INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET EN AUTOMATIQUE

Project-Team numed

Numerical Medicine

Grenoble - Rhône-Alpes

Theme : Observation, Modeling, and Control for Life Sciences

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1. Team

Research Scientists

Vincent Calvez [Researcher (CNRS)]
Benjamin Ribba [Researcher (INRIA)]

Faculty Members

Emmanuel Grenier [Team leader, Professor (ENSL), HdR]
Paul Vigneaux [Assistant Professor (ENSL)]
Marie-Aimée Dronne [Assistant Professor (Lyon I)]

Technical Staff

Violaine Louvet [Research Ing. (CNRS)]
Thierry Dumont [Research Ing Lyon I]

PhD Students

Séverine Enault [phD student (ENSL)]
Floriane Lignet [phD student (ENSL)]

Post-Doctoral Fellow

Branka Bernard [Post doc (Lyon I)]

2. Overall Objectives

2.1. Overall Objectives

The purpose of Numed is to develop new numerical methods and tools to simulate and parametrize complex systems arising in biology and medecine. Numed focuses on two axes:

- numerical methods for complex systems with several time and spatial scales. In particular: numerical simulations in complex domains, stiff reaction diffusions equations, multifluids systems, cell migration models, cell compressibility models, complex cancer models analysis.
- parametrization of complex systems using nonlinear mixed effect methods and populationnal pharmacokinetic pharmacodynamics models, with applications in oncology and virology.

Numed investigates two main applications

- Stroke: models of brain stroke (ionic exchanges, inflammation, free radicals, ...)
- Cancer: local invasion, angiogenesis, parametrization, glioma modeling.

and a few other subjects (models of prion, FIV, vaccine,...).

2.2. Highlights

Two awards:

- "Cristal du CNRS" for V. Louvet
- Blaise Pascal prize (French Academy of Science) for E. Grenier

3. Scientific Foundations

3.1. Mathematical modeling of cell motion

3.1.1. Kinetic models for bacterial collective motion

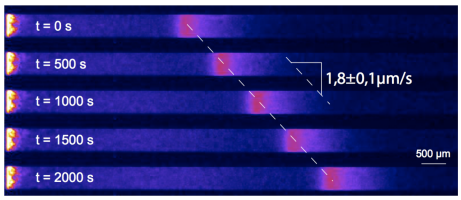

Figure 1.

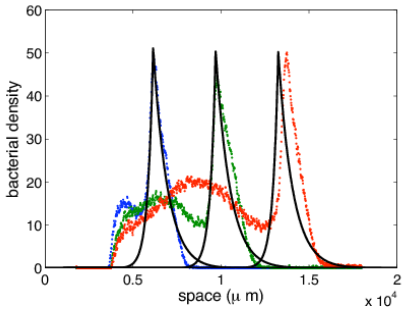

Figure 2. Bacterial waves traveling in a narrow channel (experiments and numerical simulations). The drift-diffusion limit captures well the macroscopic features of the wave (speed and asymmetric profile). (Figures taken from Saragosti et al, PLoS Comput. Biol. 2010)

We have investigated kinetic models for bacterial chemotaxis following Alt and co-authors, Erban and Othmer, Dolak and Schmeiser. First we have analysed the possible mathematical behaviours of such models. We have shown that a critical mass phenomenon occurs in dimension $N = 2$ as for the classical Keller-Segel model (with N. Bournaveas, Univ. Edimburgh). This is one of the few existing results concerning blow-up in kinetic models. The hyperbolic limit of this toy model is under investigation.

Second, we have developped a quantitative approach based on a couple of experiments performed by J. Saragosti in the team of A. Buguin and P. Silberzan (Institut Curie, Paris). These experiments describe with full statistical details solitary waves of bacteria E. coli in narrow channels. On the first set of experiments we have demonstrated that the drift-diffusion approximation of the kinetic model is valid and it fits the data very well (publication in PLoS Comput. Biol., Figure 2). On the second set of experiments we have simulated the kinetic model to obtain the best results as compared to the data in this context (work recently submitted). We believe that the full kinetic model is required to describe the data.

This leads to a new class of chemotaxis models, which differ significantly from the classical Keller-Segel model because they lack a gradient structure in the attractive field. We have started a systematic analysis of these models. This is a work in progress with N. Bournaveas (Univ. Edimburgh), F. Chardard (ENS de Lyon) and Ch. Schmeiser (Univ. Vienna). This analysis includes existence of inhomogeneous steady states, stability, speed of relaxation towards equilibrium.

