significantly improve our understanding of this classic developmental paradigm.

Predictive CC3D-based models may also be important to the development of regenerative medicine, which has been identified as a central science of the 21st century. The ability to run virtual experiments *e.g.* on limb regrowth, to identify cell-cell interactions which lead to regeneration may prove crucial to developing regenerative treatment strategies. Glazier's lab has a long-standing collaboration on regeneration with Prof. Stocum (*IUPUI*) a leading expert in regenerative medicine.

During the last 3 years I have co-mentored and supervised 5 graduate students in the Glazier group (Wendy Zhang, Abbas Shirinifard, Julio Belomonte, Susan Hester and Ruei-Jr Wu). Working with them gave me an opportunity to broaden my knowledge of biophysics and computational biology and also improved my teaching and communication skills. I learned that listening to students' ideas and treating them as partners (rather than "just students") produces better research, higher quality publications and a better scientific atmosphere. I strongly believe that maintaining this type of creative environment is essential to academic excellence.

In 2009, the Environmental Protection Agency established the Texas-Indiana Virtual STAR Center, as part of the "Virtual Tissues" (*VT*) project run by the EPA. The VT project was motivated by legislation in the USA and EU which requires the EPA and its European counterparts to publish toxicity assessments for tens of thousands of chemicals. Traditional *in-vivo* or *in-vitro* tests have inadequate throughput to provide such assessment within the required timeframe. The VT project seeks to develop predictive computational models of tissue toxicity, which coupled with high-throughput *in-vitro* experimental techniques, can dramatically expedite toxicity screening and thus improve the safety of usage of many chemicals. CompuCell3D is one of the core modeling platforms adopted by the VT. Funding under the STAR Center is partly directed towards improving the usability of CC3D in toxicity modeling. This award shows the success of my development of CC3D and my ability to lead projects with multi-institutional impact and visibility.

Future Research

During the 5 years I have spent working with Prof. Glazier, I have developed a good grasp of computational biology/biophysics and defined my scientific goals for the next several years. My experience working with scientists representing a very broad spectrum of research interests has allowed me to make deliberate decisions about my research interests. The research areas I will focus during next few years can be grouped into three main categories:

1. Large-scale software projects that address the needs of the biomedical/biophysical modeling community.
2. Domain-specific programming languages for multi-scale, multi-cell modeling.
3. Predictive multiscale models and simulations of diseases, development, and homeostasis of tissues and organs.

1) Large-scale software projects that address the needs of the biomedical/biophysical modeling community.

CompuCell3D has already transformed multi-cell biomedical simulations. By providing researchers with a comprehensive problem-solving environment for biomedical computing, it has greatly improved scientific throughput and cut simulation development time from months to days. I will continue to develop enhancements to CompuCell3D including new user interfaces, PDE solvers, modules for simulation of particular biological phenomena (*e.g*. cell tight junctions) and parallel implementations of CompuCell3D. We have established collaboration with Prof. Roshan D'Souza (University of Wisconsin, Milwaukee) who has already developed a prototype GGH implementation running on Graphical Processing Units and delivering a 20-100x speed-up as compared to a single-processor CPU-based implementation. In May 2010, together with Prof. Glazier and Prof. D'Souza, I wrote a competitive renewal NIH application for CompuCell3D, which focused on creating multiple parallel implementations (multi-core, multi-CPU, and GPU). With extended fundin,g we will deliver significantly faster CC3D versions, which would allow more detailed simulations than currently possible. Most of our current users have identified this improvement as essential for their future research.

Integrating and cross-validating biomedical models implemented using different modeling approaches and methodologies is crucial but little researched. Since multi-cell simulations are relatively new, most effort still goes into developing simulation methods and not into comparative analyses of models and methods, leaving significant gaps in our knowledge of the optimal domains for particular modeling methodologies. Other deficits include model cross-validation, mapping physical observables into model parameters and linking different modeling scales into multi-scale models. We need serious research to address these shortcomings. One strategy I have developed is to build an integrated multi-scale, multi-cell framework for biomedical modeling to allow researchers to describe tissues and organs in terms of observed cell behaviors and run simulations using multiple methodologies. In their most straightforward implementations, such environments can be thought of as translators between different model descriptions. Ultimately this approach will allow a researcher interested in modeling, *e.g.,* tumor invasion, to specify and run a model using multiple modeling methodologies (*e.g.* the GGH Model, Center Model, Subcellular Element Models, Immersed Boundary Model, *etc.*) without any additional effort. A biophysical model which passed consistency checks in this unified modeling environment would gain far greater credibility in the biomedical community (especially among clinicians) than would models run using a single methodology.

