

ED n° 474 « Interdisciplinaire Européenne Frontières du Vivant »  
Programme doctoral Liliane Bettencourt

## Fdv PhD program Courses 2009/2010

### Summary

1. Communication and Information in Medicine & Biology
2. Computational Biology 1 "Basic formal modelling"
3. Computational Biology 2 Advanced formal modelling
4. Critical analysis of research articles
5. Ecology and Evolution
6. French courses (Français Langue Etrangère)
7. English courses
8. English course online: GymGlish
9. History of Science and analysis of classical papers
10. Interfaces Physics Biology
11. Interdisciplinary Fridays
12. Modelling : Dynamical Systems
13. Scientific careers and beyond
14. Scientific Programming 1 Basics
15. Scientific Programming 2 Advanced
16. Scientific Writing
17. Signal Processing and Image Analysis
18. Statistics
19. Systems Biology

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## Communication and Information in Medicine & Biology

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Mediators : JC Thalabard, MD, PhD, University Paris Descartes & APHP

### Summary

In the land of the monolingual : *"Translating a basic finding into a new therapy requires us to speak many languages - scientific, clinical, legal and financial. Yet most of us are hopelessly monolingual, a limitation that substantially slows translational research. Steps have been taken to address this problem, but a lot remains to be done."* Nature Medicine 15, 975 (2009) To achieve this goal, in addition to original articles, the major medical journals bring regularly to their readers updates on various aspects of basic research which could potentially be translated to humans. This excursion mainly into major medical journals will help the students; i) to discover their contents, their target readership and how they are structured; ii) to summarize and present the results of both original and review articles.

### Program

The following journals will be regularly browsed to form the reading list: Lancet, New England Journal of Medicine, JAMA, Nature Medicine, PLoS Medicine An initial list of articles will be posted in the corresponding section for the course in the M1 moodle web- area. It presently includes the following topics

- Genetic and Molecular Epidemiology
- Infectious diseases
- HIV
- Modélisation of the spread of infectious disease and their prevention
- Systematic Review and Meta-analysis
- Causality
- General Hypotheses

For each session, 1- 2 papers will be selected and read by all the students, who are individually expected to prepare a written short critical review. A group of 2-3 students will be in charge of presenting the selected paper, with an open discussion based on the questions and comments raised by the audience. Sessions will be held in 2009-2010 on Mondays

## Computational Biology 1 "Basic formal modelling"

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Mediators : Gregory Batt (INRIA Rocquencourt), Vincent Danos (U. Edinburgh), Vincent Schachter

8 sessions

Basics of numerical simulation and limitations: 1 course-- (GB)

Computational aspects of numerical simulation for ODEs, conversion from stochastic to differential rates (including transport), stochastic DEs, Gillespie algorithm. Numerical errors, computational cost of numerical simulation, stiffness, dimensionality, parameter uncertainties and the question of biological significance. Spatially heterogeneous systems, crowding, diffusion limited kinetics.

Boolean and qualitative models: 2 courses, 3TDs (GB)

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24 rue du faubourg Saint Jacques 75014 Paris

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Email : [contact@fdv-paris.org](mailto:contact@fdv-paris.org)

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1st TD: (yes, we start with a TD!) modeling and basic analysis of a simple gene network

1st course: Boolean and qualitative models and their dynamics. Thomas' rules.

example "yeast robust cell cycle " <http://www.pnas.org/content/101/14/4781.abstract>

2nd TD: detailed analysis of a complex gene network (nutritional stress response in E. coli) using GNA

2nd course: computational aspects: search for steady states, formal verification, network inference

3rd TD: connection with experimental data: Saint-Savage et al.

**Model building and analysis: 2 courses, 2TDs-- (GB)**

1st course: notions of sensitivity: local, solution-based and global, sensitivities computation; notions of robustness and computational aspects

1st TD: optimizing genetic circuits by global sensitivity analysis, X.-J. Feng, S. Hooshangi, D. Chen, G. Li, R. Weiss, and H. Rabitz, *Biophys. J.*, 87(2):2195-2202, 2004. Kitano's paper on a theory of biological robustness. A general computational method for robustness analysis with applications to synthetic gene networks, <http://bioinformatics.oxfordjournals.org/cgi/content/full/25/12/i169> *Bioinformatics* paper

classical papers such as von Dassow et al and Ingolia et al.