3.1.2. Spatial complexity: collective motion of cells

- Mathematical analysis of the Keller-Segel model

[In collaboration with J.A. Carrillo and J. Rosado (UAB, Barcelona)]

Following McCann 1997 and Otto 2001, we interpret the classical Keller-Segel system for chemotaxis as a gradient flow in the Wasserstein space. The free-energy functional turns out to be homogeneous. This viewpoint helps to understand better blow-up mechanisms, and to derive rates of convergence towards self-similar profiles. We investigate more precisely linear diffusion, porous medium diffusion and fast diffusion in competition with various interaction kernels.

[In collaboration with N. Meunier (Paris 5) and R. Voituriez (Paris 6)]

Another project consists in analyzing some variant of the Keller-Segel system when the chemoattractant is secreted at the boundary of the domain. This is motivated by modeling issues in cell polarization.

- Kinetic models for bacterial collective motion

[In collaboration with N. Bournaveas (Univ. Edinburgh)]

We shed a new light on the theoretical analysis of kinetic equations for chemotaxis: we exhibited a peculiar example subject to a critical mass phenomenon as for the two-dimensional Keller-Segel system. This shows a posteriori that previous attempts to show global existence were in fact borderline with respect to this critical example.

[In collaboration with N. Bournaveas (Univ. Edinburgh), B. Perthame (Paris 6), A. Buguin, Jonathan Saragosti and P. Silberzan (Institut Curie, Paris)]

We have developed a macroscopic model for bacterial traveling pulses based on a mesoscopic description of the run-and-tumble process. We are able to capture some key features observed in the experiments (asymmetric profile, speed of the pulse).

3.1.3. Complex rheology

To investigate the growth of a tumor it is crucial to have a correct description of its mechanical aspects. Tumoral and normal cells may be seen as a complex fluid, with complex rheology.

Numerical investigations of complex flows is studied by P. Vigneaux who develops new numerical schemes for Bingham type flows (viscoplastic flows).

3.1.4. Modeling of spontaneous cell polarisation

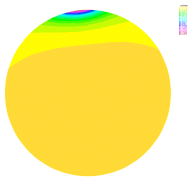

Figure 3.

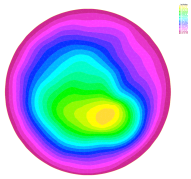

Figure 4.

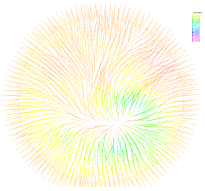

Figure 5. 2D numerical simulations of cell polarisation on a round shaped cell. (Top) The actin network carries the attractive field: polarisation occurs. (Bottom) The microtubules carry the attractive field: we observe no polarisation. (Work in progress; simulations are done with FreeFEM++)

We have analysed thoroughly recent models describing spontaneous polarisation of cells (e.g. neuron growth cones or budding yeast). These models combine a diffusive term (in the cytoplasm) plus an advective field created at the membrane and diffusing in the cytoplasm (accounting for the actin network or the microtubules). This can be compared to the classical Keller-Segel model where diffusion competes with a non-local attractive field. Going beyond linear stability analysis we have used our know-how of the Keller-Segel system to derive global existence (no polarisation) and blow-up (possibly polarisation) criteria. We have also performed some numerical experiments to determine the models which exhibit spontaneous polarisation. We have confirmed the prediction made by the physicists claiming that the microtubules cannot drive the cell into spontaneous polarisation whereas the actin network can.

3.2. Mathematical study of models of tumor growth

In her PhD thesis (defended in december 2010), S. Enault proved a serie of existence results for tumor growth models

- Incompressible models

  Let c be the density of tumoral cells and s the density of sane cells. Then as a first modelling, we assume that c and v are transported by a velocity field v deriving from a pressure p, and of course that tumoral cells multiply. This gives

$$\begin{cases} \partial_t c + v\nabla c = c(1-c) \\ \nabla \cdot v = c \\ v = -\nabla p \end{cases} \tag{1}$$

  Following the arguments of Kato on 2D incompressible Euler equations, S. Enault proves the existence of global weak solutions in R^d, for Lipschitz compact supported initial data. If the initial condition is more regular, we get global smooth solutions of this system.

- Compressible models:

  An other classical model is to consider that the tumor is incompressible whereas the sane cells are compressible. This leads to

$$\begin{cases} \partial_t c + \nabla \cdot (cv) = \alpha(p)\gamma(c) \\ (1-c)\rho_s'(p)\left(\partial_t p + v \cdot \nabla p\right) - k\rho_s(p)\Delta p = \rho_s(p)\left(\alpha(p)\gamma(c) - m(p)(1-c)\right) \\ v = -k\nabla p \end{cases} \tag{2}$$

  which is a delicate degenerated parabolic system. S. Enault proves the existence of a strong solution, in small time, in a bounded domain.

- S. Enault also compares the two previous systems to investigate the effect of compressibility on the dynamics of the tumor.