Three tools are necessary for such a modeling environment: a) A model-description language capable of describing cell behaviors independent of the specific model implementation. b) A common computer programming framework to integrate various modeling methodologies into a single platform. c) Usability and cross-validation studies to demonstrate the validity and scientific attractiveness of integrated multi-scale modeling platforms.

2) Domain-specific programming languages for multi-scale, multi-cell modeling.

Unlike systems biology, multi-cell modeling does not have a well-established domain specific-language for encapsulating key concepts. Instead we use general-purpose programming languages. While this approach works relatively well within single research groups or small research communities, it impedes collaborative research. A domain-specific computer language that can be interpreted or compiled to generate code appropriate to multiple multi-cell modeling methodologies is essential for the environment I described above.

With Prof. Nick Monk (University of Nottingham, UK), I have been working to create a new set of standards for multi-scale, multi-cell models. We have held two workshops on Cell Behavior Ontology and Model Description Standards and will hold a 3rd in October 2010 in Edinburgh, Scotland. My overarching goal in this initiative is to build an ontology for describing cell behaviors and a model-specification language based on this ontology. Success hinges on community acceptance. Therefore I continuously consult with a broad range of biomedical researchers for feedback and suggestions. Designing programming languages that can directly describe multi-cell models is an iterative process. Writing a compiler or interpreter for the new language requires language specification to be fairly advanced. To begin, I am using publically-available interpreted languages augmented with Application Programmer Interfaces (*API*s) for simulation of cell behaviors. Once the APIs are well-established and widely used, I will build a domain-specific programming language based on these APIs. The APIs and modeling language will allow researchers to describe their models in a compact standardized form and run them using different modeling methodologies, as described in 1).

3) Building predictive multiscale models and simulations of diseases, development and homeostasis of tissues and organs.

The software development in 1) and 2) ties closely to my research. Improvements in multi-scale modeling software and experimental biology/biophysics, brings us closer to conducting *in-silico* experiments on diseases and development of tissues and organs. Our recent publications show the promise of multi-scale, predictive tissue models. Proof-of-concept studies that validate our approach [**1,3,7**], include studies of somitogenesis in verterbrates, tumor growth and AMD. The cancer and AMD

studies not only increase scientific understanding but may have substantial impact in assisting clinicians and drug designers in developing new therapies. However, the model sophistication and realism needed for clinical deployment requires that we continuously refine our models.

Models of tumor growth and metastasis require: a) The ability to simulate Extra Cellular Matrix (*ECM*). Many biological models neglect ECM. However, experimental research shows that ECM plays essential roles in every stage of biological life cycles (early embryo development, wound healing, cancer progression, aging of tissues, *etc.*). b) The ability to simulate blood vessels and blood flow realistically. Our simulations of vasculogenesis and angiogenesis [**1**] replicate, with some limitations, blood-vessel growth and vascular remodeling. However, a realistic simulation of tumor growth also requires simulation of the transport of nutrients, tumor cells and chemotherapeutics due to blood flow. Our simulations currently lack flow-driven transport. c) Linking macroscopic cell behaviors to genetic, metabolic and other biochemical networks. Until recently most cell-based models used heuristic rules to define cell-cell interactions and cell properties. Often this approach is biologically validated by experiments and results in models with some predictive power. However, hand-tuning the behavior of model cells may also lead to low quality science in which the success metric is that the simulation picture looks like a microscope image. Such sloppiness impedes understanding of complex systems, because it can suggest the sufficiency of totally implausible biological mechanisms, leading to scientific confusion.

