Dynamic of actin polymerisation and depolymerisation in the cell: a microscopic continuous-space model.

IMS Annual Meeting 2026

Timothé Ringeard[1]
joint work with Amandine Véber[1], François Robin[2] and Ayman Moussa[3]

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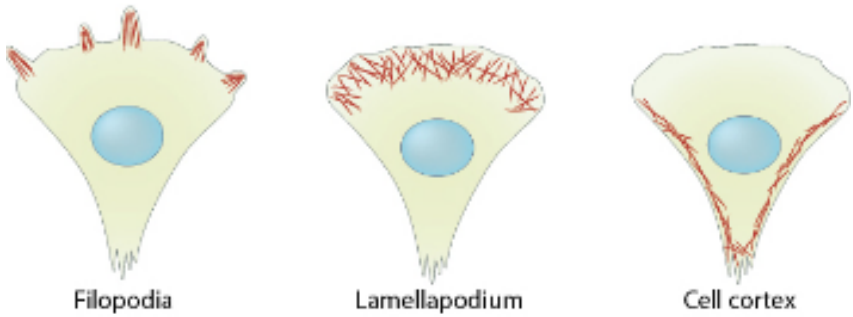
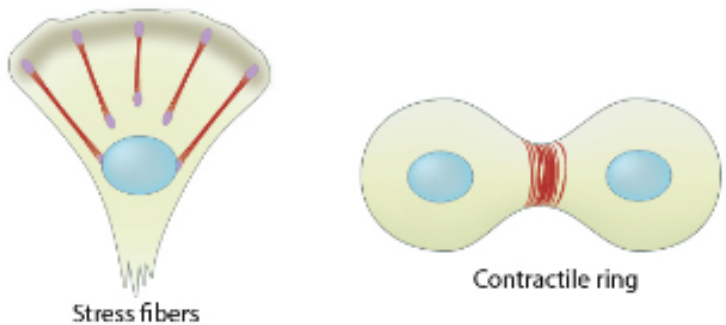
[1]MAP5, Université Paris Cité, Paris
[2]IBPS, Sorbonne Université, Paris
[3]LJLL, Sorbonne Université, Paris

In this talk

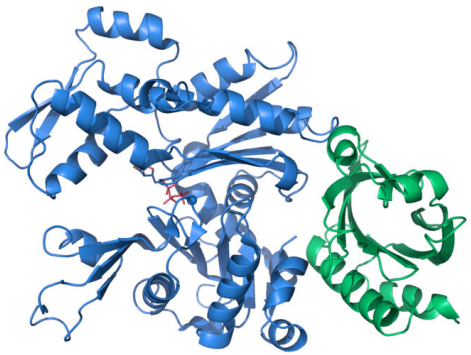
1. Biological setting
2. Construction of the model
3. Large population and small radius limits
4. Global behaviour

Actin monomers and polymers



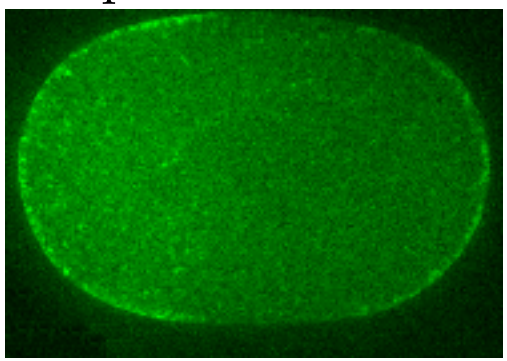


Observing actin

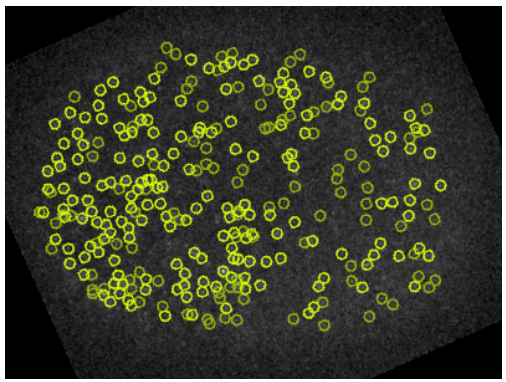


Fluorescent actin-binding proteins

Observe total intensity
$\rightsquigarrow$ Heatmap.