- In some cases it is natural to assume that sane and tumoral cells reacts with a different velocity to a gradient pressure, which leads to

$$\begin{cases} \partial_t c + \nabla \cdot (k_c c v) = \alpha c \\ \partial_t s + \nabla \cdot (k_s s v) = 0 \\ v = -\nabla p \end{cases} \tag{3}$$

  When $k_s \neq k_c$ then S. Enault proves that there exists smooth initial data leading to the apparition of a discontinuity (shock) in finite time. On the contrary when $k_s = k_c$ then for any smooth initial data there exists a unique smooth global solution.

4. Application Domains

4.1. Stroke models

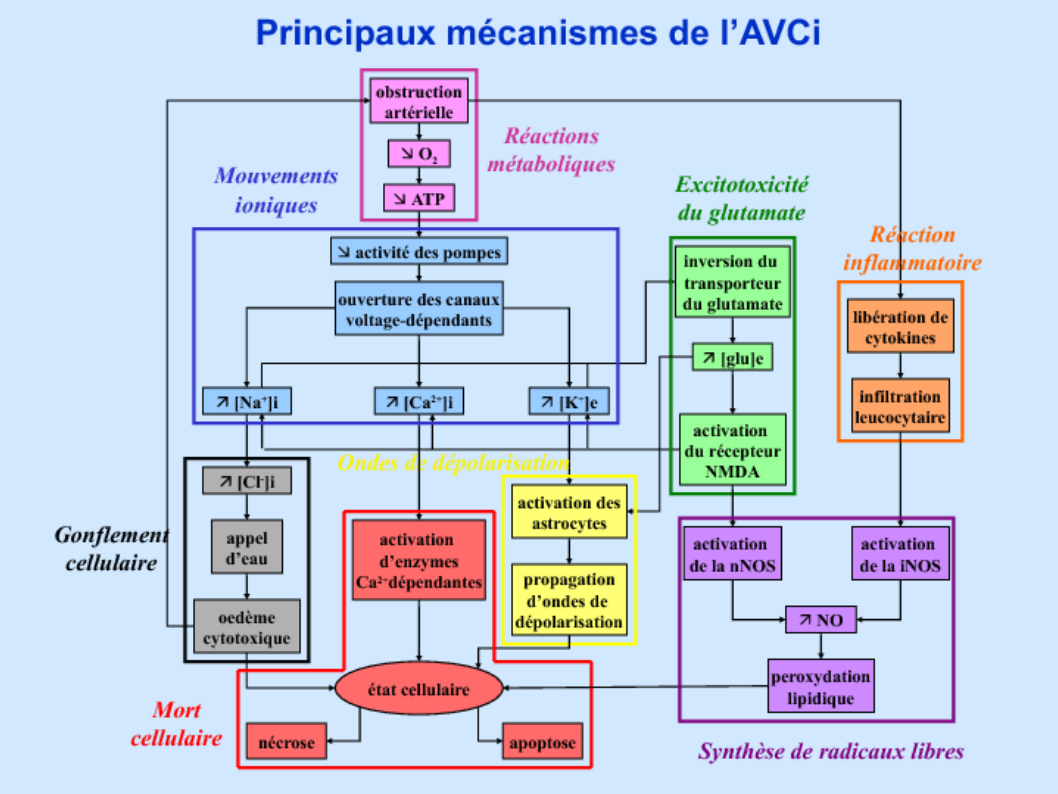

Figure 6. Models in stroke

4.1.1. Inflammation modelling

MA Dronne has designed a first model of inflammation at cellular level, based on ordinary differential equations. To take into account spatial phenomena, a first partial differential equation based model is under study. Together with Taissia Lelekov Boissard (post doc of the ANR contrat "AVC in silico"), they tried to find biological data to parametrize these models, and to build a basis of qualitative facts that must be reproduced by the model.

MA Dronne has also developped a collaboration with the Mario Negri institute (Milano) through the team "inflammation and nervous system diseases" (MG de Simoni). This teams currently runs in vivo experiments in rodent that should provide new data to investigate the temporal evolution of various variables of the model.

The study and validation of these two models of inflammation will continue with the study of in silico experiments which will simulate the action of various anti inflammatory drugs, acting at various levels of the inflammatory reaction, work in common with biologists (INSERM 842, neurooncologie et neuro inflammation, Lyon), with clinicians (Creatis, Umr 5515, Inserm U 630 Lyon).

4.1.2. Free radicals

A first model of free radical synthesis has been initiated by V. Lemesle (post doc of ANR AVC in silico). This model is under development with P. Vigneaux. A collaboration begins with Michel Plotkine (EA 2510 pharmacology of cerebral blood flow, Paris 5 university) to get experimental data on the temporal evolution of the various variables of the model.

This model will be used to manage in silico experiments in order to study the effects of various drugs.

4.1.3. Ionic motions

A mechanistic model of ionic motions has already been developped, studied and validated to study in silico the dual role of astrocytes during ischemia, and to study the effect of various ionic chanels blockers in man and roden.