2nd course: parameter estimation: identifiability, various optimization-based search methods

2nd TD: benchmarks for identification of ordinary differential equations from time series data, Gennemark and Wedelin, *Bioinformatics*, 2009; or actual parameter search on a simple but difficult example

**Metabolic networks: 3 courses and TDs (Vincent Schachter )**

Steady state assumption, admissible flows, decomposition into extreme modes, biomass production rate predictions, analysis, reconstruction

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## Computational Biology 2 Advanced formal modelling

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Mediators : Vincent Danos (U. Edinburgh), Gregory Batt (INRIA Rocquencourt), Vincent Schachter

8 sessions

**Rules and reactions: 6 courses, 3 TD**

1st course: soft introduction to the kappa basics, relation to ordinary reaction networks, refinement of rule sets (qualitative), stochastic vs. deterministic dynamics, reminder on stochastic and deterministic rate constants (units, typical magnitudes, conversion), basics of simulations, refinement of rule sets (quantitative),

TD: trivial circuits to illustrate the basic definitions, small circuits, kinase cascades

2nd course: large scale ppi network dynamics (and percolation), compositional drift

TD: simple allosteric systems, large networks, percolation experiments

3rd course: causality and stories (formal notion of pathway), model reduction

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TD: dna processing models (VD + JK,3) 4th course: thermodynamic model of complex assembly, energy functions, positional entropy model, Wegscheider conditions for reactions and rules;

Advanced allosteric models, kinetic traps.

5th course: rule-based molecular dynamics (a la Peter Dittrich, le Novere)

6th course: pde and patterns a la Meinhardt, Kholodenko, Stelling (VD)

**Membrane interactions/bigraphs (JK)**

Motivations, from rules to bigraphs [1] and bigraphical molecular systems [2,3] representing transport, dynamic compartmentalisation

[1] The Space and Motion of Communicating Agents, Cambridge University Press 2009

[2] Stochastic Bigraphs. Jean Krivine, Robin Milner and Angelo Troina. Proceedings of MFPS XXIV. Vol 218, p73-96, ENTCS 2008.

[3] A Language for the Cell. Troels C. Damgaard, Jean Krivine and Vincent Danos. RR-116 ITU Copenhagen. 2009.

**MGS and morphogenesis (Antoine Spicher ou Olivier Michel)**

### Critical analysis of research articles

Mediators : Ariel Lindner (INSERM/Paris Descartes), Pascal Hersen (CNRS/Paris Diderot)

This course is intended to develop the student's ability to read and critically interpret interdisciplinary papers from impact journals. Through this exercise the students will be exposed to a large spectra of interdisciplinary research domains and methodologies.

This 1st trimester exercise is built of a series of seminars, each prepared by two students from different backgrounds, presenting in detail a research paper of their choice. The underlying hypothesis, background and the results is discussed in detail and the different techniques explained. In addition, the students are asked to suggest further experimental/modeling approaches with respect to their conclusions from the paper at stake.

1. The articles (in PDF format) should be posted no later than a week before the presentation on the secured AIV wiki.
2. All students participating in the course have to fill their comments, including the strong and weak points of the paper as well as points not well understood no later than three days before the presentation.
3. The points raised in the student's feedbacks will be then addressed during the presentation.
4. A Short debriefing of the presenters by the AIV mentors will take place after the seminar

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## Ecology and Evolution

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Mediator : Minus van Baalen (Laboratoire d'Ecologie - UMR 7625, ENS, University Pierre et Marie Curie)  
Duration: 6\*3h

For Darwin, evolution was tightly linked to the ecology that embedded it. Indeed, even if he was not the first evolutionary biologist, with some justification one could claim that he was the first ecologist. Notwithstanding, the subsequent development was that Evolution and Ecology became complementary and almost non-interacting scientific domains.

Ecologists considered that evolution was too slow to take into account while evolutionary biologists considered that ecology was so fast that they could safely assume it was in stable equilibrium (and ignore it). However, in the 1950s and 60s, the awareness arose that one cannot always disentangle the two processes, and the discipline of Evolutionary Ecology was born.

This discipline now covers many subtopics: optimal foraging theory, evolutionary life history theory, game theory, to name a few. In the 1990s, the theory of Adaptive Dynamics was developed to put it on a sound theoretical foundation.

