Profile of Prof. Denis THIEFFRY

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Short CV

Professor of Systems Biology at the *Ecole Normale Supérieure*, Denis THIEFFRY has earned his Ph.D in 1993 at the Free University of Brussels, under the direction of René THOMAS. In between, DT spent seven years of postdocs in Mexico (UNAM), Germany (MPI) and Belgium (University of Ghent), and has been appointed as full Professor of Bioinformatics at the University of the Mediterranean (Marseilles, France, 2000-2010).
Editor of *Biosystems*, Associate Editor of *PLoS Computational Biology*, member of the editorial board of *Biological Theory* and of various scientific committees related to computational biology, DT has published about a 100 articles and book chapters, mostly in international journals, proceedings or books.

Research topics

The integration of molecular genetic data into predictive dynamical models is a key component of the emerging fields of Systems Biology. In this respect, the Computational Systems Biology team led by DT at IBENS focuses on the development of computational methods and software (logical simulations, attractor identification, regulatory circuit analysis, model reduction, etc.) to enable the design and the analysis of comprehensive models of molecular regulatory network. In collaboration with several experimental groups, this approach is used to decipher the regulatory mechanisms at the basis of cell fate decision, namely the choice between alternative cell differentiation pathways, proliferation, or programmed death, in model organisms (drosophila) and mammalian cells (mouse, human).

Selected publications

Naldi A, Carneiro J, Chaouiya C, Thieffry D (2010). Diversity and plasticity of Th cell types predicted from regulatory network modelling. *PLoS Computational Biology* **6**: e1000912.
Calzone L, Tournier L, Fourquet S, Thieffry D, Zhivotovsky B, Barillot E, Zinovyev A (2010). Mathematical Modelling of Cell-Fate Decision in Response to Death Receptor Engagement. *PLoS Computational Biology* **6**: e1000702.
Fauré A, Naldi A, Lopez F, Chaouiya C, Ciliberto A. Thieffry D (2009). Modular logical modelling of the budding Yeast cell cycle. *Molecular Biosystems* **5**: 1787–96.
Naldi A, Bérenguier D, Fauré A, Lopez F, Thieffry D, Chaouiya C (2009). Logical modelling of regulatory networks with GINsim 2.3. *BioSystems* **97**: 134-9.
Hingamp P, Brochier C, Talla E, Gautheret D, Thieffry D, Herrmann C (2008). Metagenome Annotation Using a Distributed Grid of undergraduate students. *PloS Biology* **6**: e296.
Sánchez L, Chaouiya C, Thieffry D (2008). Segmenting the fly embryo: logical analysis of the role of the Segment Polarity cross-regulatory module. *International Journal of Developmental Biology* **52**: 1059-75.
Remy E, Ruet P, Thieffry D (2008). Graphic requirements for multistability and attractive Cycles in a Boolean dynamical framework. *Advances in Applied Mathematics* **41**: 335-50.
González AG, Chaouiya C, Thieffry D (2008). Qualitative dynamical modelling of the formation of the anterior-posterior compartment boundary in the Drosophila wing imaginal disc. *Bioinformatics* **24**: i234-40.
Martínez-Antonio A, Chandra Janga S, Thieffry D (2008). Functional organisation of E. coli transcriptional regulatory network. *Journal of Molecular Biology* **381**: 238–47.
Chaouiya C, Remy E, Thieffry D (2008). Petri net modelling of biological regulatory networks. *Journal of Discrete Algorithms* **6**: 165-77.
Thieffry D (2007). Dynamical roles of biological regulatory circuits. *Briefings in Bioinformatics* **8**: 220-5.
Calzone L, Thieffry D, Tyson JJ, Novak B (2007). Dynamical modeling of syncytial mitotic cycles in drosophila embryos. *Molecular Systems Biology* **3**: 131.
González AG, Chaouiya C, Thieffry D (2006). Dynamical analysis of the regulatory network defining the dorsal-ventral boundary of the Drosophila wing imaginal disc. *Genetics* **174**: 1625-34.
Fauré A, Naldi A, Chaouiya C, Thieffry D (2006). Dynamical analysis of a generic Boolean model for the control of the mammalian cell cycle. *Bioinformatics* **22**: e124-31.
Simão E, Remy E, Thieffry D, Chaouiya (2005). Qualitative Modelling of Regulated Metabolic Pathways: Application to the Tryptophan Biosynthesis in E. Coli. *Bioinformatics* **21**: ii190-6.
Martin D, Brun C, Remy E, Mouren P, Thieffry D, Jacq B (2004). GOToolBox : Functional analysis of gene datasets based on Gene Ontology. *Genome Biology* **5**: R101.
Mendoza L Thieffry D, Alvarez-Buylla, E.R (1999). Genetic control of flower morphogenesis in Arabidopsis thaliana: a logical analysis. *Bioinformatics* **15**: 593-606.
Thieffry D, Salgado H, Huerta AM, Collado-Vides J (1998). Prediction of transcription regulatory sites in the complete genome of Escherichia coli K12. *Bioinformatics* **14**: 391-400
Thieffry D, Huerta A, Peréz-Rueda E, Collado-Vides J (1998). From specific gene regulation to global regulatory networks: a characterisation of Escherichia coli transcriptional network. *BioEssays* **20**: 433-40.
Thomas R, Thieffry D, Kaufman M (1995). Dynamical behaviour of biological regulatory networks. I. Biological role of feedback loops and practical use of the concept of the loop-characteristic state. *Bulletin of Mathematical Biology* **57**: 247-76.
Thieffry D, Thomas R (1995). Dynamical behaviour of biological regulatory networks. II. Immunity control in bacteriophage lambda. *Bulletin of Mathematical Biology* **57**: 277-295.

Title of presentation

Logical modelling of T-helper cell differentiation.

Abstract

Alternative cell differentiation pathways are believed to arise from the concerted action of signalling pathways and transcriptional regulatory networks. However, the prediction of mammalian cell differentiation from the knowledge of the presence of specific signals and transcriptional factors is still a daunting challenge. In this respect, the vertebrate hematopoietic system, with its many alternative differentiation pathways and cell types, is a compelling case study.

Based on published data, we have developed an integrated, comprehensive model of the signalling/regulatory network controlling Th cell differentiation. Our main aim is to gain insight into the potential heterogeneity and plasticity of late Th cell lineages. Since available data are mainly qualitative, we rely upon a logical formalism to perform extensive dynamical analyses. To cope with the size and complexity of the resulting network, we use an original model reduction approach coupled to a stable state identification algorithm. To assess the effects of heterogeneous environments on Th cell differentiation, we have performed a systematic series of simulations, considering various prototypic environments. As a result, we have identified stable states corresponding to canonical Th1, Th2, Th17 and Treg subtypes, but these were found to coexist with other transient hybrid cell types that co-express combinations of Th1, Th2, Treg and Th17 markers in an environment-dependent fashion.

In contrast with the classical depiction of T cell differentiation potential as a branching tree, our computational study points to a reticulate network of alternative, environment-dependent, differentiation and reprogramming events.