This model is now used to study in silico the effect of the combination of several neuroprotectors acting on ionic channels, transporters or receptors. This work should help to understand antagonist or synergic effects of blockers.

4.1.4. Spreading depression

Spreading depressions are propagative waves which travel in brain during ischemia and which may have a major role in the extension of the ischemic core. Currently 3D computations in real geometry are run to study their speed and the role of brain anatomy in their propagation.

4.1.5. Apoptosis during stroke

A collaboration has begun with Christiane Charriaut Marlangue (INSERM U676, Hopital Robert Debré) to study the apoptotic cascade during stroke.

4.2. Oncology

4.2.1. Modeling vascular tumor growth in mice

In collaboration with the group of Pr. Freyer in Lyon-Sud Hospital, we have developed a mathematical model to analyse complex vascular tumor growth in xenografted mice. This project is based on the idea that optimizing the delivery of antiangiogenic drug, a new class of anticancer medicine, would require the development of drug-disease models of vascular tumor growth incorporating histological data indicative of therapy efficacy. We formulated a model to simultaneously analyze longitudinal tumor size data together with histological markers.

The model is composed by four ODEs and focuses on the evolution of non-hypoxic, hypoxic and necrotic tissue within the tumor. It integrates an unobserved variable, the carrying capacity which accounts for the process of angiogenesis. The model is shown to correctly predict tumor growth dynamics as well as percentages of necrotic and hypoxic tissues within the tumor. The work has been published in European Journal of Cancer in 2010.

4.2.2. Modeling chemotherapy efficacy in low-grade gliomas

In collaboration with the group of Prof. Honnorat in Lyon-Est neurological hospital and INSERM, we have developed a mathematical model to analyze tumor evolution and response to chemotherapy in patients with brain tumors. Low-grade gliomas are highly diffuse brain tumors characterized by a slow and continuous evolution. Chemotherapy PCV (Procarbazine, CCNU, Vincristine) appears to be a relevant therapeutic option for large tumors. However, among clinicians, there are open questions regarding the best way to deliver this chemotherapy.

Based on the hypothesis that LGGs consist of proliferative treatment-sensitive cells and quiescent treatment-resistant cells that spontaneously undergo apoptosis we propose a mixed-effect model that accurately describes the evolution of these tumors during and after PCV chemotherapy. Model evaluation was performed in a series of 21 patients treated with first-line PCV chemotherapy in which the evolution of the mean tumor diameter (MTD) had been previously assessed. This model suggests that tailoring the time interval between PCV cycles according to LGGs individual growth characteristics might be a way to increase the efficacy of this chemotherapy regimen. This work is submitted for publication in a clinical journal.

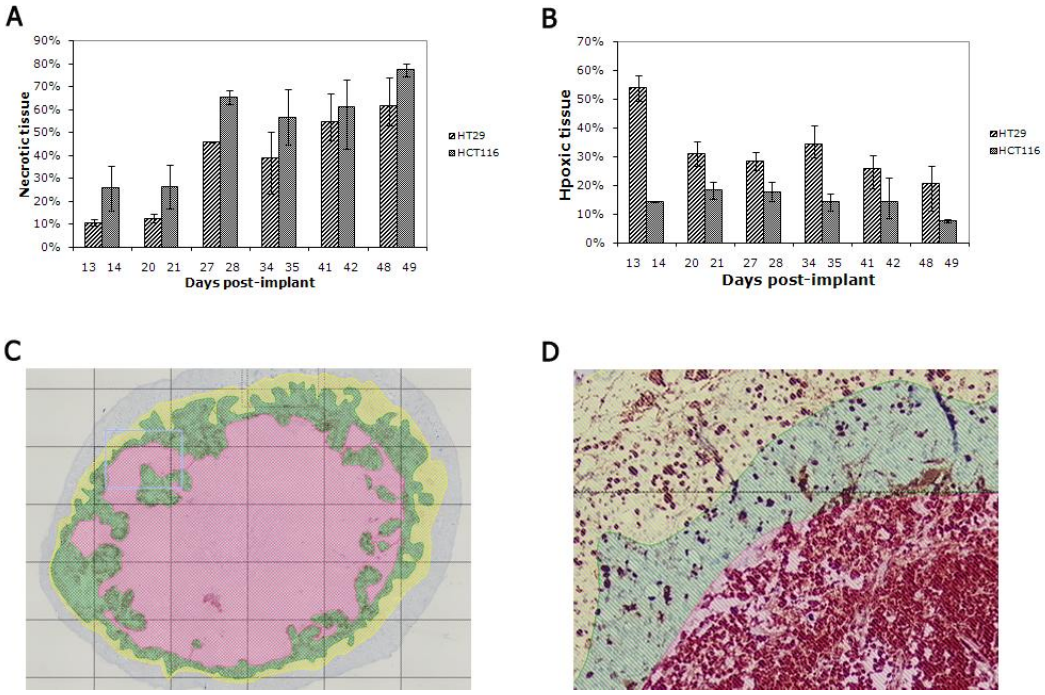

Figure 7. Data analyzed. A: percentage of necrotic tissue; B: hypoxic tissue; C: illustration of a tumor slice after immunhistochemical staining to reveal the different types of tissue; D: zoom of image C.