In this course, Minus van Baalen will attempt to cover the basic aspects of Adaptive Dynamics (6 hours) and present in some detail two examples that show how it can be applied (the Evolution of Virulence, 6 hours) and what are still exciting open problems (Population Structure and the Evolution of Communication, 6 hours).

## English courses

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Mediator: Lucy Veisblat (University Paris Diderot), for the department Études Interculturelles de Langues Appliquées (EILA) of the University Paris Diderot

**Scientific English (annual course, 48 weeks=72 hours)**

Cours d'anglais de différents niveaux (selon tests) ciblés sur l'environnement scientifique; groupes de 10 à 12 étudiants de même niveau, entraînement à la compréhension et à l'expression orales et écrites.

Cours de 1h30, le matin (8h-9h30) ou le soir (18h-19h30)

Enseignement assuré par un intervenant extérieur pratiquant la rédaction ou traduction scientifique

**Scientific English (week course, 15h over 5 days)**

Stage de préparation à la communication scientifique avec pour objectif spécifique la préparation d'une communication scientifique publique; exercices de déblocage à la prise de parole et à la compréhension orale; utilisation de documents audio, vidéo et ressources en lignes. Situations d'entretiens individuels et par groupes.

Enseignement assuré en alternance par plusieurs enseignants anglophones.

Stage de 15 heures sur 5 jours ; groupe de 5 à 6 participants.

**Scientific English : professional communication (week course, 15h over 5 days)**

Stage de préparation à la rédaction de documents professionnels en anglais : rapports, courriers, courriers électroniques, supports de présentation. Travail sur l'efficacité de la communication et la concision.

Exercices pratiques à partir de documents rédigés par les participants.

Stage de 15 heures sur 5 jours; groupe de 10 à 12 participants.

Enseignement assuré par un intervenant extérieur spécialiste de la communication professionnelle.

**General English (annual course, 48 weeks, 96 hours)**

Les doctorants souhaitant améliorer leur anglais général ont la possibilité de s'inscrire aux cours de formation continue (niveaux 1 à 5) proposés au public.

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- Cours du soir (18h-20h), d'octobre à juin soit 48 semaines
  - Stage intensif d'anglais, 30 heures, une semaine en juin
- Les doctorants ont également accès en libre-service à l'auto-formation à l'anglais dans les locaux du CRL.

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### English course online: GymGlish

Cours d'anglais par internet personnalisés <http://www.gymglish.fr/>  
GymGlish propose des cours d'anglais innovants et ludiques, fondés sur un moteur d'intelligence artificielle qui délivre chaque jour un email d'activités linguistiques personnalisées en anglais, suivi de corrections.

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### French courses (Français Langue Etrangère)

By the department Études Interculturelles de Langues Appliquées (EILA) of the University Paris Diderot  
Mediator: Lucy Veisblat (University Paris Descartes)  
The department organizes in 2010 two workshops on "French as a foreign Language" open to FDV students focussed on spoken French for professional and academic uses.  
Workshop of 30h over 5 days, 15 students maximum. Exercices on oral comprehension and expression, exploration of some aspects of French culture. (session 1: week of January 11th 2010, session 2: week of June 7th 2010).

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### History of Science and analysis of classical papers

Mediators: Michel Morange (ENS), Evelyn Keller-Fox (MIT)

Duration: 2 hours, weekly

The course is intended to evolve the students' ability to integrate information from science, in the context of philosophy and history through the examination of specific episodes in current science and the history of science.

Evelyn Fox Keller will debate on the nature and limits of Scientific Responsibility, focusing on climate science.

The students will be guided in readings of classical articles to strengthen their critical thinking skills and scientific literacy in the various interfaces of Biology with Math, Physics, Chemistry and Medicine.

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### Interdisciplinary Fridays

Mediators : François Taddei (INSERM, Paris Descartes), Samuel Bottani (University Paris Diderot), Ariel Lindner (INSERM, Paris Descartes)

Each lab hosting 2nd year FdV students for their PhD will be invited to present in the FdV lab seminar series. The whole lab and the students supervisors and tutors will be invited to attend and to initiate a dialog focused on their topics of interests. Given the interdisciplinary nature of FdV seminar series, the presentation will have to introduce the basic concepts and a zoomed-out view and then zoom-in onto the frontier of knowledge the group is trying to unravel in the thesis of the student.

