

BIRS meeting 09w5070

Multiscale Analysis of Self-Organization in Biology

Sunday, July 12 - Friday, July 17, 2009

Banff International Research Station (BIRS)

Organizers

Thomas Hillen (University of Alberta)

Benoit Perthame (Laboratoire J. L. Lions, University Pierre et Marie Curie).

Objectives

The mathematical modelling of biological systems has rapidly grown over the past decades. Positions in mathematical biology are announced in many Universities and relevant contributions are reported in the highest international journals. Most of the research is done on a model-computation-result and prediction basis. There are, however, very interesting mathematical problems related to these biological models. In this workshop we want to focus on the mathematical and analytical side of modelling, where we particularly focus on the use of integro-differential equations and partial differential equations for multi scale analysis of self organization in Biology. Here questions on finite-time blow-up, global existence, pattern formation, regularity and homogenization play an important role. Some of the models discussed here are brand new and their mathematical properties are basically unknown (for example integro differential equations).

Program

Coffee breaks are provided in Corbett Hall
morning coffee breaks are available 10:15 – 11:00
afternoon coffee breaks are available 2:30 - 3:30

Breakfast is 7:00 - 9:30 a.m.

Lunch is from 11:30 a.m. - 1:30 p.m.

Dinner 5:30 - 7:30 p.m. in the Banff Centre Dining Room.

Monday, July 12		
9:15 – 9:30	B. Perthame, T. Hillen	Welcome
9:30 – 10:15	A. Friedman	Free boundary problems in mathematical biology I
10:45 – 11:30	J.A. Carrillo	Some kinetic models in swarming
11:30 – 12:15	D. Levy	Group Dynamics in Phototaxis
4:30 – 5:15	A. Friedman	Free boundary problems in mathematical biology II
5:15 – 6:00	C. Cosner	Microscale movement and the evolution of dispersal
7:30 – 8:30	P. Babak R. Fetecau P. Hinow T. Lepoutre A. Lorz J. Wakano P. Bates S. Mirrahimi G. Raoul M. Morandotti Y. Ephsteyn S. Cuadrado H. Eberl D. Oelz	Introduction to posters
8:30 – 9:30		Poster session I
Tuesday, July 13		
9:30 – 10:15	A. Friedman	Free boundary problems in mathematical biology III
10:45 – 11:30	C. Schmeiser	Analysis and qualitative properties of a two-dimensional continuum model for cytoskeleton dynamics in the lamellipodium
11:30 – 12:15	P. Bates	Kinesin-Microtubule Interactions: Transport and Spindle Formation
2:30 – 3:30		Poster session II
3:30 – 4:15	M. Ward	Traps, Patches, Spots, and Stripes: An Asymptotic Analysis of Localized Solutions to Some Diffusive and Reaction-Diffusion Systems I

4:15 – 5:00	D. Wrzosek	Chemotaxis models with volume filling effect and singular diffusion
5:15 – 6:00	P. Laurencot	Global existence and blowup for the parabolic-elliptic Keller-Segel system with nonlinear diffusion
Wednesday, July 14		
9:30 – 10:15	M. Ward	Traps, Patches, Spots, and Stripes: An Asymptotic Analysis of Localized Solutions to Some Diffusive and Reaction-Diffusion Systems II
10:45 – 11:30	S. Cantrell	How biased density dependent movement of a species at the boundary of a habitat patch may mediate its within-patch dynamics
11:30 – 12:15	M. Lewis	Mathematical challenges in the modelling of biological invasions
Thursday, July 15		
9:30 – 10:15	M. Ward	Traps, Patches, Spots, and Stripes: An Asymptotic Analysis of Localized Solutions to Some Diffusive and Reaction-Diffusion Systems III
10:45 – 11:30	D. Kinderlehrer	Aspects of modeling transport in small systems with a look at motor proteins
11:30 – 12:15	A. Marciniak-Czopra	Hysteresis-driven pattern formation in a developmental system
2:30 – 3:30	Poster session III	
3:30 – 4:15	N. Bournaveas	Kinetic models of chemotaxis
4:15 – 5:00	R. Erban	From individual to collective behaviour of cells and animals
5:15 – 6:00	B. Kawohl	Convex sets of constant width, or why geometry can be of vital importance
Friday, July 16		
9:30 – 10:15	P. Souganidis	

