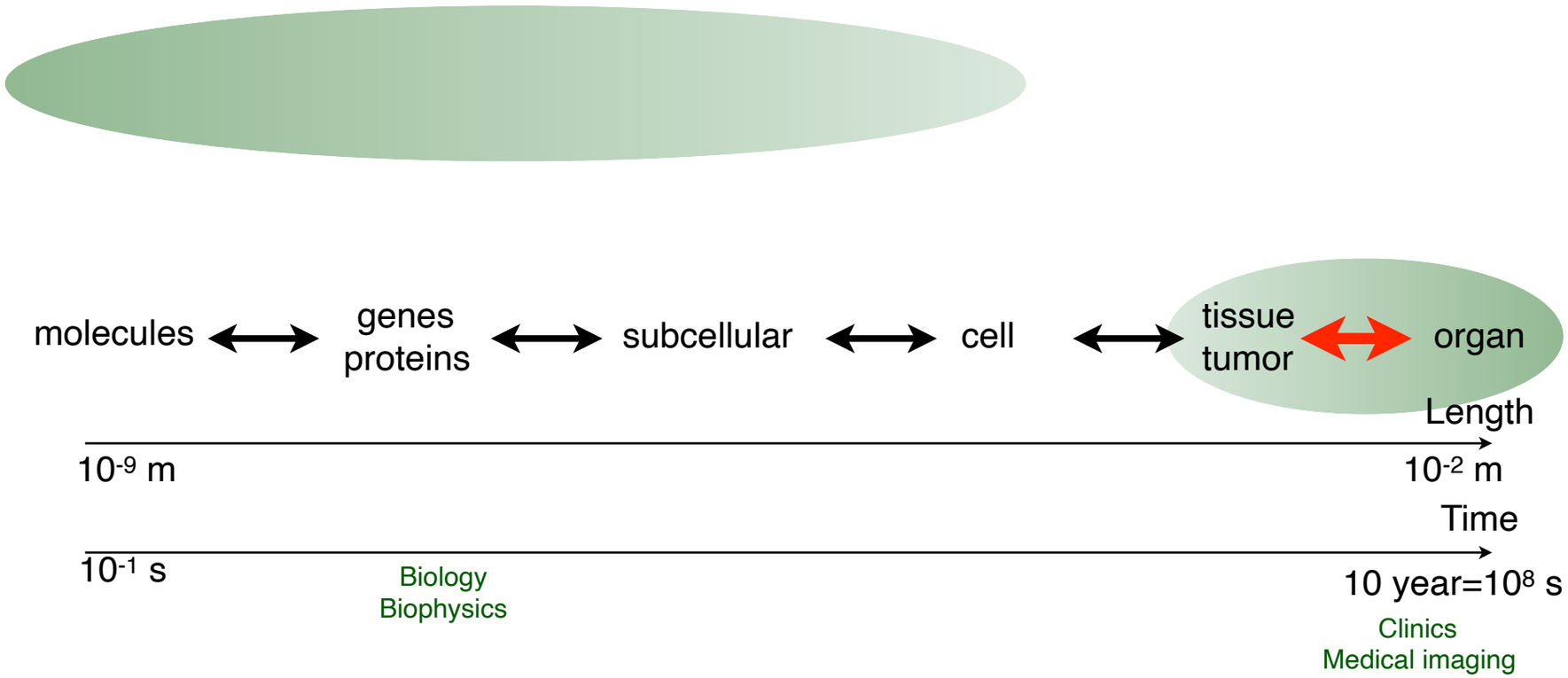
Modélisation des tumeurs : de la physique théorique des comportements collectifs des cellules vivantes à la confrontation aux données cliniques

Laboratoire IMNC, équipe MSB/Pôle Santé IJC Lab
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Basile Grammaticos (émérite), Alfred Ramani (émérite)
Léo Adenis (doctorant)
Gilberto Nakamura (post-doctorant)

Background

A growing tumor = a very complex system



How to make the link between scales? A step is missing between biology and clinics