4.2.3. Radioresistance

Within the framework of the project ETOILE, B. Bernard is part of the team that is building a predictive model of tumor responses to the conventional treatment and irradiation with carbon ions. During 2009, Branka has been working under supervision of Jean-Pierre Boissel and Benjamin Ribba. In collaboration with the group of Claire Rodriguez-Lafrasse (Radiobiology group, Hospital Lyon Sud), her research activities included the analysis of microarray data from different head and neck cancer cell lines, irradiated with X-ray and carbon ions. They detected differences in the irradiation response of different cancer cell lines that underlie their different radiosensitivities. Within GRAAL project, a lot of radiobiological information will be acquired on a several glioma cell lines and cell lines representing healthy brain tissue. Therefore, our interest is to model the dynamics of the glioma tumor growth and its response to radiation therapy.

4.3. Virology

In collaboration with MERIAL SA and Edouard Heriot Hospital in Lyon, B. Ribba develops mathematical models to describe the dynamic of Feline immunodeficiency virus (FIV) in infected cats. A translational

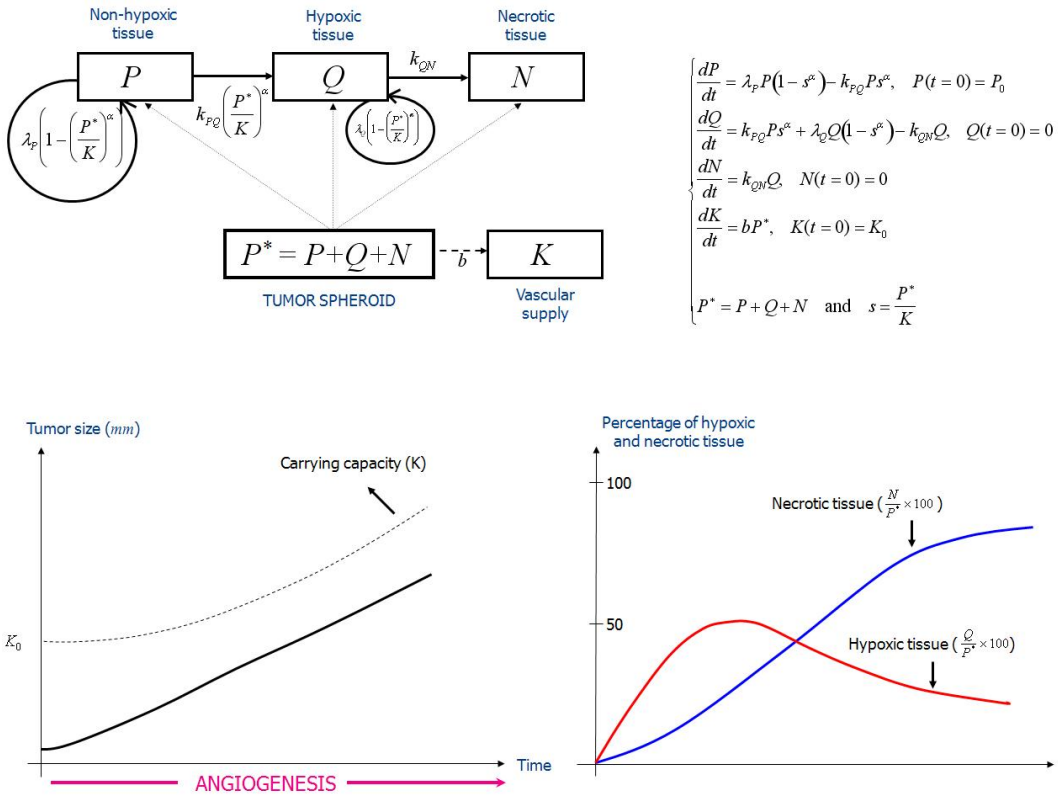

Figure 8. Schematic view of the model and time evolution of the main variables.

approach is developed in the context of parameter estimation for complex biologically-based model. He intensively uses mixed-effect modeling approaches and its SAEM algorithm implementation in MONOLIX (INRIA Saclay).