To favor informal exchanges, the seminars will open and close by moments where food and drinks will participate to the friendly and relax atmosphere.

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### Interfaces Physics Biology

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**Mediators:** Matthieu Piel (Institut Curie) , Annemiek Cornelissen (CNRS, Paris Diderot), Vincent Fleury (CNRS, Paris Diderot)

**General aim:**

In this course we propose two theoretical courses and a practical course, aimed at giving examples of what physics can tell about general biological questions, and in particular about the question of how shapes are generated, a process called morphogenesis.

The general aim is to show how it is possible to go from a specific biological question develop a quantitative experimental approach and confront data and modeling.

**Summary of content:**

A first course (3x3h) will be about the physical constraints to Evolution, presented by Vincent Fleury. It is not exactly classical Evo/Devo, but rather a physicist perspective, in the line of Darcy Thomson famous book 'On Growth and Form', on how shapes can evolve, starting with a general introduction on morphogenesis in biology, development and genetics to move towards physical modeling of developing organisms, and concentrate on a few examples, including Evolution of the hand.

A second course (3x3h) will deal with the very important morphogenetic process of angiogenesis (formation of blood vessels), from Physics to pathology. This course will be presented by Annemiek Cornelissen.

The practical course proposed (3x3h) will consist in studying formation of blood vessels during the development of the chick embryo. It required only a simple binocular microscope for observation and an incubator to control the temperature of eggs. The growth pattern of blood vessels can then be extracted and confronted to classical theories for angiogenesis.

The content above is a starting proposal, and the students interested are also welcome to propose additional topics.

During the courses researchers from various fields will come to discuss and give seminars.

We will also help the students choose and attend interesting meetings at the interface between physics and biology, the number of such meetings being now quite elevated.

The courses will be of 3 hours each time, between November 2009 and May 2010

The schedule and precise set of courses will be decided after a first meeting, in October 2009, with the student interested to follow the course.

### Modelling : Dynamical Systems

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**Mediator:** Stéphane Douady (ENS/Paris Diderot)

**Duration:** 12\*3h

Overview of dynamic systems, with small experiments and demonstrations including biological application examples.

We will study basic theoretical tools, practice specific examples and synthesize a coherent overview of :

- Non-linear notions (rabbit-fox model), dissipative model (pendulum), interactions (oscillator coupling), chaos, strange attractors (of Lorenz)
- Instability (of Faraday), Amplitude equation, derivation by symmetry argumentation, general description of bifurcations.
- Classical (phase transitions), less classic (plans, granular milieu) and biological (excitable milieu, neurons) examples of bifurcations.
- Interactions between modes and spatial motifs, spatial-temporal chaos (duality/waves). Transitions toward chaos (discrete dynamics, transition scenarios)

General cases of morphogenetic instabilities (Laplacian, of Turing: shells and tigers).

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### Scientific careers and beyond

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Mediator: Patrice Denèfle (Ph.D HDR, Qualifié PU (Section 64-65), CEDEP-INSEAD, Senior Advisor, Translational Research and Development, Healthcare Industries, Links Conseil R&D Strategic Committee, MEDICEN)

**Duration:** 12 sessions

Scientific careers can be defined as: "Professions in which people carry out or support scientific research or monitoring". This module aims to give science graduates an overview of the real world of science in action and of the diversity of careers open after a master in or a PhD in science. The course will be organized as a series of talks by science trained professionals at every level, from senior academic or industrial scientists, to patent attorneys, entrepreneurs, company managers and government officials who will present and discuss with the audience their personal story. It will present perspectives from academia in different countries, from industry in large pharmaceutical companies and small start ups, from patents agencies, government agencies etc...The module will also provide an introduction to the relationships between science, innovation and business.

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### Scientific Programming 1 Basics

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**Mediator:** Konrad Hinsen (CNRS, Synchrotron Soleil)

**Duration:** 6 sessions of 3 hours in the computer room

This series of lectures and exercises provides a practical introduction to using the programming language Python for solving common problems in computational science. Topics covered (roughly in chronological order):

- Presentation of the Python language and its use in scientific computing
- Basic language features
- Working with files
- Efficient numerical operations (NumPy library)
- Plotting (matplotlib library)
- Moving on to more complex programs: object-oriented programming and error handling

Students are expected to have experience in working with a computer: creating and editing text files, consulting documentation on the Web etc. No prior programming experience is required.

