

Genomic physics: biophysical modeling confronted to genomic data

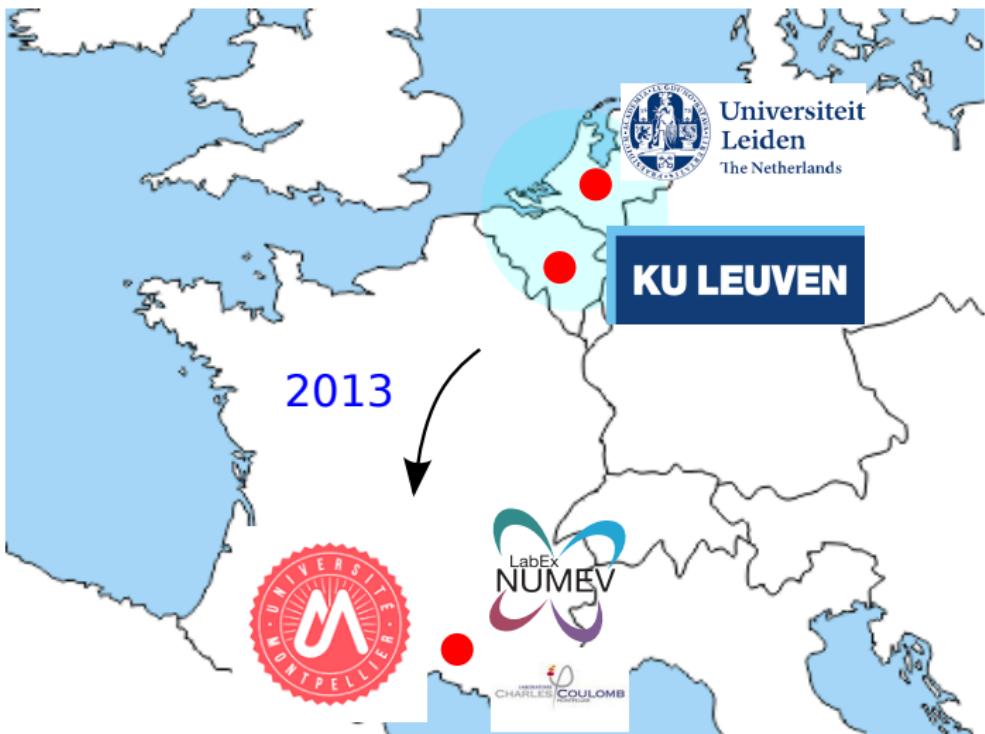
Jean-Charles WALTER

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CNRS & Université de Montpellier*

Journée Labex NUMEV
Novembre 2021



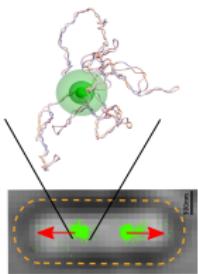
- Physical properties of DNA



- Biophysics of intracellular processes



Genomic physics



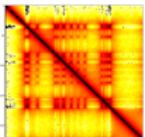
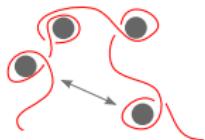
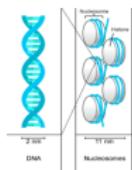
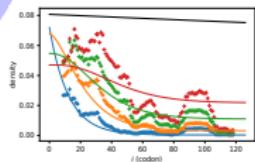
Bacterial DNA organization & segregation