10:45 – 11:30	HJ. Eberl	van Leeuwenhoek's and Hilbert's Microscopes: A spatially structured model of biofouling
11:30 – 12:15	A. Tosin	Tumor growth by a mixture theory approach: modeling and analytical issues

Participants

#	Participant	Affiliation	E-mail
1	Babak, Petro	University of Alberta	petro@ualberta.ca
2	Bates, Peter	Michigan State University	bates@math.msu.edu
3	Bournaveas, Nikolaos	University of Edinburgh	N.Bournaveas@ed.ac.uk
4	Cantrell, Stephen	University of Miami	r.cantrell@math.miami.edu
5	Carrillo, José Antonio	ICREA	carrillo@mat.uab.es
6	Cosner, Chris	University of Miami	c.cosner@math.miami.edu
7	Cuadrado, Silvia	Universitat Autònoma de Barcelona	silvia@mat.uab.es
8	Dolbeault, Jean	University of Paris Dauphine	dolbeault@ceremade.dauphine.fr
9	Eberl, Hermann J	University of Guelph	heberl@uoguelph.ca
10	Ephstejn, Yekaterina	Carnegie-Mellon University	rina10@andrew.cmu.edu
11	Erban, Radek	University of Oxford	erban@maths.ox.ac.uk
12	Fetecau, Razvan	Simon Fraser University	van@cs.sfu.ca
13	Friedman, Avner	Ohio State University	afriedman@mbi.osu.edu
14	Gong, Jiafen	University of Alberta	kgong@math.ualberta.ca
15	Hillen, Thomas	University of Alberta	thillen@ualberta.ca
16	Hinow, Peter	Institute for Mathematics and its Applications, University of Minnesota	hinow@ima.umn.edu
17	Jin, Yu	University of Alberta	yujin@math.ualberta.ca

18	Kawohl, Bernd	University of Koeln	kawohl@math.uni-koeln.de
19	Kinderlehrer, David	Carnegie Mellon University	davidk@andrew.cmu.edu
20	Laurençot, Philippe	Institut de Mathematiques de Toulouse (France)	laurenco@math.univ-toulouse.fr
21	Lepoutre, Thomas	Universite P. et M. Curie	thomas.lepoutre@inria.fr
22	Levy, Doron	University of Maryland, College Park	dlevy@math.umd.edu
23	Lewis, Mark	University of Alberta	mlewis@math.ualberta.ca
24	Lorz, Alexander	University of Cambridge	al464@cam.ac.uk
25	Marciniak-Czochra, Anna	University of Heidelberg	anna.marciniak@iwr.uni-heidelberg.de
26	Mirrahimi, Sepideh sadat	Universite P. et M. Curie	sepideh-sadat.mirrahimi@polytechnique.org
27	Morandotti, Marco	SISSA/ISAS	morandot@sissa.it
28	Oelz, Dietmar	Wolfgang Pauli Institut	dietmar.oelz@univie.ac.at
29	Perthame, Benoit	Laboratoire J. L. Lions, University Pierre et Marie Curie	benoit.perthame@upmc.fr
30	Raoul, Gael	ENS de Cachan	Gael.Raoul@cmla.ens-cachan.fr
31	Riviere, Tristan	ETH Zürich	riviere@math.ethz.ch
32	Schmeiser, Christian	University of Vienna	christian.schmeiser@univie.ac.at
33	Souganidis, Panagiotis	University of Chicago	souganidis@math.uchicago.edu
34	Tosin, Andrea	Politecnico di Torino	andrea.tosin@polito.it
35	Wakano, Joe Yuichiro	Meiji University	joe@math.meiji.ac.jp
36	Wang, Zhi An	University of Minnesota	zhiwang@ima.umn.edu
37	Ward, Michael	University of British Columbia	ward@math.ubc.ca
38	Wrzosek, Dariusz	University of Warsaw	darekw@mimuw.edu.pl

Abstracts
(alphabetically)

Participant	Title and Abstract
Babak, Petro	POSTER
Bates, Peter	POSTER and

Kinesin-Microtubule Interactions: Transport and Spindle Formation

This talk consists of two parts: Pattern formation in families of microtubules under the action of kinesin and the detailed motion of kinesin along a microtubule.