Objectives

Predictions: very important in the case of invasive gliomas

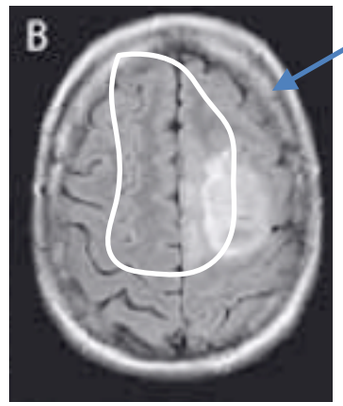
- position of the cell front
- areas of preferential growth
- effect of treatments
- etc

We develop simple mathematical models:

- with as few parameters as possible

- comparison with experimental data

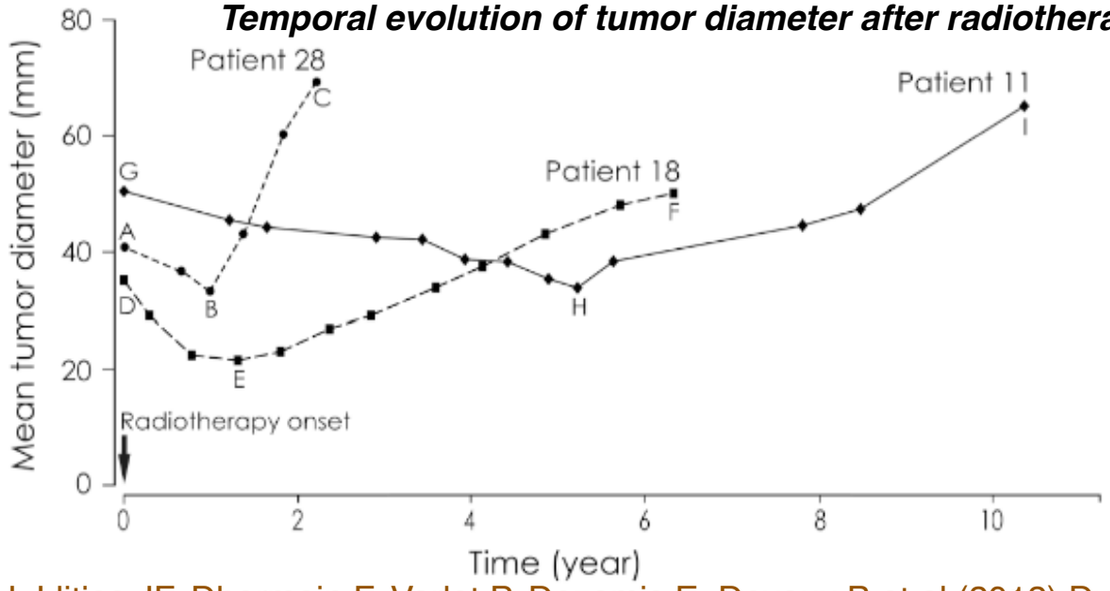
IRM T2 grade II glioma



Estimate of the real extension of the tumor

Pallud J, Mandonnet E, Les gliomes infiltrants de bas grade, Duffau H, Capelle L, (2008), *REG, Neurologies*, 11, 94-101

Temporal evolution of tumor diameter after radiotherapy



Pallud J, Llitjos JF, Dhermain F, Varlet P, Dezamis E, Devaux B et al (2012) Dynamic imaging response following radiation therapy predicts long-term outcomes for diffuse low-grade gliomas, *Neuro Oncol,* **14**, 496–505

Objectives:

- to understand better the development of gliomas, from the first cell to the tumor

- make models predictive and useful !