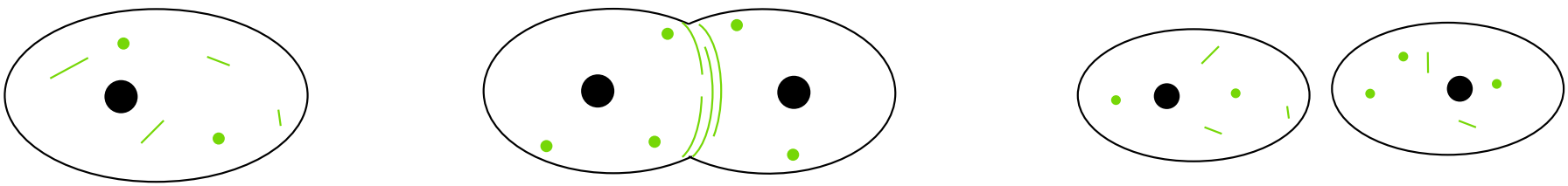
Use photobleaching to reduce the number of tagged particules to $\sim$100, and observe them one by one
$\rightsquigarrow$ Single Molecule Tracking.



How to observe a polymer entirely?
Difficulty of direct observation $\rightsquigarrow$ Models.

Choices for the model

- Macroscopic OR Microscopic
- Track the time evolution
- Spatial component

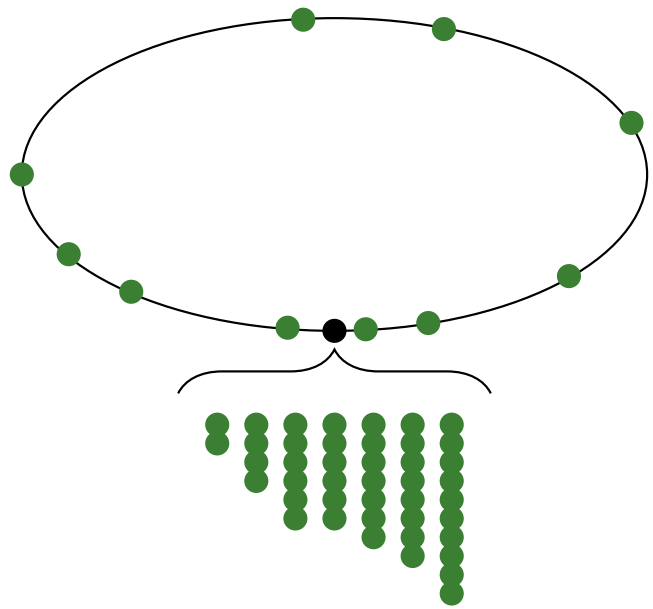


• free actin monomer
– actin polymer

Question: How do the monomers behave to the presence of very long polymers at a prescribed location in space?

The model

- The **cell** $\rightsquigarrow \mathbb{T} = \mathbb{R}/\mathbb{Z}$.
- The **cleavage furrow** $\rightsquigarrow$ the point $0 \in \mathbb{T}$.
- A **monomer** $\rightsquigarrow$ A particle evolving spatially in $\mathbb{T}$.
- A **polymer** $\rightsquigarrow$ A particle forced to stay spatially at $0 \in \mathbb{T}$, but having a trait $\ell \in \delta\mathbb{N}$ corresponding to its *length*.



- Two **reactions** of polymerisation and depolymerisation:

$$(P, 0, \ell) + (M, y, \delta) \to (P, 0, \ell + \delta) \qquad \ell \geq \delta$$
$$(P, 0, \ell) \to (P, 0, \ell - \delta) + (M, 0, \delta) \qquad \ell \geq \delta,$$

with respective rates $\lambda^+, \lambda^- > 0$.