Microtubules are long cylindrical structures (lengths being tens of microns and diameter approximately 25 nm) comprised of tubulin dimers, which self-assemble, 13 protofilaments being required side-to-side to form the circular cross section. In the first set of results, microtubules are represented as stiff, polar rods which are subject to diffusion in position and orientation and also subject to pair-wise interaction, mediated by kinesin molecular motors. The concentration of kinesin is represented by a parameter that feeds into the probability of an interaction occurring when two microtubules collide. The probability of an interaction also depends on the location of the collision point along the lengths of the microtubules, because kinesin accumulates at the positive end of each microtubule. With collision rules in place, Monte-Carlo simulations for large numbers of freely moving microtubules are performed, adjusting parameters for concentration of kinesin and polarity of the microtubules. From these studies, a phase diagram is produced, indicating thresholds for phase change to occur. Simulation results are compared to those from *in vitro* experiments.

The second part of the talk involves modeling the fine scale dynamics of a kinesin motor as it 'walks' along a microtubule. The two heads of the kinesin molecule alternately bind and unbind to the microtubule with certain mechanisms providing a directional bias to the Brownian motion expected. One bias is the shape of the head and the shape of the binding site, along with the companion electrostatic charges.

The second bias is that, utilizing ATP capture and transferal of phosphors for energy, part of the polymeric leg (neck-linker) of the bound head becomes attached towards the front of that head (the "zipped" state). The trailing head detaches from the microtubule. It then becomes subject to the biased entropic force due to the zipped state of the leading head and also preferentially (because of shape orientation) attaches in front of the currently attached head at which time ADP is released and a conformational change occurs, strengthening the binding. This motion is modeled using stochastic a differential equation. Simulations are performed with different lengths of neck-linkers and the mean speeds of progression obtained. These are compared with experimental results.

(with Zhiyuan Jia)

Boumaveas,
Nikolaos

Kinetic models of chemotaxis.

Chemotaxis is the directed motion of cells towards higher concentrations of chemoattractants. At the microscopic level it is modeled by a nonlinear kinetic transport equation with a quadratic nonlinearity. We'll discuss global existence results obtained using dispersion and Strichartz estimates, as well as some blow up results.

(joint work with Vincent Calvez, Susana Gutierrez and Benoit Perthame).

Cantrell, Stephen

How biased density dependent movement of a species at the boundary of a habitat patch may mediate its within-patch dynamics.

In this talk we will discuss some reaction-diffusion models for the propagation of a species' density in a bounded habitat. The particular models we will consider are of diffusive logistic type in the interior of the patch, subject to a nonlinear condition on the boundary of the patch of the form

$$a(u) * \text{grad}(u) \cdot \mathbf{n} + (1 - a(u)) * u = 0.$$

Here $a(u)$ is a non-decreasing nonnegative function of the species' density that takes values between 0 and 1 when u is between 0 and the local carrying capacity of the species under the logistic growth law, which is presumed to be constant on the patch. When $a(u)$ is identically constant, the prediction of the model is that all nonnegative nontrivial initial species density profiles evolve to 0 in the case of extinction or to a unique positive equilibrium profile in the case of survival. By way of contrast, in the case when $a(u)$ is non-constant, the dynamics at the scale of the patch may be more complicated. In particular, such $a(u)$ may mediate Allee effects at the scale of the patch, consistent with empirical results for the Glanville fritillary butterfly. The models demonstrate how meso-scale effects locally at the boundary of a habitat patch may mediate macro-scale effects on the patch as a whole.

This work is joint with Chris Cosner and Salome Martinez.