genomic physics

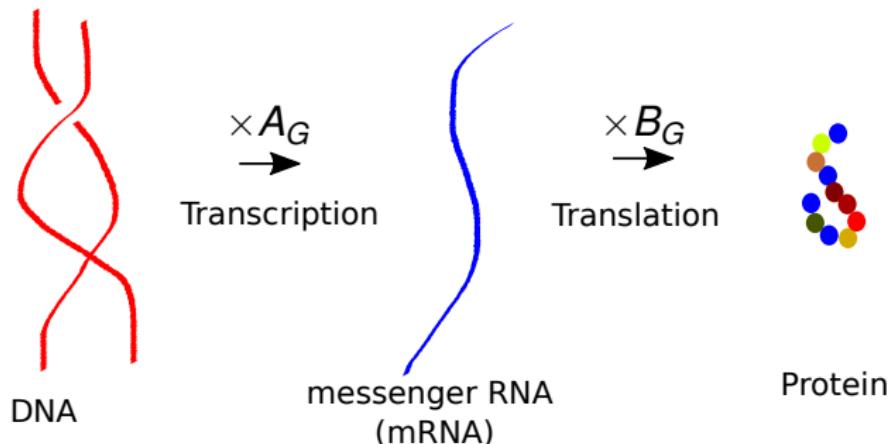


Translation of messenger RNA by ribosomes

Epigenetic regulation of eukaryotic chromatin

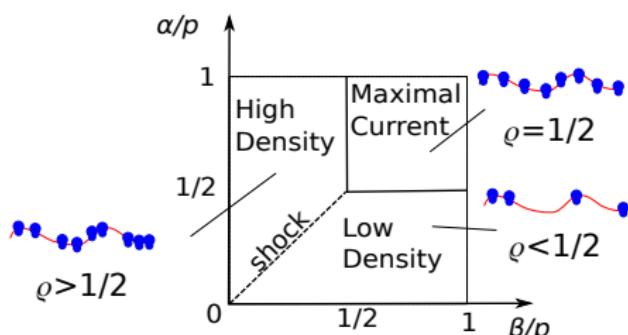
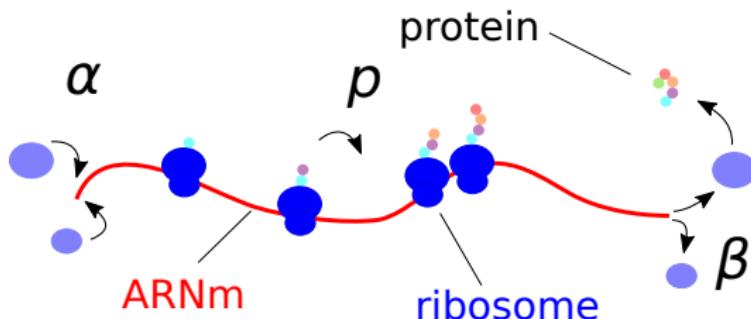


The expression of a gene depends on translation



- Expression of a gene G : $A_G \times B_G$ with $B_G \neq B_{G'}$!!
- What are the physical interactions that determine B_G ?

Translation of mRNA: the physics of 1D transport



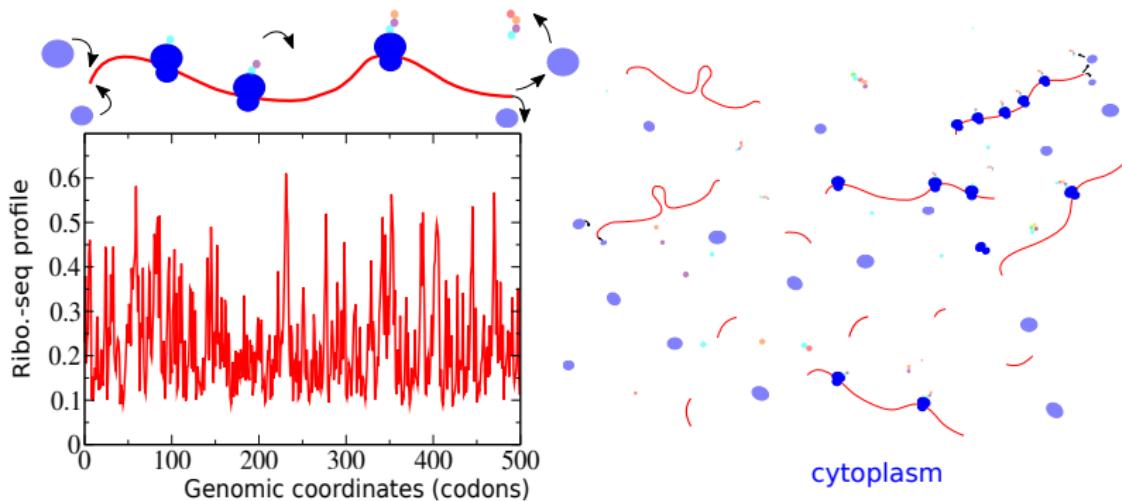
→ Finite resources:

Ciandrini*, Neri*, JCW* ... Phys. Biol. 2014

→ Finite diffusion:

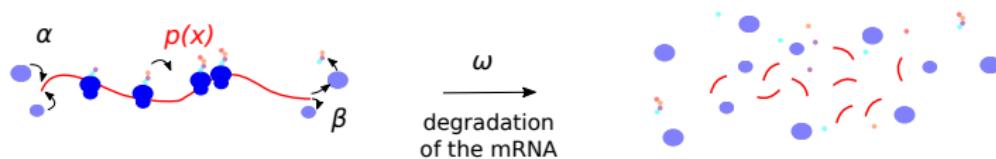
Dauloudet*, Neri*, JCW* ... Eur. Phys. J. 2021

Estimating kinetics rates with Ribo-seq data

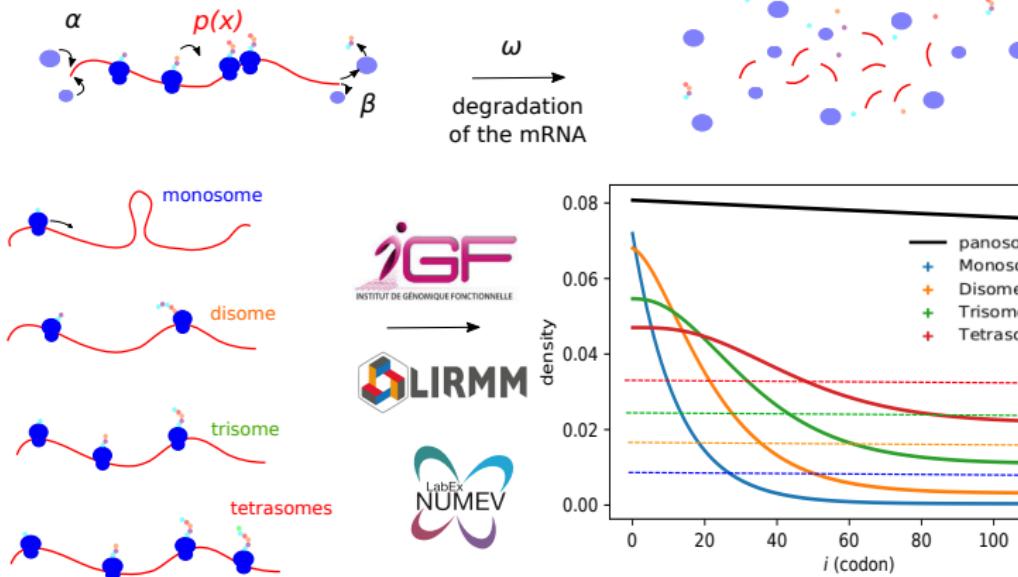


- 1 Effect of production/degradation of mRNA ?
 - 2 Normalization of experimental data for quantitative analysis?
- Gene Expression Modeling (L2C+IGF+LIRMM) – Flagship project NUMEV 2016-2020
 - Carole Chevalier & Paul Soudon (PhD students at L2C)

Estimation of the kinetic rates: mRNA degradation

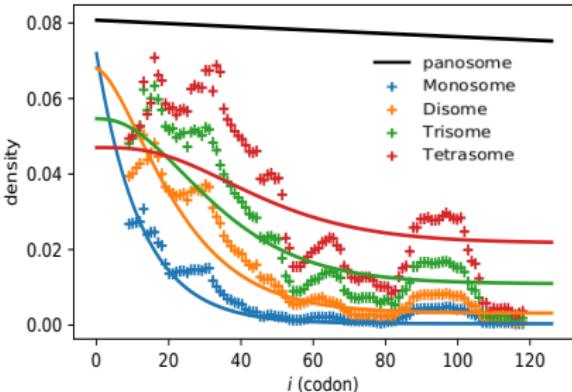
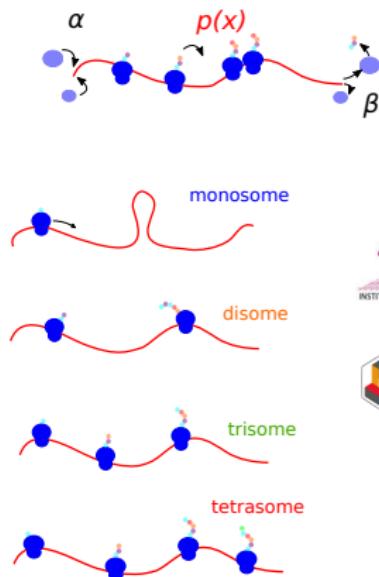


