

Genomic physics: biophysical modeling confronted to genomic data

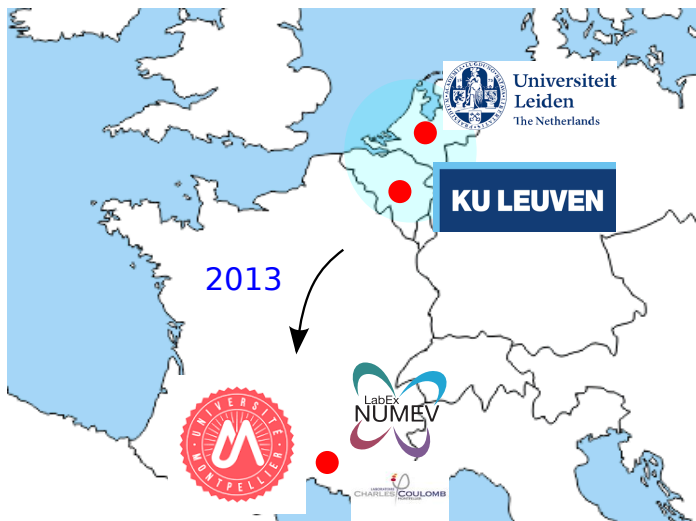
Jean-Charles WALTER

*Laboratoire Charles Coulomb (L2C)
CNRS & Université de Montpellier*

Journée Labex NUMEV
Novembre 2021



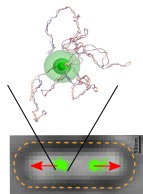
- Physical properties of DNA



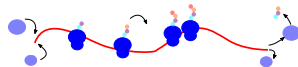
- Biophysics of intracellular processes



Genomic physics

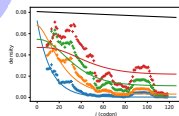


Bacterial DNA organization & segregation

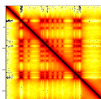
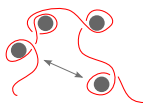
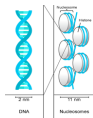


Translation of messenger RNA by ribosomes

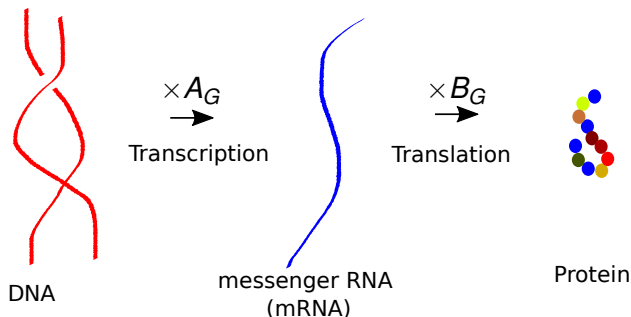
genomic physics



Epigenetic regulation of eukaryotic chromatin



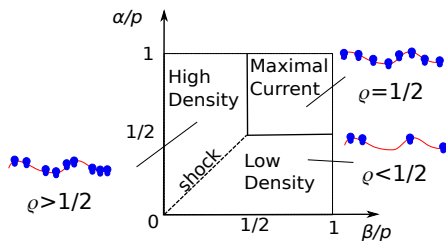
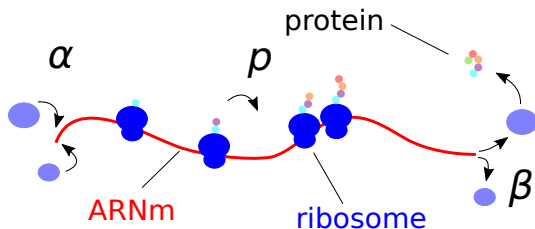
The expression of a gene depends on translation



→ 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



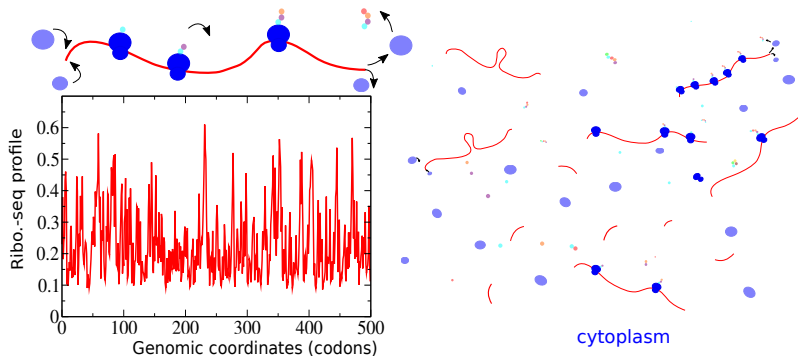
→ Finite resources:

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

→ Finite diffusion:

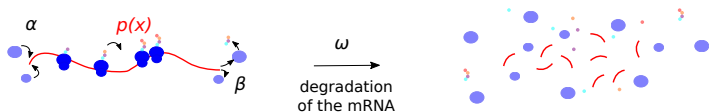
Dauloudet*, Neri*, JCW* ... *Eur. Phys. J.* 2021

