C.V. Emmanuel Grenier

1. Curriculum

Curriculum

- 1990 – 1994: Student at the Ecole Normale Supérieure (Paris)
- 1992: Master degree (University Paris 6).
- 1992: Agrégation (national competitive exam to become a teacher)
- 1995: phD thesis, under the direction of Y. Brenier (Paris 6), on "oscillatory limits in fluids and plasmas".
- 1998: habilitation thesis (required to get professor positions in France) at Paris 6.

Positions

- 1994 – 1998: junior research position at CNRS (Paris 6)
- 1998 - now: professor at Ecole Normale Supérieure de Lyon ("second class", then "first class", then "exceptional class")
- 2000 – 2012: associate professor at Ecole Polytechnique.
- 2008 - now: leader of the INRIA team "Numed" (Numerical Medicine). (INRIA is the national institute for computer science and automatics in Frannce, with a strong applied mathematics component).

Awards

- 2000: Peccot Prize from the "Collège de France", for a series of works in mathematical fluid mechanics.
- 2000: European Mathematical Society (EMS) prize, for a series of works in mathematical fluid mechanics.
- 2006: Prize from the "Annales Henri Poincaré".
- 2009: "La Recherche - Aréva " Prize (collective prize), for a series of works in mathematical geophysics.
- 2010: Blaise Pascal Prize from the French Academy of Sciences, for a series of works on stroke modeling.
- 2011: "La Recherche" Prize (collective prize), for a series of works on cancer modeling.

2. Research

Domains of interest

- Partial differential equations:

  In particular: inviscid limit of the Navier Stokes equations, incompressible limit of Navier Stokes equations, massless and gyro-kinetic limits in plasma physics, qualitative properties of reaction diffusion equations.

- Modeling in biology and medicine:

  In particular: modeling of glioma, of stroke, of apoptosis, of drug resistance, of dormance.

- Applications of mathematics and industrial collaborations

  In particular: modeling of the degradation of vaccines, pharmacokinetics and pharmacodynamics, quality control of industrial processes.

Five favorite results

1) Inviscid limit of Navier Stokes equations:

   The study of the limit behavior of solutions of Navier Stokes equations in an half space when the viscosity goes to 0 is a widely open question. Let u^ν be a sequence of solutions of the incompressible Navier Stokes equations

   $$\partial_t u^\nu + (u^\nu.\nabla)u^\nu + \nabla p^\nu - \Delta u^\nu = 0,$$

   $$\nabla.u^\nu = 0$$

   on an half space, with boundary condition $u^\nu = 0$. As ν goes to 0, one may expect that u^ν converges to solutions of Euler equations (similar equations, with $\nu = 0$ and $u.n = 0$ on the boundary, where n is the normal to the boundary), up to a boundary layer correction (so called Prandtl's boundary layer). It turns out that the situation is much more complex.

   In a series of papers (some of them in collaboration with Y. Guo and T. Nguyen), I proved that any shear layer flow is linearly unstable provided the viscosity is small enough. It is also nonlinearly unstable in L^∞, up to $O(1)$ for a particular class of shear layer profiles, and up to $O(\nu^{1/4})$ for generic profiles.

   This in particular proves that there exists no asymptotic expansion of Prandtl's type in Sobolev spaces to describe the limiting behavior of solutions of Navier Stokes equations as the viscosity goes to 0, whatever the initial data is.

2) Ekman boundary layers

In geophyics, oceanography or meteorology, the Coriolis force created by the rotation of the Earth is a predominant driving force. This motivates the study of Navier Stokes equations in a fast rotating frame

$$\partial_t u + (u.\nabla)u + \nabla p - \nu\Delta u + \epsilon^{-1} e \times u = 0,$$

$$\nabla . u = 0$$

where e is a given fixed vector, and ϵ a small parameter.

In a series of paper, I completely described the limit $\epsilon \to 0$ which both involves the propagation of fast waves (called Rossby waves) and boundary layers (so called Ekman layers).

This series of paper was awarded an ECM prize.

3) Semi classical limit of nonlinear Schrödinger equation before caustics

Description of the limit of Schrödinger equation as the Planck's constant goes to 0, in the WKB regime.