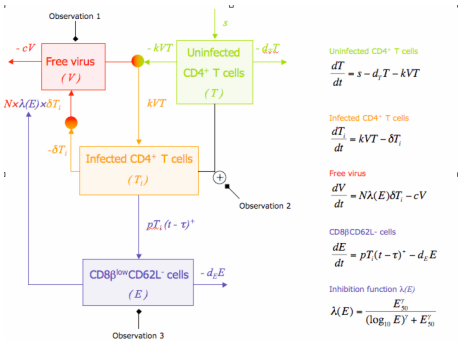

Figure 9. Model of FIV

4.4. Misc.

4.4.1. Prion

[In collaboration with M. Doumic (INRIA Rocq.), P. Gabriel and B. Perthame (Paris 6) – ANR TOPPAZ]

We study mathematically and numerically the polymerization/fragmentation equation involved in prion aggregation. We have investigated first the case of a size-dependent polymerization rate motivated by recent experiments. We now focus on some issue in optimization of protocol. This is closely related to recent challenges in fitness optimization, and optimal control.

4.4.2. Atheroma

[In collaboration with N. Meunier (Paris 5)]

Following El Khatib et al. (2007) we have proposed a mathematical model for the inflammatory processes driving the growth of early atherosclerotic plaques. This model is coupled with blood flow, with particular emphasis on the influence of shear stress.

5. Software

5.1. Wombats

Under construction by P. Vigneaux: A Navier-Stokes code for 2D and 3D bifluid flows with surface tension. It combines Finite-Volumes and Level Set methods for interface capturing, as well as penalization methods to take into account solid obstacles inside the flow. This code has been developed and validated in close collaboration with physicists from the Rhodia Laboratory of the Future (Pessac, France) : good agreement is achieved between numerical simulation and physical experiments in microchannels. Various mixing hydrodynamics has been exhibited numerically. This code (in F90) is now private and is still in development to implement some models dedicated to the simulation of cell motility.

5.2. Bingham Flows

A 1D and 2D code with a new method for the computation of viscoplatic flows with free-surface. It essentially couples Optimization methods and Well-Balanced Finite-Volumes schemes for viscous shallow-water equations (induced by the viscoplastic nature of the fluid). Currently applied to avalanches of dense snow, it is a private code currently actively developed (in C++). One of the key feature is that its well-balanced property allows to obtained the stationary states which are linked to the stopping of the snow avalanche for this highly non-linear type of fluid.

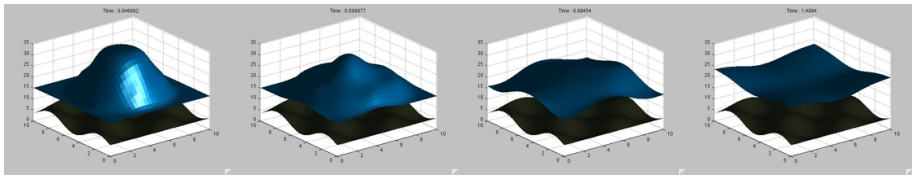

Figure 10. An academic dam break simulation with BINGHAM FLOWS code

5.3. Zebre

Participant: Thierry Dumont [correspondant].

Thierry Dumont is currently developping a toolbox to solve stiff reaction diffusion equations using splitting methods, together with refined numerical schemes for ODEs (RADO 5).

This code was first designed to serve as demonstrator of the theoretical results of Descombes and Massot on the solution of stiff reaction–diffusion systems by alternate directions methods, and as a first step towards complex chemistry simulations. Later it was used and improved to solve the ionic model of strokes, and incorporated stabilized explicit Runge Kutta methods for diffusion steps. Coded in C++, it solves stiff systems with various schemes in dimension 1, 2 and 3, in complex geometries. The code is multithreaded.

5.4. Non uniform tabulation

To study complex systems which are very long to compute (as complex partial differential equations in complex geometries), a simple idea is to precompute them. To be efficient this "tabulation" should not be done on a uniform grid, but rather on an adaptative grid, which is refined where the output of the complex systems changes rapidly.

V. Louvet and E. Grenier have developped a serie of routines (C++ and Matlab) to tabulate on nonuniform grid complex systems. These routines are on Inria Forge and will soon be released.

These routines have be used in real context, for human skin reflectance study.

5.5. Cancer modeling

A large serie of routines has been developped to simulate qualitative systems of tumor growth. These models combine nutriment diffusion, chemotaxis, angiogenesis, cell cycle, pharmacokinetics and pharmacodynamics. They are written in scilab and take the form of a serie of modules which may be combined to simulate the effects of drugs.

These routines are currently on Inria Forge.