Our approach

We combine several **complementary competences**:

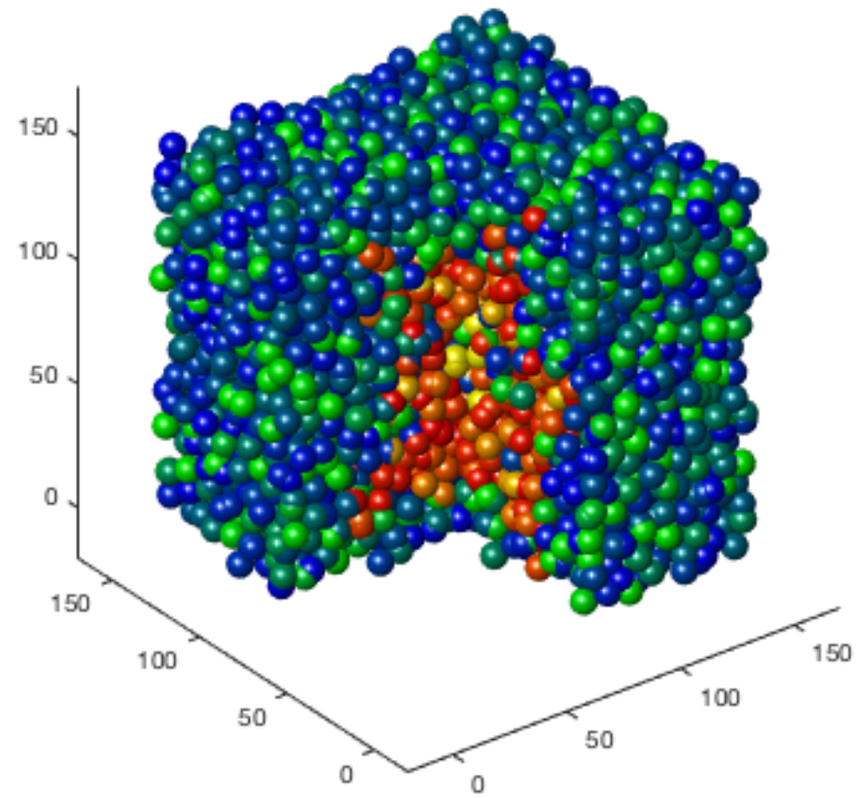
- image analysis

- data analysis

- modelling (models based on partial differential equations or cellular automata)

- numerical simulations

- statistical physics



Dufour A et al, (2018), Modeling the dynamics of oligodendrocyte precursor cells and the genesis of gliomas, *PLoS Comput Biol.*, **14**, e1005977.

To get data, we **collaborate** with :