Ideally we would look closely at the biology of individual cells and try to infer their macroscopic properties from the dynamics of their molecular-level mechanisms. However, the scale of tissue simulations is far coarser than the scale of single cells, so modeling heterogeneity within a single cell is impractical. Modeling molecular mechanisms via reaction-kinetics network models is a useful intermediate-scale approach, combining the complex behaviors of intracellular biochemical reactions with relatively simple mathematical descriptions and implementations. Defining cell-level observables such as cell-cell contact forces, cell growth and proliferation rates, *etc.,* as functions of subcellular molecular concentrations largely eliminates hand tuning of cell behaviors. However, adding biochemical networks to models is not a full solution because we still need to quantify the relations between the state of the biological network and the cell-level parameters. Paradoxically, this mapping has been little studied experimentally. Exploring the ways in which, *e.g.,* concentrations of proteins, growth factors, gene expression levels, *etc*., determine physical cell properties and behaviors remains an important experimental and computational task. How a gene or combination of genes regulates cellular behavior is often so unclear that designing experiments is difficult. An educated guess in the form of a model which hypothesizes interactions and calculates their results, can help guide experiments, creating a positive feedback loop, where modeling and experiment work in tandem to improve our understanding of complex biological systems. From a software point of view, including biological network simulators in multi-cell models is relatively straightforward. Dedicated packages such as Systems Biology Workbench (*SBW),* which specialize in implementing biological networks, have well developed programmer interfaces and I have already included support for SBW models in CC3D. Defining a language to describe the relations between cell-level and subcellular simulators is more challenging. However, an active community of researchers is genuinely interested in addressing these issues and I anticipate that within two to three years the first multi-cell modeling standards will be deployed and used.

I will focus on the relations between biological network dynamics and cell-level behaviors to produce a clear and unambiguous procedure for linking the two scales. Since our group is also involved in synthetic biology projects, I will have the opportunity to compare the real behaviors of cultures of carefully engineered cells with virtual experiments. Based on these comparisons, I will be able to map the dynamics of molecular cell networks into parameters describing macroscopic cell behaviors, beginning with simple two-cell-type cell-sorting and proceeding to more complex phenomena such as tumorgenesis or AMD.

Publications (H-index 7):

1. "A Computer Simulation of Long-Range Patterning in the Drosophila Pupal Eye," David Larson , Ruth Johnson, **Maciej Swat**, J. Cordero, James Glazier, Ross Cagan, *PLoS Comput Biol* **6,** e1000841. doi:10.1371/journal.pcbi.1000841(2010).
   Role: Developed core modules for the paper, trained David Larson in CC3D modeling and wrote sections of the paper. **30% effort**.
2. "Workflows for Parameter Studies of Multi-Cell Modeling," Randy W. Heiland, **Maciej Swat**, Benjamin L. Zaitlen, James A. Glazier, Andrew Lumsdaine, *HPC2010 Conference Proceedings*, Orlando, FL, April 12-15 (2010).
   Role: Co-developed workflow approach to do parameter studies in CC3D. Reviewed and edited the paper. **30% effort**.
3. "3D Multi-Cell Simulation of Tumor Growth and Angiogenesis," Abbas Shirinifard, John S. Gens, Benjamin L. Zaitlen, Nikodem J. Popławski, **Maciej Swat**, James A. Glazier, *PLoS ONE* **4**: e7190, doi:10.1371/journal.pone.0007190 (2009).
   Role: Developed main modules and PDE solvers used in cancer simulation. Reviewed and edited sections of the paper. **40% effort**.
4. "Front Instabilities and Invasiveness of Simulated Avascular Tumors", Nikodem Popławski, Ubirajara Agero, J. Scott Gens, **Maciej Swat**, James A. Glazier, *Bulletin of Mathematical Biology*, **5**(71), pp. 1189-1227 (2009).
   Role: Developed modules and PDE solvers used in cancer simulation. Reviewed and edited sections of the paper. **30% effort**.
5. "Multi-Cell Simulations of Development and Disease Using the CompuCell3D Simulation Environment," **Maciej Swat**, Susan D. Hester, Randy W. Heiland, Benjamin L. Zaitlen, James A. Glazier. In Ivan V. Maly ed., *Systems Biology Series: Methods in Molecular Biology*, pp. 138-190.
   Role: Wrote most of the publication. **70% effort.**
6. "Coordinated Action of N-CAM, N-cadherin, EphA4, and ephrinB2 Translates Genetic Prepatterns into Structure during Somitogenesis in Chick," James A. Glazier, Ying Zhang, **Maciej Swat**, Benjamin Zaitlen and Santiago Schnell, *Current Topics in Developmental Biology* **81**, 205-247 (2008).
   Role: Co-developed simulation code and wrote sections of the paper. **50% effort**.
7. "Simulation of Single-species Bacterial-Biofilm Growth using the Glazier-Graner-Hogeweg Model and the CompuCell3D Modeling Environment," Nikodem J. Popławski, Abbas Shirinifard, **Maciej Swat** and James A. Glazier, *Mathematical Biosciences and Engineering* **5**, 355-388 (2008).
   Role: Developed main modules and PDE solvers used in biofilm simulations. Reviewed and edited sections of the paper. **40% effort**.
8. "From genes to organisms via the cell: a problem-solving environment for multicellular development," Trevor Cickovski, Karim Aras, Mark S. Alber, Jesus A. Izaguirre, **Maciej Swat**, James A. Glazier, Roeland M.H. Merks, Tilmann Glimm, H. George E. Hentschel, Stewart A. Newman, *Computers in Science and Engineering* **9**, 50-60 (2007).
   Role: Co-Developed CompuCell3D - problem solving environment. Wrote sections of the paper. **30% effort**.
9. "The Glazier-Graner-Hogeweg model: extensions, future directions, and opportunities for further study," Ariel Balter, Roeland M. H. Merks, Nikodem J. Popławski, **Maciej Swat**, James A. Glazier, in: Alexander R. A. Anderson, Mark A. J. Chaplain, Katarzyna A. Rejniak, eds., *Single-Cell-Based Models in Biology and Medicine*, pp. 151-168. Mathematics and Biosciences in Interaction, Birkhauser, Basel, Boston and Berlin (2007).
   Role: Reviewed and edited manuscript, participated in discussions about the paper. **20% effort**.