The process

- The system at any given time is represented by a counting measure on the space $\mathcal{P} = \{M\} \times \mathbb{T} \sqcup \{P\} \times \mathbb{R}_+$.
- The process $\mu = (\mu_t)_{t \geq 0}$ belongs to the space of all càdlàg functions taking their values in $\mathcal{M}_p(\mathcal{P})$, denoted by $\mathbb{D}(\mathbb{R}_+, \mathcal{M}_p(\mathcal{P}))$.
- Monomers diffuse according to independent Brownian motions, until they are absorbed into a polymer.
- Each polymer depolymerises at a constant rate λ^-.
- Each polymer polymerises at a rate λ^+ times the number of monomers in a viscinity of $0 \in \mathbb{T}$, i.e., at a rate $\lambda^+ \int_{\mathbb{T}} \Gamma(x) \mu_t(M, dx)$, where Γ is a smooth probability kernel centered at 0.

Construction of the process

To construct this process, we start at the time $t_0 = 0$ with a given counting measure $\mu_0 \in \mathcal{M}_p(\mathcal{P})$.

1. Draw the Brownian trajectories of the monomers $(\overline{\mu}_t)_{t \geq t_0}$.
2. Draw two independent exponential variables $\mathcal{E}^-$ and $\mathcal{E}^+$ with mean 1. Set

$$\tau^- = \inf \left\{ t \geq 0 : \int_{t_0}^{t} \lambda^- \mu_{t_0}(P, \mathbb{R}_+^*) ds \geq \mathcal{E}^- \right\}$$

$$\tau^+ = \inf \left\{ t \geq 0 : \int_{t_0}^{t} \lambda^+ \mu_{t_0}(P, \mathbb{R}_+^*) \int_{\mathbb{T}} \Gamma(x) \overline{\mu}_s(M, dx) ds \geq \mathcal{E}^+ \right\}.$$

3. Set $\tau_1 = \tau^- \wedge \tau^+$, and define $t_1 = t_0 + \tau_1$.
4. Choose a polymer uniformly among the extant polymers, and a monomer according to the law $\Gamma(x)\overline{\mu}_{t_1}(M, dx) / \left(\int_{\mathbb{T}} \Gamma(y)\overline{\mu}_{t_1}(M, dy) \right)$.
5. Define the process μ to be equal to $\overline{\mu}$ on the time interval $[t_0, t_1)$, and apply the reaction corresponding to τ_1 at time t_1.
6. Repeat from the first step with $t_0' = t_1$.

Large population limit

- Number of monomers $\sim N$.
- Number of polymers $\sim N'$.
- Typical length of a polymer $\sim N/N'$.

We are interested in the limit $N, N', N/N' \to \infty$ (e.g. $N' = N^\alpha$, with $0 < \alpha < 1$).
We construct the process $\mu^N = \mu^{N,M} + \mu^{N,P}$, that we normalize as follows

$$\widetilde{\mu}^N = \frac{1}{N}\mu^{N,M} + \frac{1}{N'}\mu^{N,P}.$$

Hypotheses:

- The scaled initial condition converges in law: $\widetilde{\mu}_0^N \underset{N\to\infty}{\longrightarrow} \mu_0 = (m_0, p_0)$.
- As $N, N' \to \infty$, the rates scale as

$$\begin{cases} \frac{N'}{N}\lambda^{-,N} & \to \lambda^-, \\ N'\lambda^{+,N} & \to \lambda^+. \end{cases}$$

- There is a constant $C_0 < \infty$ such that a.s. $\sup_N \langle \widetilde{\mu}_0^N, (1, 1+l)\rangle \leq C_0$.

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Theorem

Under the regularity assumption $p_0 \in W^{1,1}(\mathbb{R}_+)$, the process $\widetilde{\mu}^N$ converges in law to a deterministic process $\mu = (m, p) \in \mathcal{C}(\mathbb{R}_+, \mathcal{M}_+(\mathcal{P}))$, which is the only weak solution in this space to

$$\begin{cases} \partial_t m_t &= D\Delta m_t + \left(\lambda^-\delta_0 - \lambda^+\Gamma m_t\right)\langle p_t, \mathbb{1}_{l>0}\rangle, \\ \partial_t p_t &= \left(\lambda^- - \lambda^+\langle m_t, \Gamma\rangle\right)\partial_\ell p_t, \\ \partial_t \langle p_t, \mathbb{1}_{l=0}\rangle &\geq 0. \end{cases}$$

Large population limit: ideas of the proof

3 steps proof :

1. The sequence $\widetilde{\mu}^N$ is tight in the space $\mathbb{D}([0,T],\mathcal{M}_+(\mathcal{P}))$ $\rightsquigarrow$ Criteria from Roelly, Aldous-Rebolledo.
2. Any limit μ of a converging subsequence satisfies the desired equation. $\rightsquigarrow$ Martingale problem + specific arguments.
3. The limiting equation has a unique solution in the space where μ can live. $\rightsquigarrow$ Grönwall argument.