- biologists: O. Seksek, M. Juchaux, D. Crespin, IJC lab

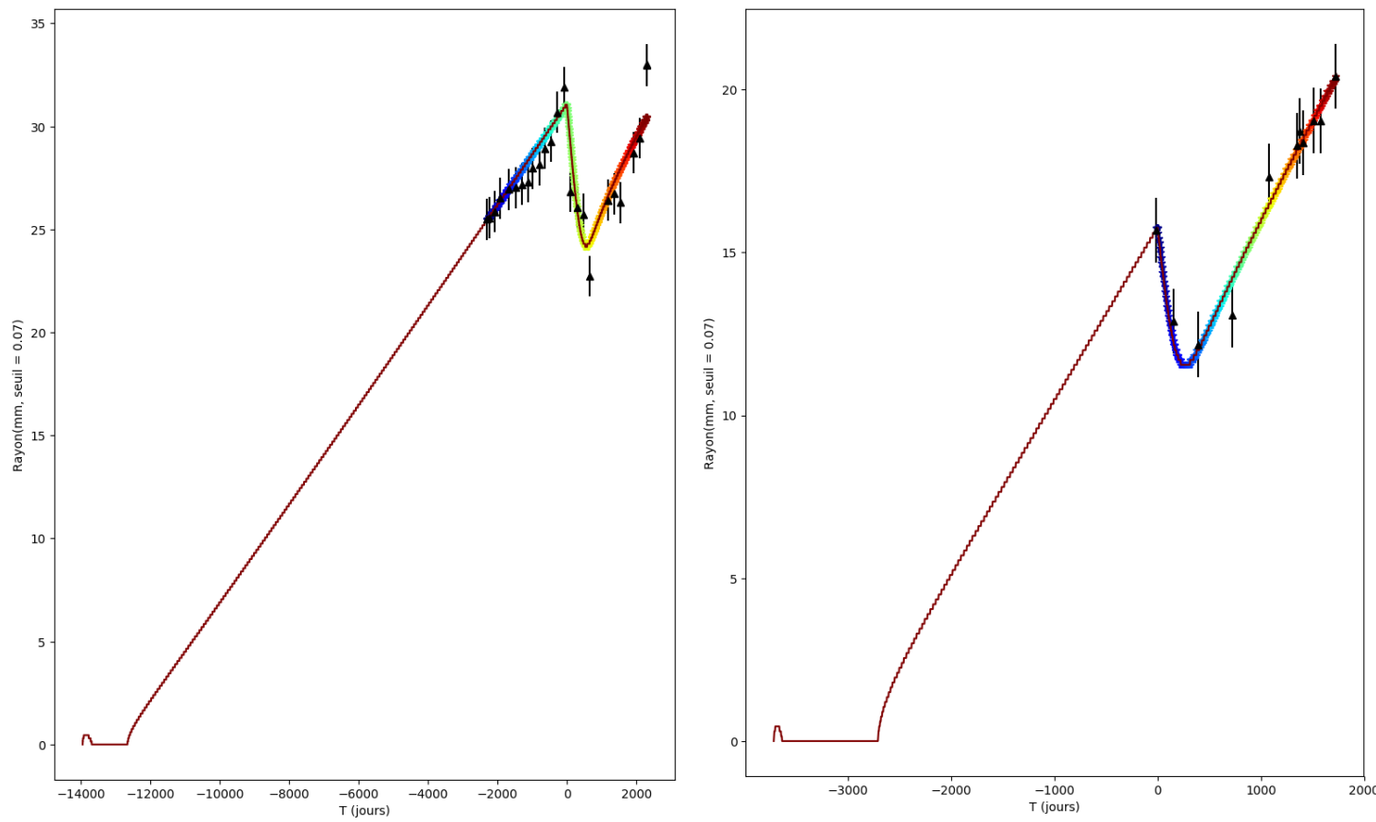
- clinicians: hospitals Sainte-Anne, Lariboisière, Saint-Louis, Necker (Paris)

Our projects

Modeling clinical data

- Effect of radiotherapy on gliomas in patients: (we are trying to predict the time of regrowth)
- Glioma growth in pregnant women
- Effect of chemotherapy
- Anaplastic transformation

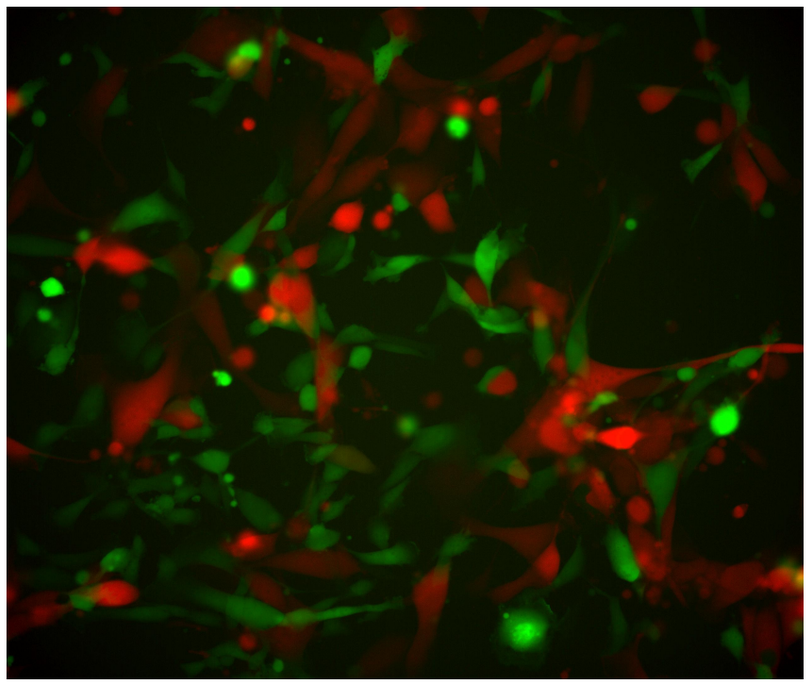
Leo Adenis PhD, 2017-2020



Temporal evolution of tumor diameter after radiotherapy, model and data points

Modeling biological data

- Interaction between irradiated and non-irradiated cell populations
- Cell-of-origin (OPCs)