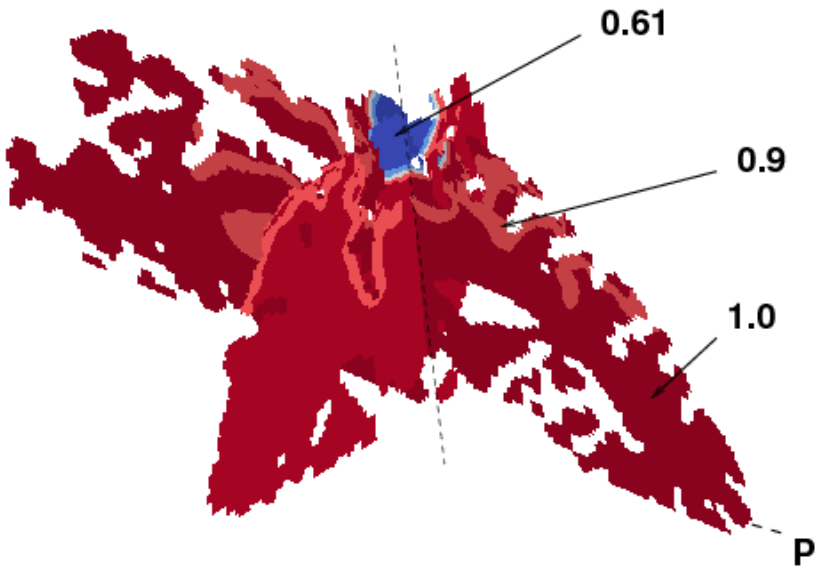

Figure 11. Propagation of a spreading depression in brain, using Zebre

6. Contracts and Grants with Industry

6.1. Contracts with Industry

- Sanofi-Pasteur: "Stability and integrity vaccine modeling and prediction" (study and transfert contract)
- L'Oréal: study of skin refractance (contract for Cemracs 2009).

6.2. Regional initiatives

Etoile is a research consortium on hadrontherapy. B. Ribba is responsible for the modeling part and focuses on the study tumor growth models.

6.3. National Initiatives

- P. Vigneaux is a participant of ANR JCJC Rugo (head: David Gérard Varet) on the mathematical study of rugosity effects.
- MA Dronne, T. Dumont, E. Grenier and F. Lignet are part of ANR Bimbo project (head: F. Gueyffier): this project is devoted to the study or atheroma. Numed members has the task to help to parametrize the various models which will emerge from this project.
- ANR AVC in silico: 2007 - 2009: the ANR Biosys projet "AVC in silico" which gathers biologists, clinicians and mathematicians to study various aspects of stroke (inflammation, free radicals, ionic motions, ...).
- ANR Sechelles: 2009-2011: participants T. Dumont and V. Louvet.

  The ANR Sechelles is joint group incorporating physicists and mathematicians. The goal is the modelization and the numerical solution of stiff multiscale systems of PDEs, with emphasis on combustion, plasma hysics and Stroke simulation. The main numerical developments concern numerical analyslis and implementation of Multiresolution schemes, efficient time step control for alternate directions methods, parallelism on massively parallel machines, fast evaluation of chemical reactions. Members belong to mathematical laboratories in Lyon and Nice, Physical labs in Ecole Centrale Paris and Rouen.

6.4. International Initiatives

B. Ribba is involved in the PhD direction of Floriane Lignet (MSc) on the modeling of in vivo tumor growth data from the Weizmann Institute of Science (on-going collaboration with Prof. Yossi Yarden, dept Biological Regulation).

7. Dissemination

7.1. Animation of the scientific community

- P. Vigneaux is member of the redaction committee of "Images des Mathématiques": construction and animation of the website.
- Organisation of JERAA 2010 (V. Calvez, P. Vigneaux): the JERAA days are a workshop which gathers all the mathematics departements of the region (Chambéry, Grenoble, Lyon, Saint Etienne, Clermont Ferrand).
- Organisation of Cemracs 2009 (V. Calvez, P. Vigneaux, E. Grenier): long summer school (6 weeks) composed of a week of lectures followed by a workshop of 5 weeks (talks and work on projects). More than hundred participants, publication of proceedings.

- B. Ribba: 17/03 - Journee ARC Lyon
- B. Ribba: 4-8/10 - Organization of the workshop "Modeling angiogenesis: joining cell, math and computers" with Roeland Merks, Leiden (Pays-Bas)
- B. Ribba: 2/12 - Organization with M. Badoual (IMNC) of a thematic workshop of GdR STIC SANTE: "Modeles mathematiques et imagerie en cancerologie"
- E. Grenier: head of GDR (groupement de recherches) of CNRS "MABEM" (mathematics applied to biology and medecine): 2007 - 2010.

7.2. Teaching

- Introduction to mathematical modeling, master M2 IXXI, Lyon (E. Grenier)
- Introduction to numerical analysis at ENS Lyon (E. Grenier and P. Vigneaux).