We extensively use the martingale property satisfied by μ^N, which describes the process on a macroscopic level.
The difficult part is to show that $\partial_t \langle p_t, \mathbb{1}_{l=0} \rangle \geq 0$, as it is not a macroscopic property.

Influence of the reaction radius in the limiting process

What happens if the reaction radius $\varepsilon \to 0$, i.e., if $\Gamma \to \delta_0$?

Kernel $\Gamma^\varepsilon = \frac{1}{\varepsilon}\Gamma^1(\frac{\cdot}{\varepsilon}) \quad \rightsquigarrow \quad$ Solutions m^ε and p^ε.
Let $q_t^\varepsilon = p_t^\varepsilon - p_t^\varepsilon(\{0\})\delta_0$.

Proposition

Assume that $m_0 \in \mathrm{L}^2(\mathbb{T})$. Then, as $\varepsilon \to 0$, we have the strong convergence $m^\varepsilon \to \mathfrak{m}$ in $\mathrm{L}^2([0,T], \mathrm{H}^1(\mathbb{T}))$ and $q^\varepsilon \to \mathfrak{q}$ in $\mathrm{L}^\infty([0,T], \mathrm{L}^1(\mathbb{R}_+))$, for a pair $(\mathfrak{m}, \mathfrak{q})$ which is a weak solution to

$$\begin{cases} \partial_t \mathfrak{m}_t &= D\Delta \mathfrak{m}_t + \Big(\lambda^- - \lambda^+ \mathfrak{m}_t\Big)\delta_0 ||\mathfrak{q}_t||_1, \\ \partial_t \mathfrak{q}_t &= \Big(\lambda^- - \lambda^+ \mathfrak{m}_t(0)\Big)\partial_\ell \mathfrak{q}_t, \\ \partial_t ||\mathfrak{q}_t||_1 &\leq 0. \end{cases}$$

The result comes from a structural stability result on the previous equations with smooth Γ: for solutions $(m^1, p^1), (m^2, p^2)$ respectively associated with kernels Γ^1, Γ^2, we show that

$$||m^1 - m^2||_{\mathrm{L}^2(\mathrm{H}^1)} + ||p^1 - p^2||_{\mathrm{L}^\infty(\mathrm{L}^1)} \leq C\, ||\Gamma^1 - \Gamma^2||_{\mathrm{H}^{-1}}.$$