10. "Adhesion between cells, diffusion of growth factors, and elasticity of the AER produce the paddle shape of the chick limb," Nikodem J. Popławski, **Maciej Swat**, J. Scott Gens and James A. Glazier, *Physica A* **373**, 521-532 (2007).
    Role: Co-developed simulation code and reviewed and edited the paper. **50% effort**.
11. "A Partial Wave analysis of the pi- pi- pi + and pi0 pi0 pi- and the Search for JPC=1-+ Meson," Alexander Dzierba, Maciej Swat, Ryan Mitchel, Adam Szczepaniak, Scott Teige, *Physical Review D* **73**, 072001 (2006).
    Role: Wrote high-performance code for Partial Wave Analysis and performed significant part of the "discovery phase" data analysis. Wrote sections of the paper. **60% effort**.
12. "Reply to Comments on "The Evidence for a Pentaquark Signal and Kinematic Reflections," Alexander Dzierba, Dan Krop, **Maciej Swat**, Adam Szczepaniak, Scott Teige, *Physical Review D* **71**, 098502,(2005).
    Role: Participated in discussions about this short paper. Reviewed and edited the paper. **10 % effort**.
13. "The evidence for a pentaquark signal and kinematic reflections," Alexander Dzierba, Dan Krop, Maciej Swat, Adam Szczepaniak, Scott Teige, *Physical Review D*, **69**, 051901 (2004).
    Role: Participated in discussions about the paper, ran auxiliary Monte Carlo simulations. Reviewed and edited the paper. **20 % effort**.
14. "Exotic meson searches: E852 data analysis", **Maciej Swat**, *Proceedings of 10th International Conference on Hadron Spectroscopy, Aschaffenburg, Germany, AIP Conf.Proc.***717**:462-466,(2004).
    Role: Wrote Partial Wave Analysis code for analyzing the data and performed most of data analysis. Wrote most of the paper. **80% effort**.
15. "Study of the eta pi and eta' pi Spectra and Interpretation of Possible Exotic $J^{PC} = 1^{-+}$ Mesons," Adam Szczepaniak, **Maciej Swat** *et al*., *Physical Review Letters* **91**, **09** (2003).
    Role: Wrote Partial Wave Analysis code for analyzing the data and performed most of data analysis. Wrote sections of the paper. **50% effort**.
16. "Search for a $J^{PC} = 1^{-+}$ Exotic Meson in the eta pi0 System," Alexander Dzierba, **Maciej Swat**, Adam Szczepaniak, Scott Teige, *Physical Review D*, **67**, 094015 (2003).
    Role: Wrote Partial Wave Analysis code for analyzing the data and performed most of data analysis. Wrote sections of the paper. **70% effort**
17. "Role of Photoproduction in Exotic Meson Searches," Adam Szczepaniak, Maciej Swat, *Physics Letters B*, **516**, 72-76 (2001).
    Role: Did part of the theoretical calculations. Wrote sections of the paper. **30% effort**.
18. "Fuzzy modeling of dynamics of chamber resistance furnaces," Jacek Kucharski, Maciej Swat, *Proceedings of 5th International Symposium on Methods and Models in Automation and Robotics MMAR'98* (1998).
    Role: Developed the model and implemented it in software. Wrote sections of the paper.**70% effort.**

Recent Grants Written/Funded:

1. National Institutes of Health, National Institute of General Medical Sciences, 1R01 GM077138-01A1 "Development and Improvement of Tissue Simulation Toolkit – CompuCell3D," (9/1/07-8/31/10, approx. $1,590,000). PI James A. Glazier - **60% effort**.
2. National Institutes of Health, National Institute of General Medical Sciences, 2 R01 GM077138-04 "Competitive Renewal of Development, Improvement and Extension of the Tissue Simulation Environment – CompuCell3D," September 2009 – rejected - **60% effort**.