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### Scientific Programming 2 Advanced

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**Mediator:** Konrad Hinsen (CNRS, Synchrotron Soleil)

**Duration:** 5 sessions of 3 hours in the computer room

This series of lectures and exercises addresses advanced topics in scientific computing.

Topics covered:

- Basic parallelization using task farming
- Graphical user interfaces (Tk library)

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- Managing source code (and more) with a version control system (Mercurial)
- 3D visualization and animation with VPython

Possible additional topics (chosen according to the students' preferences):

- Interfacing C and Fortran code with Python
- Debugging, profiling, optimization
- Performance boosting using Pyrex/Cython
- Handling large data sets (HDF library, Pytables library)
- Advanced visualization using MayaVi

Students are expected to have a working knowledge of the Python language. Some of the additional topics (Interfacing C and Fortran code, Performance boosting using Pyrex/Cython) also require a working knowledge of the C language.

## Scientific Writing

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**Mediator:** Jean-Luc Lebrun

**Duration** Two and a half days

### Course Synopsis

This course is based on the book "Scientific Writing: A Reader and Writer's Guide". It helps identify and articulate the differences between efficient and deficient scientific writing. Through many in-class exercises, it promotes good scientific writing habits such as conciseness and clarity. The course material is mostly provided by the participants: they bring a published or unpublished paper (6 to 8 pages) to the course and learn how to evaluate and improve documents of the same type.

Good scientific writing skills open up many opportunities to the researcher: publications, conference or seminar attendance. They also lead to better patents, better research partnerships and better funded research. Clarity and efficiency in scientific writing is a testimony to the quality of a researcher; It influences career promotion.

### Course structure

- Introduction: "Write to be read" - a reader and reviewer perspective
- Module 1: The 'Why' and the 'How' of each item in a standard scientific paper structure: title, abstract, introduction, body (headings, subheadings, tables and graphs), conclusion
- Module 2: Literature review, role and rules
- Module 3: Elementary principles of composition: reaching clarity, conciseness, precision and fluidity in writing
- Module 4: Identification of writing problems: a walkthrough process to detect structural problems at the sentence, paragraph and paper level

### Requirements

- A scientific paper written by the student (not a review) published, submitted, or draft
- Highlighters of various colours
- The companion book: "Scientific Writing: a Reader and Writer's Guide" World Scientific Publishing 2007 will be provided to the participants.

**Class size** :20 participants

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**The trainer**

Jean-Luc Lebrun has managed research programs while working at Apple Computer in its Advanced Technology Research group for over ten years. He subsequently invested his energy in the commercialization of research. He teaches scientific writing at the following A-Star\* research Institutes: BII, BTI, CMM, DSI, GIS, I2R, IBN, ICES, IHPC, IME, IMRE, SBIC, Simtech, and SSCC as well as medical research centres: SGH, NCCS.

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**Signal Processing and Image Analysis**

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**Mediator:** Christophe Zimmer (Pasteur Institute)

**Duration:** 7 sessions of 3h with practice

**Image formation:**

Light microscopy: principles and variants  
Fluorescence  
Point spread function and resolution  
Noise

**Basic image processing techniques**

Image restoration:

denoising  
deblurring  
registration

Detection:

automatic thresholding  
correlation  
other methods

Image segmentation:

adaptive thresholding  
edge filters  
region based methods

Tracking

detection and association  
correlation tracking  
optical flow

**Advanced methods: examples**

Inverse deconvolution methods  
Deformable models  
Statistical detection and estimation

**Highlights of image processing in biological research:**

Single molecule dynamics  
Super-resolution microscopy  
Automated phenotyping and lineage tracing  
Reconstruction of neuronal circuitry

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## Spatio-temporal Modeling and Simulation in Biology

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Mediator: Ivo Sbalzarini (ETH-Zürich)

Duration: 4 full days

The large amount of data generated by modern experimental assays frequently requires computational analysis ("data mining") in order to allow interpretation. At the same time, imaging capabilities have evolved to a point where it becomes possible to study the dynamics of intra-cellular processes in space and time with the help of computational models and simulations. This opens a need for spatio-temporal modeling based on first principles from physics, and the numerical simulation of these models using computers. In order to benefit from these new methods, life scientists will have to become increasingly computationally literate. Unfortunately, most lectures, books, and papers describing computational methods are not easily accessible to life science students due to heavy use of jargon and assumed prior knowledge. This has important implications for our education programs, but is only slowly realized in universities throughout the world.