Estimating kinetics rates with Ribo-seq data

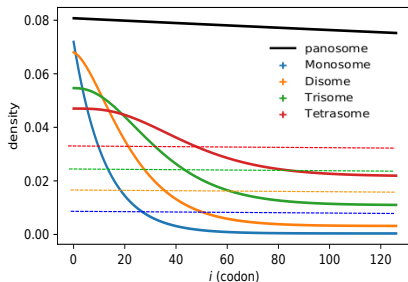
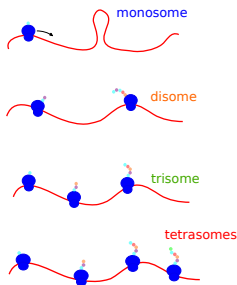
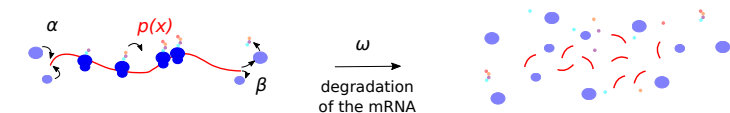


- 1 Effect of production/degradation of mRNA ?
 - 2 Normalization of experimental data for quantitative analysis?
- Gene Expression Modeling (L2C+IGF+LIRMM) – **Flagship project NUMEV 2016-2020**
 - **Carole Chevalier** & Paul Soudon (PhD students at L2C)

Estimation of the kinetic rates: mRNA degradation

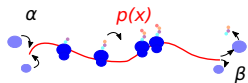


Estimation of the kinetic rates: mRNA degradation

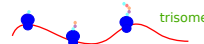


$$\alpha \approx 0.05s^{-1}, \omega \approx 5.10^{-4}s^{-1}, p \approx 1 \text{ codon/s}$$

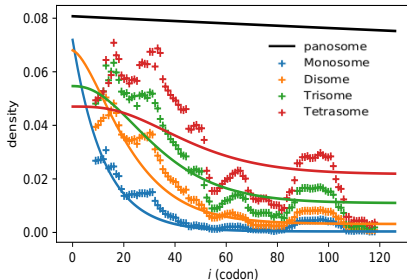
Estimation of the kinetic rates: mRNA degradation



ω
degradation
of the mRNA

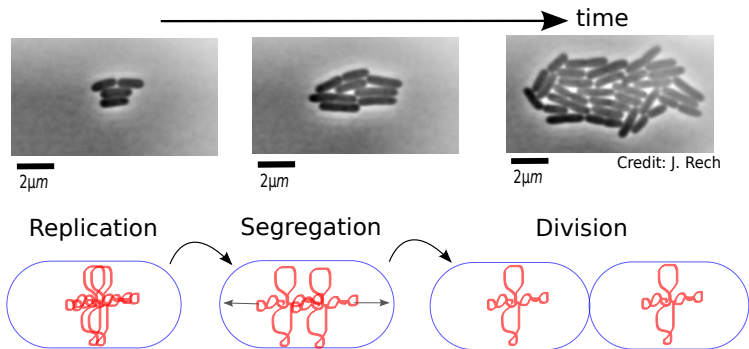


INSTITUT DE GÉNÉTIQUE FONCTIONNELLE

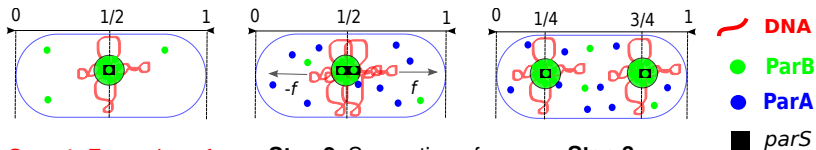


$$\alpha \approx 0.05s^{-1}, \omega \approx 5.10^{-4}s^{-1}, p \approx 1 \text{ codon/s}$$

The bacterial DNA segregation



The ParABS system



Step 1. Formation of ParBS

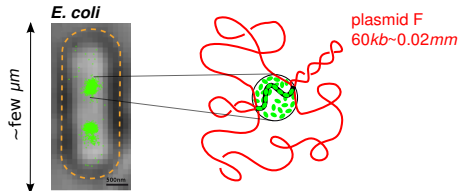
Equilibrium LLPS ?

Step 2. Separation of DNA copies

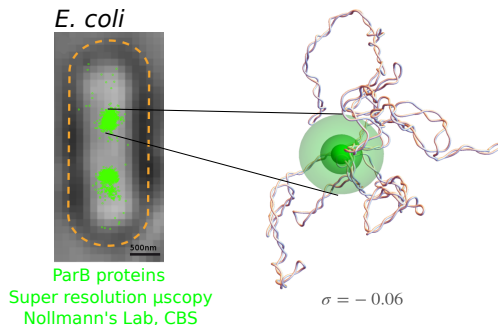
Non-eq. phase separation (ATP)