3. National Institutes of Health, National Institute of General Medical Sciences, 2 R01 GM077138-04A1 "Competitive Renewal of Development, Improvement and Extension of the Tissue Simulation Environment – CompuCell3D," May 2010, resubmission, under review - **60% effort**.
4. National Institutes of Health, National Institute of General Medical Sciences, R01 GM76692-04 "Competitive Renewal of Multiscale Studies of Segmentation in Vertebrate Embryos," (10/1/08-9/30/12, approx. $2,800,000) PI James A. Glazier, co-PIs Santiago Schnell, Charles Little, Herbert Sauro – **20% effort**.
5. Environmental Protection Agency, National Center for Environmental Research, "The Texas-Indiana Virtual STAR Center: Data-Generating *in vitro* and *in silico* Models of Development in Embryonic Stem Cells and Zebrafish," (11/1/09-10/31/12, $750,000), PI Jan-Åke Gustafsson, co-PI James A. Glazier – CompuCell3D was included in this grant as a core simulation toolkit for studies of tissue toxicity - **5 % effort**, **however one of the main reasons Glazier's lab was on the grant was CC3D** .

6. National Academies Keck Futures Initiative Seed Grant, "Virtual Oogle Human – towards a Cell Behavior Ontology," February 2009, rejected – **50 % effort**.

Referees:

1. Prof. Philip K. Maini
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Philip Maini received his B.A. in mathematics from Balliol College, Oxford, in 1982 and his DPhil in 1985 under the supervision of Prof J. D. Murray, FRS. After completing his studies he spent a year as an Assistant Master at Eton College before returning to the CMB in 1987 as a Junior Research Fellow at Wolfson College, Oxford. In 1988 he was appointed Assistant Professor in the Mathematics Department at the University of Utah, Salt Lake City for two years, before returning to Oxford, initially as a University Lecturer and then as Professor and Director of the CMB. He is currently on the editorial boards of a large number of journals, including serving as the managing editor for the *Bulletin of Mathematical Biology*. He has also been an elected member of the Boards of the Society for Mathematical Biology (*SMB*) and European Society for Mathematical and Theoretical Biology (*ESMBTB*). Recently he was elected to the Council of the IMA.

His research projects include the modelling of avascular and vascular tumours, normal and abnormal wound healing, collective motion of social insects, bacterial chemotaxis, rainforest dynamics, pathogen infections, immunology, vertebrate limb development and calcium signalling in embryogenesis. He has over 280 publications in the field and has held visiting positions at the Universities of Ancona, Cambridge, Central de Venezuela, Degli Studi Di Modena E Reggio Emila, Pierre et Marie Curie (Paris VI), Minnesota, South Florida, Sydney, Washington, Williams College, Queensland University of Technology, National Tsing Hua University of Taiwan and was Distinguished Foreign Visiting Fellow, Hokkaido University (2002). He co-authored a Bellman Prize winning paper (1997), was awarded a Royal Society Leverhulme Trust Senior Research Fellowship for 2001-2 and a Royal Society-Wolfson Research Merit

Award (2006-11). In 2005 he was elected Honorary Guest Professor, University of Electronic Science Science and Technology of China, Chengdu. In 2006 he was appointed to a 3-year Adjunct Professorship at the School of Mathematical Sciences, Queensland University of Technology, Brisbane. In 2010 he was appointed to a 3-year Adjunct Professorship at Lincoln University, Christchurch, New Zealand and appointed Distinguished Research Fellow at the African Institute for Mathematical Sciences (*AIMS*), South Africa. In 2009 he received the LMS Naylor Prize and Lectureship.

Prof. Maini and Dr. Swat have met multiple times at conferences, workshops and during Prof. Maini's sabbatical at IU. They have never collaborated directly.