Carrillo, José
Antonio

Some kinetic models in swarming

I will present a kinetic theory for swarming systems of interacting, self-propelled discrete particles. Starting from the particle model [\cite{DCBC}](#), one can construct solutions to a kinetic equation for the single particle probability distribution function using distances between measures [\cite{dobru}](#).

Moreover, I will introduce related macroscopic hydrodynamic equations. General solutions include flocks of constant density and fixed velocity and other non-trivial morphologies such as compactly supported rotating

mills. The kinetic theory approach leads us to the identification of macroscopic structures otherwise not recognized as solutions of the hydrodynamic equations, such as double mills of two superimposed flows.

I will also present and analyse the asymptotic behavior of solutions of the continuous kinetic version of flocking by Cucker and Smale \cite{CS07}, which describes the collective behavior of an ensemble of organisms, animals or devices. This kinetic version introduced in \cite{HT08} is obtained from a particle model. The large-time behavior of the distribution in phase space is subsequently studied by means of particle approximations and a stability property in distances between measures. A continuous analogue of the theorems of \cite{CS07} will be shown to hold for the solutions on the kinetic model. More precisely, the solutions concentrate exponentially fast their velocity to their mean while in space they will converge towards a translational flocking solution.

The presentation is based in works in collaboration \cite{CCR,CDP,CFRT}.

\bibitem{CCR}

J. A. Carrillo, J. A. Cañizo and J. Rosado. Well-posedness of the swarming equations in the space of measures, work in preparation.

\bibitem{CDP}

J. A. Carrillo, M. R. D'Orsogna and V. Panferov. Double milling in self-propelled swarms from kinetic theory, to appear in \textit{Kinetic and Related Models}.

\bibitem{CFRT}

J. A. Carrillo, M. Fornasier, J. Rosado and G. Toscani. Asymptotic Flocking Dynamics for the kinetic Cucker-Smale model, preprint.

\bibitem{CS07}

F. Cucker and S. Smale. Emergent behavior in flocks. \emph{IEEE Trans. Automat. Control}, \textbf{52} (2007), 852--862.

\bibitem{dobru} R. Dobrushin. Vlasov equations.

\emph{Funct. Anal. Appl.}, \textbf{13} (1979), 115--123.

\bibitem{DCBC}

M.R. D'Orsogna, Y.-L. Chuang, A. L. Bertozzi, L. Chayes. Self-propelled particles with soft-core interactions: patterns, stability, and collapse. \emph{Phys. Rev. Lett.}, \textbf{96} (2006), 104302-1/4.

\bibitem{HT08} S.-Y. Ha and E. Tadmor. From particle to kinetic and hydrodynamic descriptions of flocking. \emph{Kinetic and Related Models}, \textbf{1} (3) (2008), 415-435.

The dispersal of organisms is clearly a significant aspect of many ecological processes, but the evolution of dispersal is still not well understood. In the setting of reaction-advection-diffusion models and their discrete analogues there is evidence that in spatially variable but temporally constant environments the dispersal strategies that are evolutionarily

stable are those that allow populations to distribute themselves to match the distribution of their resources. Such strategies produce population distributions where fitness is zero everywhere (since all resources are used) and there is no net movement at equilibrium. Those features characterize populations that are distributed according to the ideal free distribution, where each individual locates itself to maximize its fitness. Whether or not a diffusion process derived from a simple random walk can support such an ideal free dispersal strategy depends on microscale assumptions about local movement probabilities. Classical physical diffusion as described by Fick's law cannot support such strategies without additional advection terms, and in fact if dispersal strategies are restricted to classical diffusion there is selection for lower diffusion rates. However, changing the assumptions about microscale movement can lead to diffusion models that can support some type of ideal free dispersal. At the mesoscale, adding advection to classical diffusion can achieve similar results. This talk will describe these ideas and some of their implications.