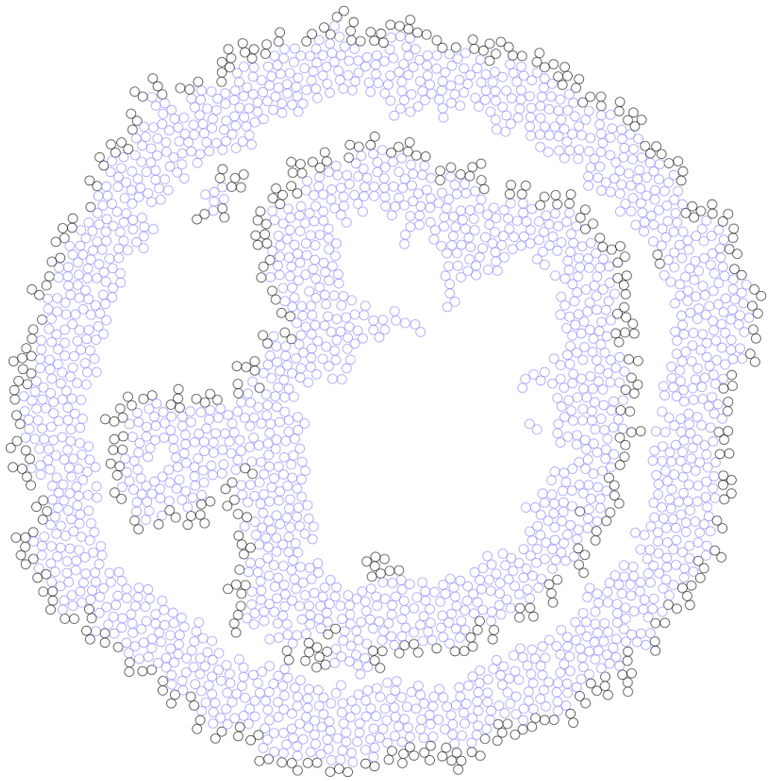


Red cell population: irradiated with 30 Gy; green cell population: non irradiated

Our projects

Statistical physics

- Influence of the polarisation of cells on the invasion front
- Influence of the shape of cells in migration/invasion
- Study of the homeostasis in the brain for cell populations