2. Prof. Mark Chaplain

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Prof. Chaplain is the Head of the Mathematics Department at the University of Dundee, Scotland. He has published about 130 scientific papers on mathematical and computational biology, 11 book chapters and edited 3 books. He has received multiple awards for scientific achievement including being a Fellow of The Royal Society of Edinburgh, Scotland and the London Mathematical Society Whitehead Prize.

Prof. Chaplain invited Dr. Swat to present a talk at the Cancer Modeling Workshop in Dundee, Scotland, Aug, 2010. Dr. Swat has also visited Dundee to train students in CompuCell3D modeling. Dr. Swat and Prof. Chaplain have not published any peer reviewed articles together.

3. Dr. Thomas Knudsen
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Dr. Tom Knudsen is a Developmental Systems Biologist at the US Environmental Protection Agency's National Center for Computational Toxicology. He received his Ph.D. in Anatomy from Thomas Jefferson University and postdoctoral training at the Children's Hospital Research Foundation in Cincinnati and Emory University. Before joining the EPA, held the rank of Professor at the University of Louisville. Dr. Knudsen's research focuses on predictive models of developmental toxicity, using high-throughput screening data, multicellular models and computational systems biology. In addition to his research at EPA, Dr. Knudsen is Adjunct Professor at the University of Louisville, Editor in Chief of *Reproductive Toxicology* and Past-President of the Teratology Society. He has received multiple NIH and NSF research

grants. He co-leads the Virtual Tissues project in the National Center for Computational Toxicology. He has published approximately 65 peer-reviewed articles

Dr. Swat and Dr. Knudsen have met multiple times at conferences and workshops. They have not published any scientific articles together.

4. Prof. Andreas Deutsch

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Prof. Deutsch is head of the department "Innovative Methods of Computing" in the Center for Information Services and High Performance Computing (Technische Universität Dresden). The Deutsch group possesses special expertise in the analysis of spatio-temporal pattern formation in biological systems at the molecular and cellular scale (Deutsch and Dormann, 2005). Applications focus on microorganismic pattern formation, organization principles of cellular and intracellular signalling networks and cancer.
Prof. Deutsch has published approximately 60 peer reviewed papers, 2 books and several book chapters. He is a Board Member of European Society for Mathematical and Theoretical Biology.

Prof. Deutsch and Dr. Swat have met multiple times at workshops, conferences and summer schools but have not collaborated directly.

5. Prof. Herbert Sauro

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Prof. Sauro is Associate Professor of Bioengineering at the University of Washington, Seattle. His research interests include: metabolic and systems transduction networks, computer simulation, non-linear dynamics and control analysis. He received an Award for Outstanding Technical Achievement from DARPA in 2005. He has published approximately 50 peer reviewed papers and written two textbooks. He is Senior Scientific Advisor to the NIH on Systems Biology and a founding member of the Systems Biology Markup Language standards committee. He has been recipient of multiple NIH, DOE and DARPA research grants.

Prof. Sauro and Dr. Swat have met multiple times at conferences and workshop. They have never collaborated on any publications

6. Prof. Nick Monk
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Prof. Monk is Associate Professor in the Department of Applied Mathematics at the University of Nottingham. He has published approximately 50 papers on computational biology and on cellular signaling networks and is an editor of one book.

Prof. Monk and Dr. Swat have met multiple times at conferences, but have never collaborated on any publication.

7. Dr. Yi Jiang
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Dr. Jiang is a Technical Staff Member in the Mathematical Modeling and Analysis Group of Los Alamos National Laboratory and Adjunct Associate Professor in the Department of Mathematics at the University of Notre Dame. Her research interests include soft condensed matter, biophysics, materials modeling, nonlinear and non-equilibrium dynamics, pattern formation, complex fluids and networks. She has published approximately 45 peer-reviewed papers and edited 2 books.

Dr. Swat and Dr. Jiang have met at conferences and workshops, but have not collaborated on any publication. Dr. Jiang invited Dr. Swat to present a CC3D tutorial at the Q-Bio 2008 Conference, which she co-organized.

8. Prof. Shane Hutson
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Prof. Hutson is Associate Professor of Physics and Biological Sciences at Vanderbilt University. He has published approximately 40 papers and one book chapter. He has received National Science Foundation Faculty Early Career Development (CAREER) Award and a Jeffrey Nordhaus Award for Excellence in Undergraduate Teaching in the College of Arts & Sciences at Vanderbilt University.

Dr. Swat and Prof Hutson have met multiple times at conferences and workshops but have never collaborated directly.