This practical course provides a prime format to introduce students to basic computational methods in a compact and concise way. We will present ready-to-use recipes and methods (akin to experimental protocols), without intricate (and mostly unnecessary) mathematical formulations and proofs. After the course, the participants will be familiar with a simple but versatile particle method to simulate dynamic processes in space and time. Particle methods are exceptionally well suited for biological systems due to their intimate link to the simulated processes, their appropriateness for complex geometries (as predominant in biological systems), and their robustness and stability. From a didactic point of view, particle methods are the best choice since they can be understood intuitively and a real-world meaning can be attributed to each variable and operation. This is in contrast to other numerical methods, such as finite differences or finite elements, that require a much more mathematical approach in order to be understood.

The course starts by introducing the concepts of Eulerian and Lagrangian control volumes, from which the numerical particle method is then derived. Rather than giving a general and abstract overview of these methods and the equations that are being solved, we focus on the most important examples of spatio-temporal processes in biological systems. These include diffusion, reaction-diffusion (Turing patterns), flows, and waves. For each transport phenomenon, we will derive the corresponding governing equation using the modeling tools introduced at the beginning of the course. During the whole process, we emphasize the biological meaning of the various terms in the equations and the intuitive understanding of their meaning, while the mathematical formulation is placed in the background. Once the governing equations for the considered transport processes are derived and understood, we will simulate each process in the computer using particle methods. This will be done in tutored hands-on exercises where each participant will have her/his own computer workstation in order to implement and try out the knowledge acquired in the lectures. Playing with the equations and the process parameters further enhances intuitive understanding of the methods and leads to a fusion of system, model, equation, and simulation. The participants realize that computational modeling and simulation is a straightforward process, following simple algorithms that resemble experimental protocols. This demystification of computational methods, and the insight that they are not perfectly accurate, allows the students to take advantage of this powerful new tool. With the help of the tutors, they start playing with and using the various techniques as well as judging their utility and accuracy. It is important that the students realize where the pitfalls and limitations of computational methods are,

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such that they can later avoid the most common mistakes and are able to critically judge the quality and reliability of computational results obtained by others.

day 1:	day 2:	day 3:	day 4:
<ul style="list-style-type: none"> <li>* Modeling spatial effects / the Reynolds transport theorem (2h)</li> <li>* Introduction to particle methods for simulating spatio-temporal systems (2h)</li> <li>* Exercise: implementing a skeleton particle simulator (4h)</li> </ul>	<ul style="list-style-type: none"> <li>* particle methods to simulate diffusion processes (2h)</li> <li>* simulating reaction-diffusion processes and morphogenesis (2h)</li> <li>* Exercise: implement a PSE diffusion solver and do convergence studies (4h)</li> </ul>	<ul style="list-style-type: none"> <li>* simulating advection-diffusion (2h)</li> <li>* simulating flows (2h)</li> <li>* Exercise: implement a morphogenesis simulation with Turing patterns (4h)</li> </ul>	<ul style="list-style-type: none"> <li>* simulating waves (2h)</li> <li>* Exercise: simulation of moving and deforming shapes using advection-diffusion (6h)</li> </ul>

This corresponds to chapters 4 to 10 of the lecture notes (available upon request)

**Prerequisites:** in order for the students to be able to follow the course, they need to be familiar already with:

- \* programming in Matlab or Octave
- \* vector analysis
- \* dynamic (ODE) models
- \* dimensional analysis and dimensionless groupings
- \* the concept of conservation laws and balance equations
- \* partial differential equations

These prerequisites can be acquired or checked by reading chapters 1 to 3 and 11 of the lecture notes (available upon request).