Cuadrado, Silvia	POSTER
Dolbeault, Jean	
Eberl, Hermann J	van Leeuwenhoek's and Hilbert's Microscopes: A spatially structured model of biofouling
	<p>When studying microbial population and resource dynamics, mathematical biologists and experimental microbiologists have traditionally focused on suspended bacterial populations. In fact, the well-developed theory of the chemostat can be considered one of the biggest success stories in Mathematical Biology. However, it is becoming more and more accepted now that most bacterial populations live in fact as spatially structured microbial depositions on surfaces, usually in aqueous environments. These biofilms play beneficial roles in environmental processes (pollution degradation), and detrimental roles in industrial (biofouling, biocorrosion) and medical contexts (bacterial infections, health risks). In the past decade a variety of mathematical models of these biofilms have been proposed, focusing on different aspects and time-scales of biofilm processes and utilizing a variety of mathematical model concepts (ranging from individual based models to cellular automata and models of continuum mechanics). We discuss in some detail a density-dependent diffusion-reaction model for population and resource dynamics in a single-species/single-substrate biofilm and show in some examples how this modeling concept can be applied to more involved biofilm processes. This model is a meso-scopic model of spatial organisation; we will also comment on but not present solutions to multi-scale challenges in biofilm modeling.</p>
Ephsteyn, Yekaterina	POSTER
Erban, Radek	From individual to collective behaviour of cells and animals

In this talk, we focus on two model systems: flagellated bacteria and locust nymphs. In both cases, the individual behaviour can be described as a biased random walk, although the nature of the bias and the corresponding mathematical models differ. We present methods for inferring collective properties from the individual-based models.

Flagellated bacteria are modelled as the velocity jump process with internal dynamics. We show that this framework can be used for relating the coefficients of macroscopic partial differential equations (which describe the evolution of the density of cells) to parameters of the intracellular signal transduction mechanism. Moreover, we also show that the velocity jump process with (metabolic) internal variables can be used to study travelling waves in the density of cells.

Locusts are modelled using a modified self-propelled particle model. Systematic analysis of the experimental data reveals that individual locusts appear to increase the randomness of their movements in response to a loss of alignment by the group. We show how properties of individual animal behaviour can be implemented in the self-propelled particle model to replicate the group-level dynamics seen in the experimental data.

Fetecau, Razvan	POSTER
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Friedman, Avner	Free boundary problems in mathematical biology I, II, III
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In this talk I will give a brief overview of some general free boundary problems, such as variational inequalities and Hele-Shaw problems. I will then focus on mathematical models of tumor growth, wound healing, cartilage growth, etc. For some of the models I will describe the shape of the free boundary, bifurcation of the free boundary, and asymptotic stability results. Open problems will be described.

Gong, Jiafen	
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Hillen, Thomas	
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Hinow, Peter	POSTER
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Jin, Yu	
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Kawohl, Bernd	Convex sets of constant width, or why geometry can be of vital importance.
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When does a steel pipe have an exactly circular cross section? When it features constant exterior width from each angle? That could easily be verified with a big caliper or slide gauge, and this what used to happen in the process of assembling booster rockets for the space shuttle. The authors of the corresponding manuals had overlooked that there are geometric shapes, so-called sets of constant width, that are not circles. This was a contributing factor to the Challenger disaster in 1986. In my talk I will point out that these odd sets show up in our daily life, and that there are interesting mathematical questions connected with them. The

talk is directed at a general audience.

Kinderlehrer,
David

Aspects of modeling transport in small systems with a look at
motor proteins

Motion in small live systems has many challenges. Prominent environmental conditions are high viscosity and warmth. It is difficult to move and maintaining a course is compromised by immersion in a highly fluctuating bath. We discuss some possibilities for motor proteins, which transduce chemical energy into directed mechanical energy. Such nanoscale motors, like conventional kinesin, have a role in intracellular transport, separating the mitotic spindle, and many other cellular functions. Our approach is to formulate a dissipation principle connected to the Monge-Kantorovich mass transfer problem. We show how this leads to a system of evolution equations. We then discuss how various elements of the system must be related in order that transport actually occur. Finally, what opportunities do these ideas offer? We examine some 'hybrid variational problems' and discuss unresolved issues.