Estimation of the kinetic rates: mRNA degradation



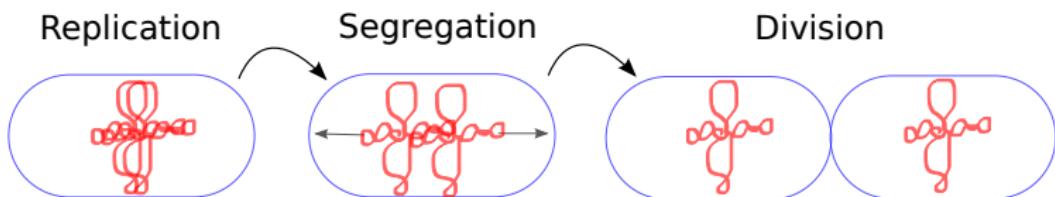
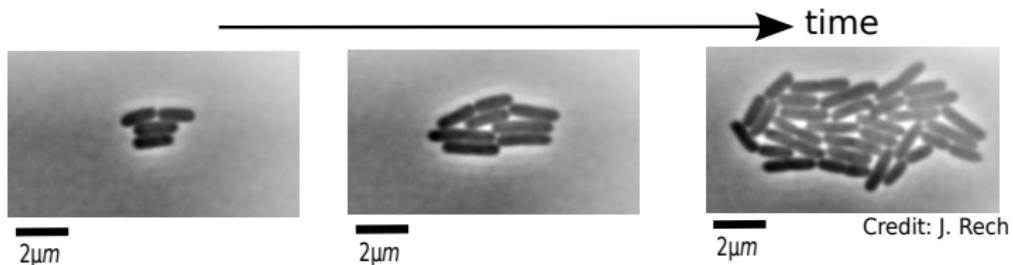
$$\alpha \approx 0.05 s^{-1}, \omega \approx 5 \cdot 10^{-4} s^{-1}, p \approx 1 \text{ codon/s}$$

Estimation of the kinetic rates: mRNA degradation

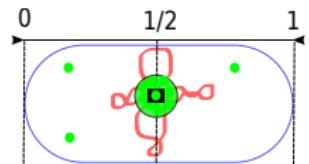


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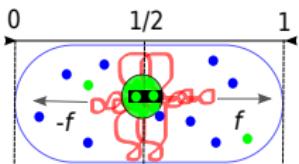
The bacterial DNA segregation



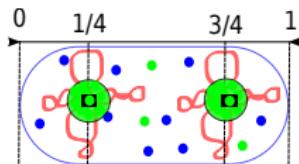
The ParABS system



Step 1. Formation of ParBS
Equilibrium LLPS ?



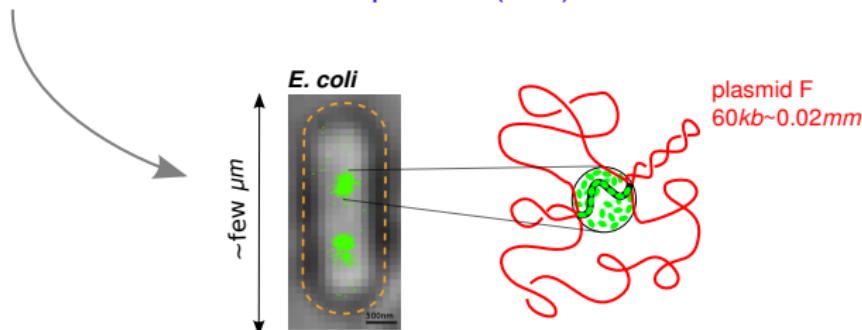
Step 2. Separation of DNA copies
Non-eq. phase separation (ATP)



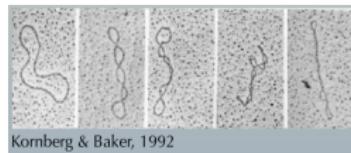
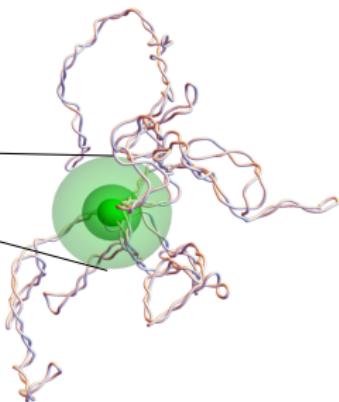
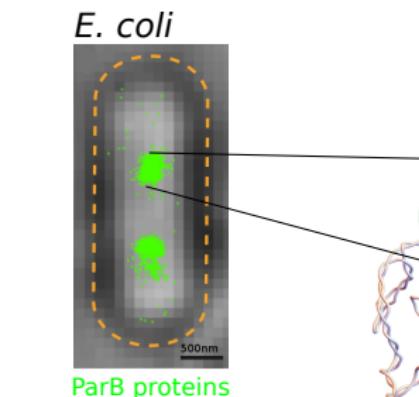
Step 3.
Equipoioning