## Statistics

**Mediators:** Stéphane Robin (INA-PG), Pierre-Yves Bourguignon (Genopole, Paris Diderot), Sophie Schbath (INRA), Grégory Paul (INSERM Paris Descartes)

In order to face the diversity of needs encountered by PhD students, the lecture is divided into 3 modules corresponding to different points of view and practices. The lectures share the same overall organization:

- workshops on statistical analysis of actual data from original graduate research
- lectures/ journal club to improve statistical knowledge/skills
- reading of historical papers

In addition, two initiatives should benefit from (and be beneficial to) these courses:

- creation of a user's group on computational tools such as R
- development of a knowledge database on statistics using collaborative tools (e.g. wiki)

**Centre de Recherches Interdisciplinaires**

Faculté de médecine Université Paris Descartes - Site Cochin 2<sup>ème</sup> étage

24 rue du faubourg Saint Jacques 75014 Paris

Tél : 01 44 41 25 22 - Fax : 01 44 41 25 29

Email : [contact@fdv-paris.org](mailto:contact@fdv-paris.org)

Web : [www.fdv-paris.org](http://www.fdv-paris.org)

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A short introduction on probability theory (probability space, random variable, convergence theorems, etc.) and on simulation of random variables will be given as practical exercises dedicated to improve the intuition of the participants and to ensure a common background among students.

**Module 1 : Statistical inference (M1)**

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This module is dedicated to the essential elements of statistical inference. Fundamental notions will be rigorously presented in order to set the ground for the next modules. The course on the bayesian approach will provide an opportunity to review the basics of statistical inference: fixed and stochastic distinction, parameter/variable, etc...

The courses are accompanied by practical work illustrating the notions introduced during the lecture with practical examples, owing largely to simulations.

- 1 Reminder of probabilities (2 sessions)
- 2 Statistical inference (3 sessions)
- 3 Bayesian Inference (2 sessions)

**Module 2: Linear model and introduction to R**

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This module sets into practice the basics of statistics introduced during the first module using the framework of the much used classical linear model. Due to the simplicity and generality of its formalism, this model is very relevant for a large number of analyses in biology.

A central part of the course will be dedicated to modeling and interpretation of the results. The last days will be dedicated to the generalization of the linear gaussian model to discrete data and dependent data. These courses will remain introductory, and will require further investigation from the interested students.

Duration : 25 hours

Format : Each day 3 h course + 2 h tutorial

schedule	Morning	Afternoon
Monday	Regression	Tutorial
Tuesday	Anova	Tutorial
Wednesday	General linear model(Gaussian)	Tutorial
Thursday	Introduction to the generalized linear model (discrete data)	Tutorial
Friday	Introduction to the mixed generalized linear model. (dependent data)	Tutorial

**Module 3: Statistical modelling**

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The aim of this very advanced module is to perform a statistical modeling project (with the associated inference) on a precise example, for instance in the domain of evolution or of phylogeny.

After a detailed presentation and exploration of the data during the first day, the students will be asked to define themselves a list of biological questions pertaining to the data set and to propose relevant models to propose answers.

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The following days will be dedicated to courses on models and methods useful for the considered examples. Possible courses are:

- which probability distribution?
- mixing models, EM algorithm
- Markov chains
- Selection of models
- Graphs/networks
- Non linear regression
- Models of evolution
- Models for trees
- Kernel methods
- Classification
- Multidimensional methods
- Small n, large p
- 

This module corresponds to the workshop "Modélisation statistique et analyse de données biologiques" in common with the doctoral schools GGC, SdV, et ABIES.  
[http://moulon.inra.fr/~mag/ue\\_modelstat.html](http://moulon.inra.fr/~mag/ue_modelstat.html)

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## Systems Biology

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Mediator: Andrew Murray (Harvard/CRI)  
Duration: 12 sessions of lecture (2h)+discussion(2h)

### Course Philosophy - What is systems biology?

Our definition is studying how little things come together to produce big things that have interesting properties that none of the little things exhibit in isolation, with an emphasis on understanding the general principles behind these transformations. This includes understanding how a linear chain of amino acids becomes a protein with a specific structure and function, how a group of proteins interact with each other to produce devices for receiving information, processing it, and inducing cellular responses (such as biological clocks), and how the accumulation of mutations leads to the evolution of such sophisticated machines.

The course will use several examples (the Lac operon, decisions in the development of flies and bacteria, clocks, chromosome segregation, evolution, and sex) to explore the existence of general principles that explain the function and evolution of cells and their components. By concentrating on concepts, we hope to make the course accessible both to students from physics and mathematics whose background in biology is weak and to biology students with little exposure to mathematics. The ancestral version of this class included basic instruction in computer programming, but within the format of the AIV/FdV this material will be covered in other classes and you will be encouraged to use these skills to improve your understanding of the material presented in this class.