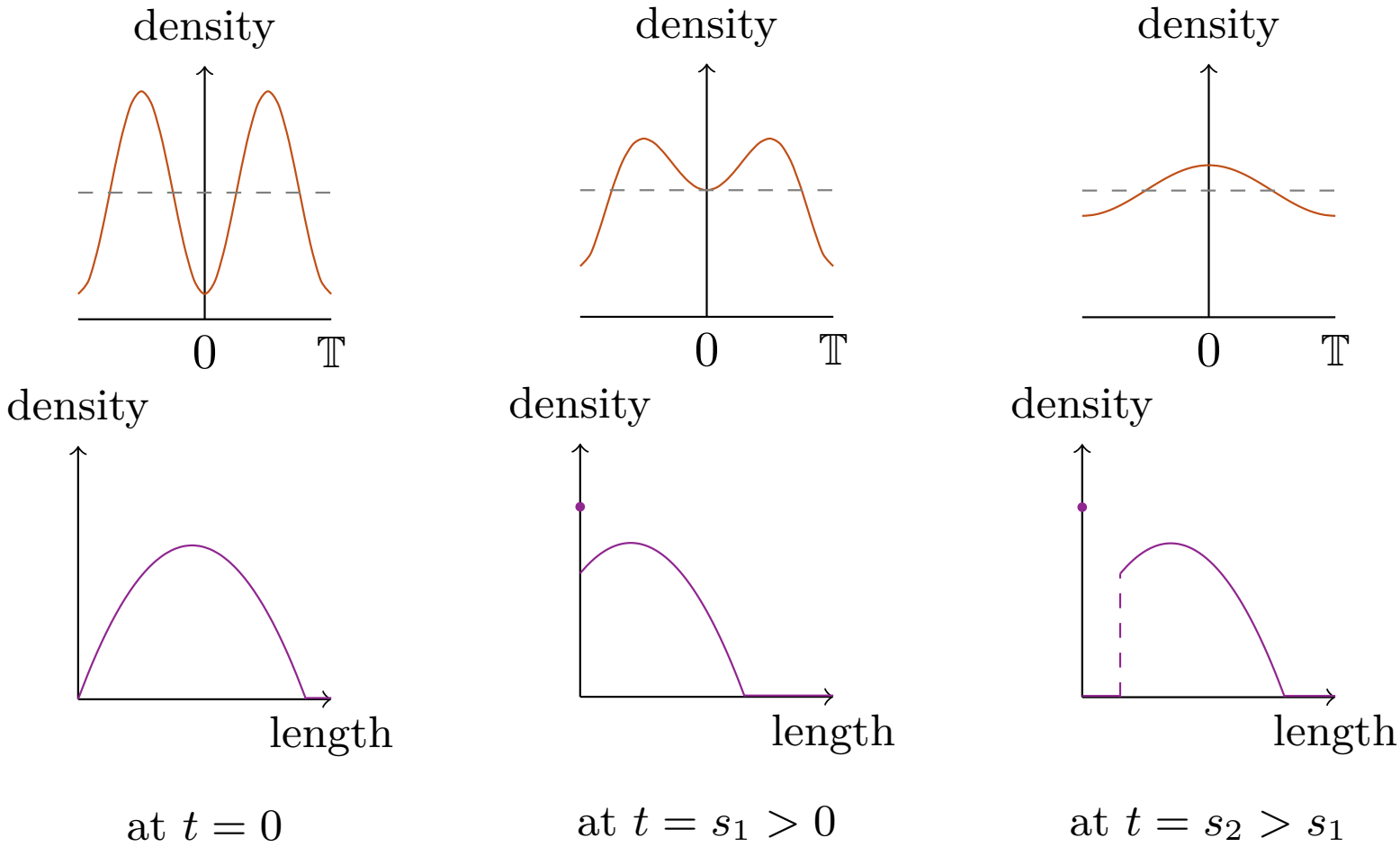

Figure: Example of a solution $(\mathfrak{m}, \mathfrak{q})$ to the limiting equations with kernel $\Gamma = \delta_0$.

Behaviour of the solutions

Equilibrium state:

- Spatially constant density d of monomers,
- Any profile $p(\ell)$ of polymer lengths
- The monomers concentration is linked to the polymer profile via

$$d = d_0 - \int_0^\infty \ell p(\ell) d\ell,$$

  where d_0 is the total concentration of monomers if all polymers were to empty.
- The profile $p(\ell)$ typically has a gap in a interval of the form $(0, \ell^*)$: there are no polymers of very small length.
- d is very difficult to predict from the inital condition.

The solutions can also exhibit several oscillations between global polymerisation and global depolymerisation.

A larger class of models

Framework developped in Popovic & Véber (2023):

- Any number of **species** $A_1, \dots, A_n$, **diffusing** in a compact space E.
- Any number of **reactions** r, of any type, e.g.

$$A_1 + 2A_2 \mapsto 2A_1 + A_3, \qquad A_1 + A_3 \mapsto \emptyset, \qquad 2A_2 \mapsto 3A_2 \dots$$

- Reaction **rates** $\lambda_r(y, \mu_t)$ depending on the location and current process state.
- Interactions of the species via a kernel Γ, modelling the **radius** of the reactions.

The model presented earlier has:

- Molecules with **traits** (length).
- A limit as the reaction **radius goes to zero**.

Outlook for future work

- Confront model with **experimental data**: Which quantities are measurable?
- Model **other actin structures**, for example branched actin networks.
- Add **accessory proteins**, such as formin, cofilin, in the model.

- Study the **combined limit** large population + small radius.

Thank you for listening!