4) Stroke modeling

Ischemic brain stroke is one of the main cause of death in Western countries. In the years 2000, a series of drugs (ionic channel blockers) were successful on rat, but appeared to have no effect on human (and even to have negative effects). To try to understand this series of failure, together with medical doctors from Lyon and Grenoble neurological hospitals, I designed models of ionic exchanges in brain during the acute phase of stroke. These models underline the protective role of astrocytes during stroke and the differences in the effects of drugs between astrocytes and neurons. The astrocyte / neuron ratio is much larger in Human than in rodent. This difference of ratio by itself may explain that drugs efficient in Rat are not efficient in human.

This work was awarded the "Blaise Pascal prize" by the French Academy of Sciences.

5) Modeling of vaccine degradation

The prediction of the speed of degradation of vaccines is a crucial issue for pharmaceutic companies. These companies have to certify that a vaccine will remain efficient after a given time at a given temperature. They also want to know whether a given vaccine will remain efficient after a thermal excursion, which may occur during a long travel, in particular in underdeveloped countries.

In collaboration with Sanofi Pasteur (a big French pharmaceutic company), I have written a software used

- in early studies of new vaccines (twenty different vaccines have been studied with this software inside Sanofi's company).

– in certification procedures (this software has been used to certify a new production procedure by the F.D.A.)

– in the "last mile kilometer program" (W.H.O.): the problem is to know whether a vaccine is still safe just at the injection time, in particular in remote areas. A small chip on the vaccine continuously measures temperature, and the software uses this record to predict the concentration of active product in the vaccine. This indicates the doctor whether he shall use this vaccine.

A patent has just been filed on these problems by Sanofi.

3. Grants, teaching, administration

Industrical grants

- 2000, 2002 and 2003: annual contracts with the French CEA (Centre for Atomic Studies) on turbulence modeling.
- 2008: L'Oréal (French cosmetic manufacturer), on the modeling of skin color.
- 2009 - now: successive contracts with Sanofi Pasteur company (large French pharmaceutic company), on the modeling of vaccine degradation.
- 2012: Tiama (French small company): glass quality control.
- 2014: Servier (French large pharmaceutical company): dose optimization in mice
- 2017: Voice (French small company): evaluation of human motion
- 2018: Paint Up (French small company): automatic painting optimization.

National grants and regional grants

- $2003-2006$: national grant on the modeling of brain stroke
- $2005-2008$: national grant on mathematical models in biology
- 2009 to now: recurrent grants by INRIA
- $2011-2014$: INSERM grant on glioma modeling (INSERM is a French national institute devoted to medical research).
- $2018-2019$: three joints project with the "Centre Léon Bérard" (hospital specialized in cancer treatment in Lyon), for $150k$ euros.
- 2019 to now: INSERM grant for the modeling of the combination of two drugs in the treatment of cancer ($700k$ euros)

Former phD students

- D. Gérard Varet (Professor, Paris 7)
- G. Chapuisat (Assistant Professor, Marseille)
- M. Giacalone (high school teacher)
- T. Zhang (Assistant Professor, China)
- S. Enault (undergraduate teacher)
- F. Lignet (junior researcher, Merck company)
- E. Ollier (medical doctor at Saint Etienne Hospital)

Teaching

Analysis, PDEs, complex analysis, ODEs, modeling, numerical analysis at undergraduate and graduate levels.

Administration

- $2002 - 2006$: chair of the mathematical department at Ecole Normale Supérieure de Lyon.
- $2000 - 2004$: elected member of the administrative council of Ecole Normale Supérieure de Lyon
- $2000 - 2004$: in charge of the preparation to the "agrégation" competitive exam (graduate level).
- 2010 - now: in charge of the first year of graduate studies.
- $2004 - 2008$: in charge of a national network, gathering all the mathematics departments interesting in biomedical modeling ("Mabem" GdR, funded by CNRS).

Expertise

- Member of various program committees for the INSERM (national health and medical research institute), and European Commission.
- Member of the Scientific Committee of the CLARA (Regional Center for Cancer Research, which pilots the cancer research of the various hospitals and universities).
- Member of the academic panel for technologic innovations of the CLARA.

4. Publications

86 in mathematical journals, 2 books, 14 in journals from other academic disciplines

Publications in mathematical journals

Books

1) Chemin JY, Desjardins B, Gallagher E, Grenier, E: Mathematical geophysics: an introduction to rotating Navier Stokes equations, *Oxford Lecture Series in Mathematics and its applications*, 2006.