Laurençot,
Philippe

Global existence and blowup for the parabolic-elliptic Keller-
Segel system with nonlinear diffusion

Whether solutions to the parabolic-elliptic Keller-Segel system with nonlinear diffusion are global or blow up in finite time is investigated in one space dimension and in several space dimensions for radially symmetric initial data. The study mainly relies on an alternative formulation of the problem and virial identities.

Lepoutre, Thomas POSTER

Levy, Doron

Group Dynamics in Phototaxis

Microbes live in environments that are often limiting for growth. They have evolved sophisticated mechanisms to sense changes in environmental parameters such as light and nutrients, after which they swim or crawl into optimal conditions. This phenomenon is known as "chemotaxis" or "phototaxis." Using time-lapse video microscopy we have monitored the movement of phototactic bacteria, i.e., bacteria that move towards light. These movies suggest that single cells are able to move directionally but at the same time, the group dynamics is equally important. Following these observations, in this talk we will present a hierarchy of mathematical models for phototaxis: a stochastic model, an interacting particle system, and a system of PDEs. We will discuss the models, their simulations, and our theorems that show how the system of PDEs can be considered as the limit dynamics of the particle system. Time-permitting, we will overview our recent results on particle, kinetic, and fluid models for phototaxis.

This is a joint work with Devaki Bhaya (Department of Plant Biology, Carnegie Institute), Tiago Requeijo (Math, Stanford), and Seung-Yeal Ha (Seoul, Korea).

Lewis, Mark

Mathematical challenges in the modelling of biological
invasions

Biological invaders are introduced locally, and then spread spatially into new environments, often impacting ecosystems. Models for invasions track the front of an expanding wave of population density. The underlying equations are often systems of parabolic partial differential equations and related integral formulations.

I will structure this talk around three challenges in the analysis of biological invasions where mathematical theory has provided new insight:

(i) Reid's paradox of rapid plant migration. How were trees able to migrate very quickly behind retreating ice sheets after the last ice age?

(ii) Multispecies competition paradox. Why do classical mathematical methods, based on linearization, fail to predict the rate of competitive spread of one species into another?

(iii) Reid's paradox in multispecies communities. Pollen data indicates that secondary species can spread very quickly into regions already occupied by a close competitor. How can this spread occur so quickly?

Each of these challenges will be addressed using mathematical analysis to provide insight regarding the behaviour of the biological models. I will finish by suggesting some new mathematical challenges where biological invasion theory and mathematical models meet.

Lorz, Alexander

POSTER

Marciniak-
Czochra, Anna

Hysteresis-driven pattern formation in a developmental
system

It is becoming increasingly clear that multistability plays an important role in cell signalling. Coupled with the diffusion process, it may give rise to spatial patterns in chemical and biological systems, such as Liesegang rings formed by precipitating colloids and bacterial growth patterns. Processes containing switching between different pathways or states lead to new types of mathematical models, which consist of nonlinear partial differential equations of diffusion, transport and reactions, coupled with dynamical systems controlling the transitions. Diffusion tries to average different states and is the cause of spatio-temporal patterns. Based on these concepts we propose a model for pattern formation in a fresh-water polyp, hydra, a simple organism, which can be treated as a prototype for axis formation in higher organisms. The proposed model shows how the hysteresis in intracellular signalling may result in spatial patterning. In particular, it demonstrates that bistability in the dynamics of the growth factor controlling cell differentiation explains the experimental observations on the multiple head formation in hydra, which is not

possible to describe using classical Turing-type models. Depending on the type of nonlinearity stationary and oscillatory patterns are found. The model is discussed in the context of recent experimental findings of the Wnt and Dkk overexpression during regeneration.

Mirrahimi, Sepideh sadat	POSTER
Morandotti, Marco	POSTER
Oelz, Dietmar	POSTER
Perthame, Benoit	
Raoul, Gael	POSTER
Riviere, Tristan	
Schmeiser, Christian	Analysis and qualitative properties of a two-dimensional continuum model for cytoskeleton dynamics in the lamellipodium.