Step 3. Equipositioning

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



The Stochastic Binding model



$L=60kb$

F plasmid

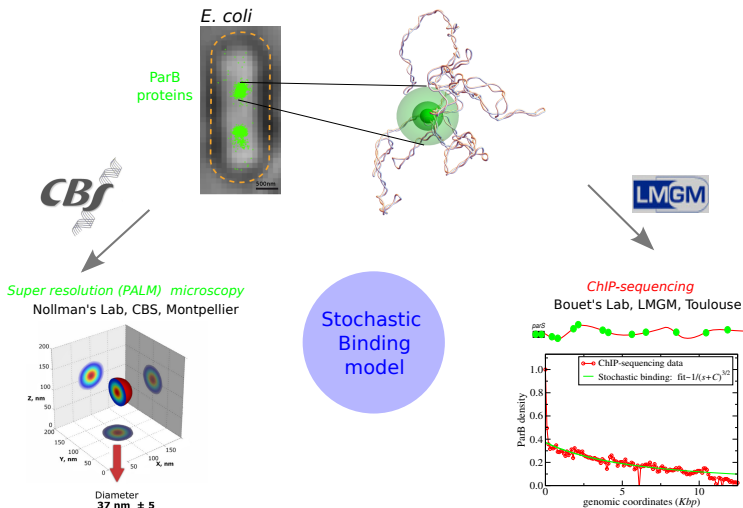
$l_p=150bp$

Monte Carlo simulations:
bending+twist+loop $\rightarrow \sigma$

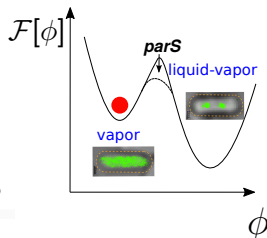
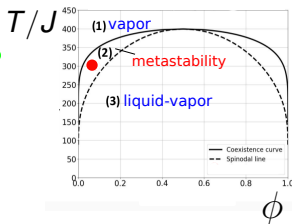
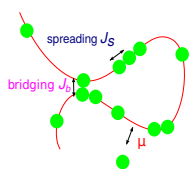
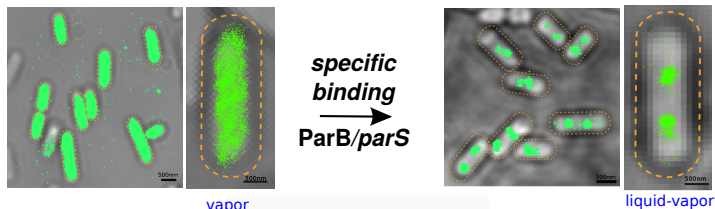
Sanchez... Bouet *Cell Syst.*, 2015
Diaz... JCW* & Bouet* *Mol. Syst. Biol.*, 2018
JCW... Brøedersz *New J. Phys.*, 2018
JCW* ... Bouet* *iScience*, 2020

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

The Stochastic Binding model

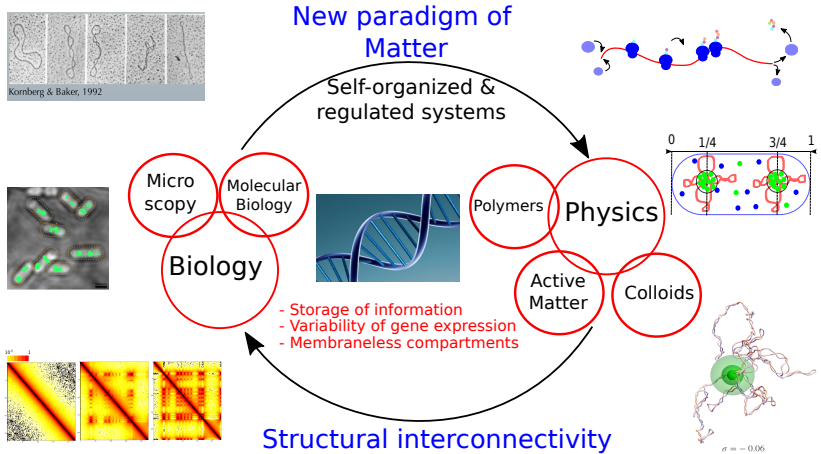


Liquid-liquid phase separation of proteins













Guilhas, JCW, ... Nollmann *Mol. Cell.* 2020
David, JCW, ... Palmeri *Phys. Rev. Res.* 2020

Conclusion: feedback between Physics and Biology



Thank you for your attention!

<p>J Dornnac F Geniet J Palmeri A Parmeggiani N-O Walliser</p> <p>Biophysical modeling</p> <p>C Chevalier G David P Soudon</p> 	<p>A David A Choquet</p> <p>Molecular biology</p> 		
<p>B Guilhas D Cattoni A Le Gall M Nollmann</p> <p>Super resolution microscopy</p> 	<p>Bioinformatics</p> <p>E Rivals</p> 	<p>N Wingreen</p> <p>PRINCETON UNIVERSITY</p> <p>C Broedersz</p>  	
<p>R Diaz-Debaugny C Mathieu-Demazière J Rech J Bouet</p> <p>Molecular biology</p>  	<p>UGA Université Grenoble Alpes</p> <p>TIMC</p> <p>I Junier T Lepage</p> <p>Numerical Simulations</p>	