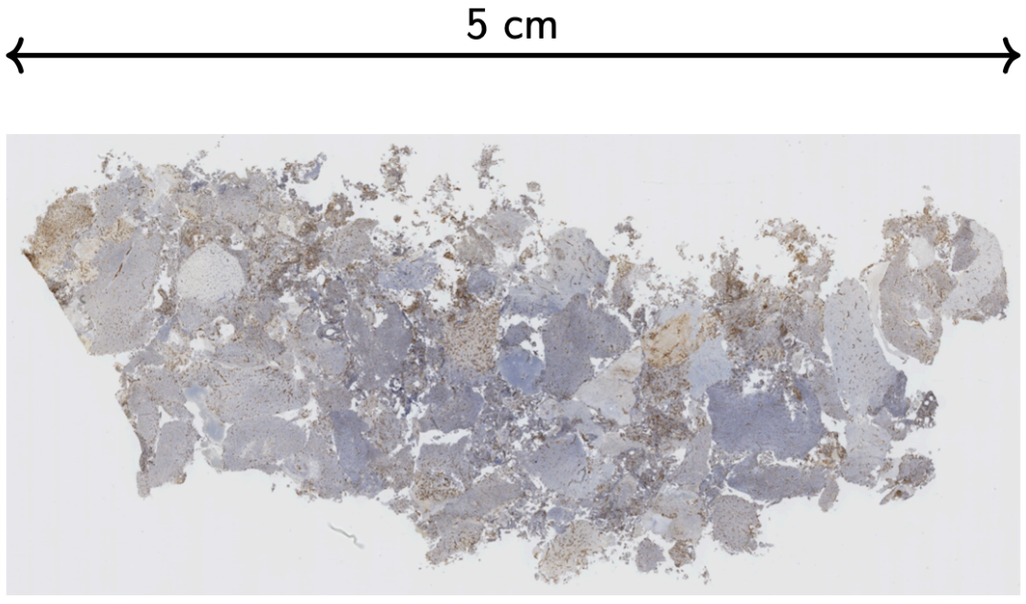
OPCs forming moving fronts

Our projects

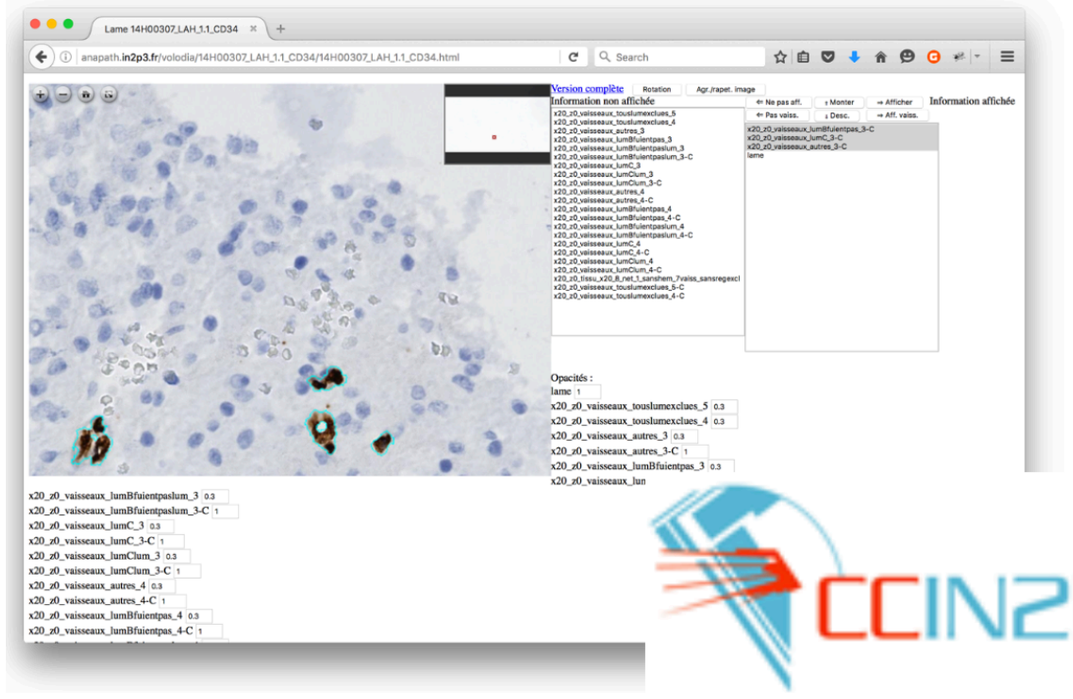
Big data approach for gliomas

- Transparisation and reconstruction of the 3D tumor and blood vessel architecture of rodent brain, to study effect of radiotherapy.

- In clinics: some algorithms to open and analyse quantitatively tissues from biopsies (cell, blood vessel, proliferating cell counts) have been developed and are now used by a lot of persons around the world. The objective now is to develop a software that could be used by clinicians.



Images are huge (this one : 138240×62976 pixels).



Deroulers C, Dangouloff-Ros V, Badoual M, Varlet T, Boddaert N (2016) Automatic quantification of the microvascular density on whole slide images, applied to paediatric brain tumours, *Diagnostic Pathology*, **2**, 209