A recently developed continuum model for the dynamics of the actin cytoskeleton in lamellipodia will be presented. It is derived from a microscopic description of the bending, polymerization and depolymerization of individual cross-linked actin filaments taking into account substrate adhesion and mechanical effects of the leading edge. The model can be seen as a generalized gradient flow, however, equipped with a number of peculiarities like nonconvexity of the energy functional and of the manifold of admissible states, as well as energy gain and loss through (de)polymerization and the building and breaking of cross-links and adhesions. Aspects of the existence and numerical analysis and of qualitative properties of simplified model problems will be presented (joint work with D. Oelz and N. Sfakianakis).

Souganidis, Panagiotis	
Tosin, Andrea	Tumor growth by a mixture theory approach: modeling and analytical issues

Resorting to the theory of deformable porous media, we address tumors as a mixture of abnormal and healthy cells within a porous extracellular matrix (ECM), which is wet by a physiological extracellular fluid. In the talk, we will focus mainly on the modeling of the mechanical interactions between a growing tumor and the host tissue, their influence on tumor growth, and the attachment/detachment mechanisms between cells and ECM. Then, by weakening the role of the extracellular matrix, we will derive a system of PDEs describing the evolution of the cell density coupled to the dynamics of some nutrient, e.g., oxygen, whose higher and lower concentration levels determine proliferation or death of cells, respectively, and we will briefly discuss some related analytical issues.

Wakano, Joe Yuichiro	POSTER
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A survey of the development and application of singular perturbation methods to treat a variety of both linear and nonlinear PDE models of diffusion and reaction-diffusion type with localized solutions is presented. Many of the problems considered have certain key common elements, notably related to the Neumann Green's function and the reduced-wave Green's function, and their regular parts. We highlight some of these key elements, and suggest some open problems and possible further directions.

In the first lecture we focus on three different linear diffusive problems; the narrow escape problem for diffusion from within a sphere to small traps on its boundary, the analysis of free diffusion on the boundary of a sphere with small traps, and the determination of the persistence threshold for the diffusive logistic model in a highly patchy spatial environment. For the first two problems we derive two discrete variational problems, related to classical Fekete points, that are central to determining the mean first passage time.

In the second lecture, we study localized spot-type solutions to certain non-variational reaction-diffusion systems, notably the Gray-Scott and Schnakenburg models, in a two-dimensional spatial domain. The dynamics of spots will be determined, and three different (but generic) types of instabilities for spot-patterns will be discussed and analyzed: spot self-replication, spot-annihilation, and spot oscillations. Phase diagrams indicating parameter regimes where these instabilities occur will be constructed. The asymptotic analysis to construct quasi-equilibrium spot patterns is shown to be rather similar to that used to treat the linear diffusive problems in the first lecture.

In the third lecture, we highlight some results for the analysis of localized stripe solutions to some reaction-diffusion systems in planar domains. In many instances a stripe or ring pattern is unstable to a breakup instability, which leads to the disintegration of the stripe or ring into a sequence of spots. In other cases, a stripe is de-stabilized by a transverse or zigzag instability, leading to a wiggled stripe. In certain cases, this wiggled stripe is the precursor to a complicated space-filling labyrinthian pattern. Our analysis of stripe stability involves a combination of singular perturbation theory, the spectral theory of nonlocal eigenvalue problems, and

numerical eigenvalue computations.

Wrzosek, Dariusz Chemotaxis models with volume filling effect and singular diffusion.

A quasilinear parabolic system of Keller-Segel type in which it is assumed that 1) there is a critical threshold value the density of cells cannot exceed and 2) the diffusion of cells becomes singular when the density approaches the threshold. The structure of the model includes recent models by Wang and Hillen (2007) with fast diffusion and that of Lushnikov (2008) with superdiffusion. It is proved that for some range of parameters describing the relation between the diffusive and the chemotactic part of a cell flux there are global-in-time classical solutions which in some cases are separated from the threshold uniformly in time. For the case of fast diffusion existence and uniqueness of global weak solutions and stationary solutions are studied. Applications of general results to particular models are shown.