2) Grenier E, Nguyen, T: Stability of shear flows, *accepted for publications by Springer*

Publications in medical or biological journals

1) Giacalone M, Frindel C, Robini M, Cervenansky F, Grenier E, Rousseau D. Robustness of spatio-temporal regularization in perfusion MRI deconvolution: An application to acute ischemic stroke. *Magn Reson Med.* 2017 Nov;78(5):1981-1990.

2) Ollier E, Mazzocco P, Ricard D, Kaloshi G, Idbaih A, Alentorn A, Psimaras D, Honnorat J, Delattre JY, Grenier E, Ducray F, Samson A. Analysis of temozolomide resistance in low-grade gliomas using a mechanistic mathematical model. *Fundam Clin Pharmacol.* 2017 Jun;31(3):347-358.

3) Parra-Guillen ZP, Berraondo P, Grenier E, Ribba B, Troconiz IF. Mathematical model approach to describe tumour response in mice after vaccine administration and its applicability to immune-stimulatory cytokine-based strategies. *AAPS J.* 2013 Jul;15(3):797-807.

4) Lignet F, Calvez V, Grenier E, Ribba B. A structural model of the VEGF signalling pathway: emergence of robustness and redundancy properties. *Math Biosci Eng.* 2013 Feb;10(1):167-84.

5) Ribba B, Kaloshi G, Peyre M, Ricard D, Calvez V, Tod M, Cajavec-Bernard B, Idbaih A, Psimaras D, Dainese L, Pallud J, Cartalat-Carel S, Delattre JY, Honnorat J, Grenier E, Ducray F. A tumor growth inhibition model for low-grade glioma treated with chemotherapy or radiotherapy. *Clin Cancer Res.* 2012 Sep 15;18(18):5071-80.

6) Ribba B, Watkin E, Tod M, Girard P, Grenier E, You B, Giraudo E, Freyer G. A model of vascular tumour growth in mice combining longitudinal tumour size data with histological biomarkers. *Eur J Cancer.* 2011 Feb;47(3):479-90.

7) Chapuisat G, Dronne MA, Grenier E, Hommel M, Boissel JP. In silico study of the influence of intensity and duration of blood flow reduction on cell death through necrosis or apoptosis during acute ischemic stroke. *Acta Biotheor.* 2010 Sep;58(2-3):171-90.

8) Lelekov-Boissard T, Chapuisat G, Boissel JP, Grenier E, Dronne MA. Exploration of beneficial and deleterious effects of inflammation in stroke: dynamics of inflammation cells. *Philos Trans A Math Phys Eng Sci.* 2009 Dec 13;367(1908):4699-716.

9) Billy F, Ribba B, Saut O, Morre-Trouilhet H, Colin T, Bresch D, Boissel JP, Grenier E, Flandrois JP. A pharmacologically based multiscale mathematical model of angiogenesis and its use in investigating the efficacy of a new cancer treatment strategy. *J Theor Biol.* 2009 Oct 21;260(4):545-62.

10) Boissel JP, Ribba B, Grenier E, Chapuisat G, Dronne MA. Modelling methodology in physiopathology. *Prog Biophys Mol Biol.* 2008 May;97(1):28-39.

11) Dronne MA, Grenier E, Chapuisat G, Hommel M, Boissel JP. A modelling approach to explore some hypotheses of the failure of neuroprotective trials in ischemic stroke patients. *Prog Biophys Mol Biol.* 2008 May;97(1):60-78.

12) Dronne MA, Grenier E, Dumont T, Hommel M, Boissel JP. Role of astrocytes in grey matter during stroke: a modelling approach. *Brain Res.* 2007 Mar 23;1138:231-42.

13) Dronne MA, Boissel JP, Grenier E. A mathematical model of ion movements in grey matter during a stroke. *J Theor Biol.* 2006 Jun 21;240(4):599-615.

Publications in geophysics

1) Desjardins B, Dormy E, Grenier E: Instability of Ekman-Hartmann Boundary layers, with application to the fluid flow near the Core-Mantle Boundary, *Physics of the Earth and Planetary Interiors*, $123-1$: $15-27$ (2001).