JCW* ... Geniet Phys. Rev. Lett., 2017

- DNA
- ParB
- ParA
- parS



The Stochastic Binding model

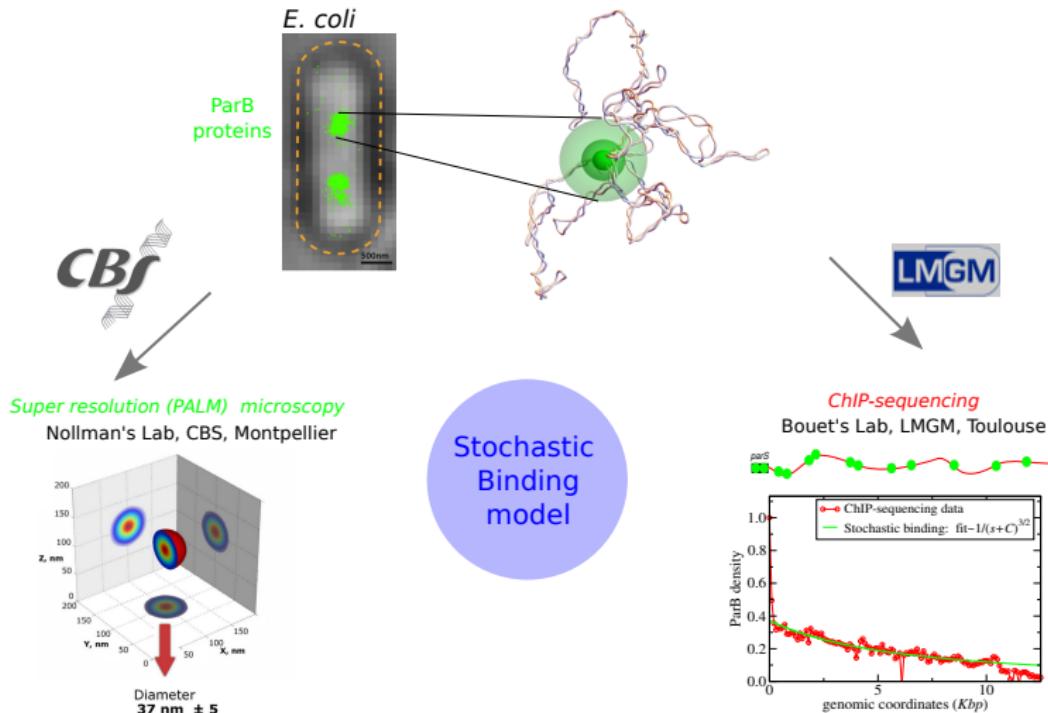


$L=60\text{kb}$
 F plasmid
 $l_p=150\text{bp}$
Monte Carlo simulations:
bending+twist+loop $\rightarrow \sigma$