7.3. Invitations

- P. Vigneaux: 2 months (15 Oct - 16 Dec 2010) at the Institute of Mathematics of the University of Seville, Spain
- P. Vigneaux: Morningside Center for Mathematics, Chinese Academy of Sciences, Beijing, China (3 weeks, january 2010)
- B. Ribba: 21-24/06 - Pampelune (I. Troconiz, pharmacology department)

7.4. Conferences

- B. Ribba: 14/01 - Novartis : "Multiscale dynamical modeling of vascular tumor growth in vivo"
- B. Ribba: 17/03 - "Modelisation de l'action du Sunitinib sur la croissance tumorale en combinant des donnes de tailles tumorales et des marqueurs histologiques"
- B. Ribba: 16/04 - IMNC (Orsay): "Modeling response to anticancer treatments"
- B. Ribba: 8-11/06 - Conference PAGE: poster: "Combined analysis of tumor size and histological markers"
- B. Ribba: 21-24/06 - Pampelune:
  + "A model of vascular tumor growth in mice combining longitudinal tumor size with histological biomarkers"
  + "A K-PD model of the effect of the antiangiogenic drug Sunitinib in xenografted mice"
  + "Modeling tumor response to anticancer treatment: A multiscale integrated framework initiative"
- B. Ribba: 16-20/08 - Summer School, Dundee (Scotland) : three talks.
- B. Ribba: 17-20/11 - Workshop "Modeling and simulation for PK/PD", Salamanque
- M.-A. Dronne: december 2010: Fontevraud, Groupe de réflexion en recherche cardiovasculaire.
- P. Vigneaux: CNRS - NSFC Chinese - French Math. Institute on "Stress Tensor Effects on Fluid Mechanics", Beijing, China. January 2010.
- P. Vigneaux: Seminar at the Institute of Mechanics. Chinese Academy of Sciences. Beijing, China. January, 22, 2010
- P. Vigneaux: CANUM 2010, Carcan, 31 Mai - 4 Juin 2010.
- P. Vigneaux: Conference ICCFD6 - St-Petersburg, Russia, July 12-16, 2010.
- P. Vigneaux: WCCM 2010, the "9th World Congress on Computational Mechanics". Sydney, Australia. July 2010. Keynote Lecture.

- P. Vigneaux: Fluid Mechanics Seminar at the University of Queensland, Brisbane, Australia. August 19, 2010.
- P. Vigneaux: Conference at the Institute of Mathematics of the University of Seville (IMUS), Spain. November 10, 2010.
- P. Vigneaux: Seminar at the Department of Numerical Analysis, University of Malaga, Spain. November 18, 2010.
- P. Vigneaux: Conference at the Institute of Mathematics of the University of Seville (IMUS), Spain. December 9, 2010.
- V. Calvez: Septembre 2010 : Cambridge, Newton Institute conference "Fluid-Kinetic Modelling in Biology, Physics and Engineering"
- V. Calvez: Jun 2010 : Barcelone, SIAM conference DSPDES
- V. Calvez: May 2010 : Banff, Canada workshop "Nonlinear Diffusions and Entropy Dissipation: From Geometry to Biology"
- V. Calvez: April 2010 : Edimburgh conference "Nonlinear PDEs arising in mathematical biology: cell migration and tissue mechanics" (perturbee par le volcan islandais)
- V. Calvez: Mars 2010 : Banff, Canada workshop "Deterministic and stochastic front propagation"
- V. Calvez: February 2010 : La Havane, Cuba conference ICOR
- V. Calvez: December 2009 : Lyon entretiens Jacques Cartier
- V. Calvez: November 2009 : Tozeur, Tunisie conference "International Workshop on Biomathematics and Biomechanics"
- V. Calvez: October 2009 : IHP, Paris conference SMF : "Application des Mathématiques en Sciences du vivant"
- V. Calvez: Mars 2009 : Brasil workshop "Mathematical methods and modelling of biophysical phenomena"
- V. Calvez: January-Jun 2009 : Barcelone program "Mathematical Biology: Modelling and Differential Equations"
- E. Grenier: Workshop on recent progresses in fluid mechanics (Y. Guo), Beijing, july 2010.
- E. Grenier: chinese academy of science, july 2010.

8. Bibliography

Publications of the year

Articles in International Peer-Reviewed Journal

[1] N. BOURNAVEAS, V. CALVEZ. *The one-dimensional Keller-Segel model with fractional diffusion of cells*, in "Nonlinearity", 2010.

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[13] D. BRESCH, E. F. NIETO, I. IONESCU, P. VIGNAUX. *Augmented lagrangian / well-balanced finite volume method for compressible viscoplastic flows*, in "Proceedings of International Conference on Computational Fluid Dynamics (ICCFD6)", St. Petersburg, Russia, July 12-16, 2010 2010.

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[15] V. CALVEZ, L. CORRIAS, M. EBDE. *Blow-up, concentration phenomenon and global existence for the Keller-Segel model in high dimension*, 2010, submitted.

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