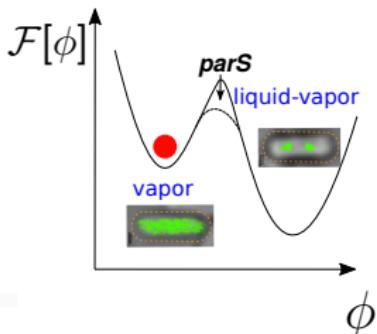
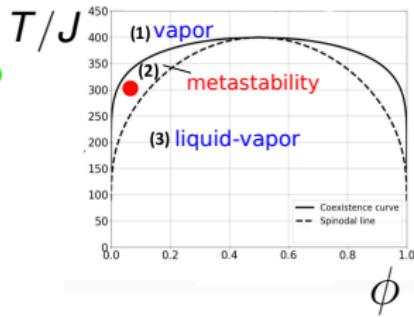
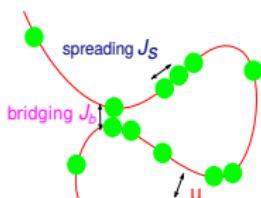
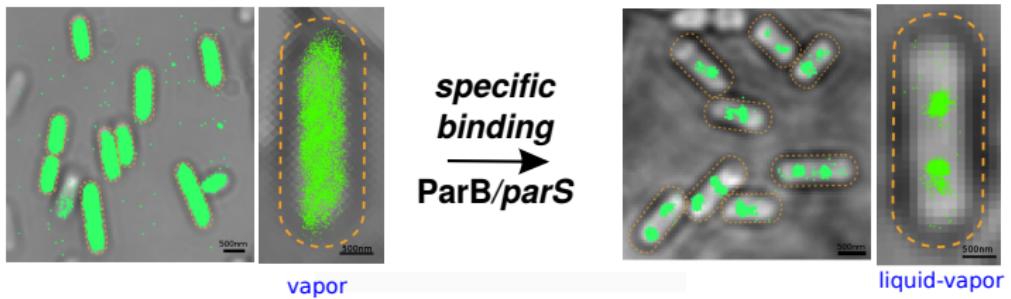
Sanchez... Bouet *Cell Syst.*, 2015
Diaz... JCW* & Bouet* *Mol. Syst. Biol.*, 2018
JCW... Brødersz *New J. Phys.*, 2018
JCW* ... Bouet* *iScience*, 2020

JCW* ... Junier* *PLOS Comp. Biol.*, 2020
In collaboration with I Junier (Grenoble-Alpes Univ.)

The Stochastic Binding model



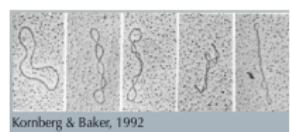
Liquid-liquid phase separation of proteins



Guilhas, JCW, ... Nollmann Mol. Cell. 2020

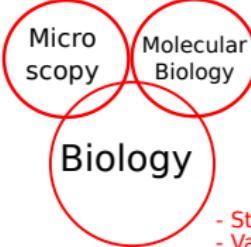
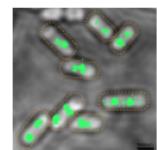
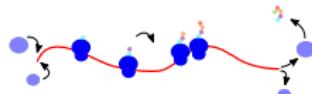
David, JCW, ... Palmeri Phys. Rev. Res. 2020

Conclusion: feedback between Physics and Biology



New paradigm of Matter

Self-organized & regulated systems

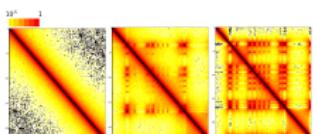
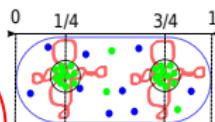


Physics

Polymers

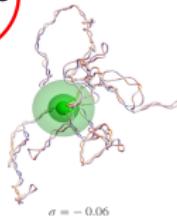
Active
Matter

Colloids



Structural interconnectivity

- Storage of information
- Variability of gene expression
- Membraneless compartments



Thank you for your attention!

The collage consists of several rectangular boxes containing text and logos, arranged over a photograph of a sandy beach with wooden fence posts in the background.

- Top Left Box:** J Dorignac, F Geniet, J Palmeri, A Parmeggiani, N-O Walliser. **Biophysical modeling**. Logos: C Chevalier, G David, P Soudon. **LABORATOIRE CHARLES COULOMB MONTPELLIER**.
- Top Middle Box:** A David, A Choquet. **Molecular biology**. Logo: **iGF INSTITUT DE GÉNOMIQUE FONCTIONNELLE**.
- Top Right Box:** **cnrs** (danser les frontières).
- Middle Left Box:** B Guilhas, D Cattoni, A Le Gall, M Nollmann. **Super resolution microscopy**. Logo: **CBS**.
- Middle Center Box:** **Bioinformatics**. E Rivals. Logos: **LIRMM**, **LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN**.
- Middle Right Box:** N Wingreen, **PRINCETON UNIVERSITY**. C Broedersz.
- Bottom Left Box:** R Diaz-Debaugny, C Mathieu-Demazière, J Rech, JY Bouet. **Molecular biology**. Logos: **LMGM**, **UNIVERSITÉ TOULOUSE III PAUL SABATIER**.
- Bottom Center Box:** I Junier, T Lepage. **Numerical Simulations**. Logos: **UGA Université Grenoble Alpes**, **TiMC**.
- Bottom Right Box:** **LabEx NUMEV**.