


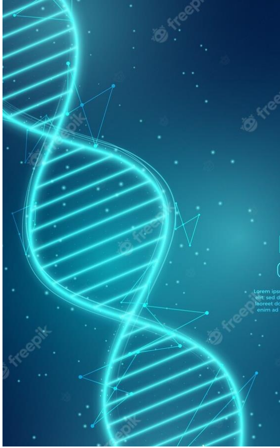

Phase segregation drives RNA-Protein dynamics

Andrea Signori, AIMS Conference, Wilmington, 02/06/23

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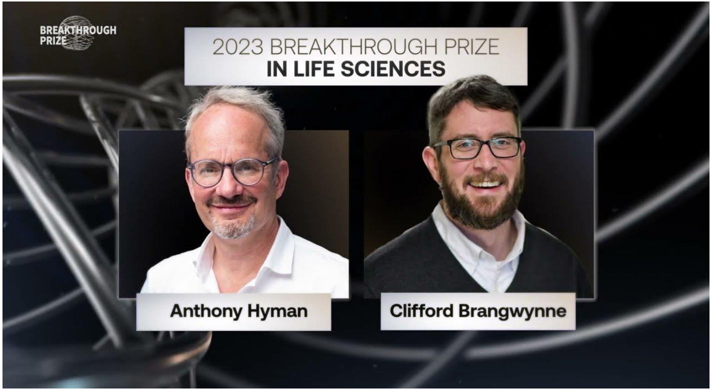

"For discovering a fundamental mechanism of cellular organization mediated by ***phase separation*** *of* ***proteins*** *and* ***RNA*** *into membraneless* ***liquid droplets****."*

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On a Phase Field Model for RNA-Protein Dynamics

Authors: Maurizio Grasselli, Luca Scarpa, and Andrea Signori | AUTHORS INFO & AFFILIATIONS

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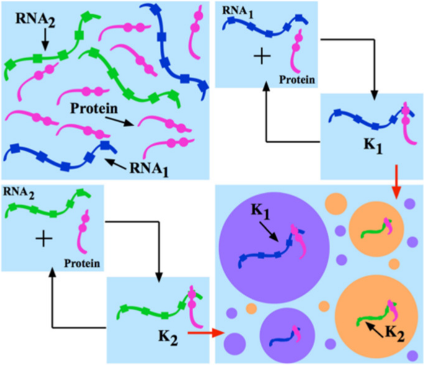
Modeling background

Two species of RNA competing for a pool of shared protein. The φ_i complex, $i = 1, 2$, is formed when the RNA R_1 interacts with a free protein P. Both protein–RNA complexes are capable of driving phase separation and forming distinct droplets.



- Protein: P;
- RNA-species: R_1 and R_2;
- Protein-RNA complexes:
  $R_1 + P \rightsquigarrow \varphi_1, \quad R_2 + P \rightsquigarrow \varphi_2.$

- K. Gasior, M.G. Forest, A.S. Gladfelter and J.M. Newby. Modeling the mechanisms by which coexisting biomolecular RNA-Protein condensates form. *Bull. Math. Biol.* **82**:153, 2020.
- K. Gasior, J. Zhao, G. McLaughlin, M.G. Forest, A.S. Gladfelter and J. Newby. Partial demixing of RNA-protein complexes leads to intradroplet patterning in phase-separated biological condensates. *Phys. Rev. E* **99**:012411, 2019.

RNA-Protein model

Let $\Omega \subset \mathbb{R}^3$, bdd and smooth domain, and $T > 0$. We set

$$\boldsymbol{\varphi} := (\varphi_1, \varphi_2), \quad \boldsymbol{\mu} := (\mu_1, \mu_2), \quad \mathrm{R} := (R_1, R_2).$$

Then, the `RNA-Protein` system we are going to analyse reads as

$$
\begin{aligned}
&\partial_t \boldsymbol{\varphi} - \Delta \boldsymbol{\mu} = \mathrm{S}_{\boldsymbol{\varphi}}(\boldsymbol{\varphi}, P, \mathrm{R}) && \text{in } Q := \Omega \times (0,T),\\
&\boldsymbol{\mu} = -\Delta \boldsymbol{\varphi} + \Psi_{\boldsymbol{\varphi}}(\boldsymbol{\varphi}) && \text{in } Q,\\
&\partial_t P - \Delta P = S_P(\boldsymbol{\varphi}, P, \mathrm{R}) && \text{in } Q,\\
&\partial_t \mathrm{R} - \Delta \mathrm{R} = \mathrm{S}_{\mathrm{R}}(\boldsymbol{\varphi}, P, \mathrm{R}) && \text{in } Q,\\
&\partial_{\mathbf{n}} \boldsymbol{\varphi} = \partial_{\mathbf{n}} \boldsymbol{\mu} = \partial_{\mathbf{n}} \mathrm{R} = 0, \quad \partial_{\mathbf{n}} P = 0 && \text{on } \Sigma := \partial\Omega \times (0,T),\\
&\boxed{\boldsymbol{\varphi}(0) = \mathbf{0},} \quad \mathrm{R}(0) = \left(\tfrac{1-P_0}{2}\right)\mathbf{1}, \quad P(0) = P_0 \in (0,1) && \text{in } \Omega,
\end{aligned}
$$

being $\mathbf{0} = (0,0)$ and $\mathbf{1} = (1,1)$, $\Psi_{\boldsymbol{\varphi}} := \nabla \Psi$.

Working Framework

The order parameter $\boldsymbol{\varphi} = (\varphi_1, \varphi_2)$ lives in the 2D simplex:

$$\Delta_\circ := \{\boldsymbol{\varphi} = (\varphi_1, \varphi_2) \in \mathbb{R}^2 : \min\{\varphi_1, \varphi_2\} > 0, \varphi_1 + \varphi_2 < 1\}, \quad \Delta_\bullet := \overline{\Delta_\circ},$$

and the multi-well potential Ψ is of Flory-Huggins type. Namely, $\Psi = \Psi^{(1)} + \Psi^{(2)}$, where the `entropy` part $\Psi^{(1)}$ is

$$\Psi^{(1)}(\boldsymbol{\varphi}) = \begin{cases} \sum_{i=1}^{2} \varphi_i \ln \varphi_i + (1 - \varphi_1 - \varphi_2) \ln(1 - \varphi_1 - \varphi_2) & \text{if } \varphi_1 \geq 0,\ \varphi_2 \geq 0,\ \varphi_1 + \varphi_2 \leq 1, \\ +\infty & \text{otherwise,} \end{cases}$$

whereas the `demixing` term $\Psi^{(2)}$ is such that

$$\Psi^{(2)} \in C^2(\mathbb{R}^2), \qquad \nabla\Psi^{(2)} := \Psi^{(2)}_{\boldsymbol{\varphi}} : \mathbb{R}^2 \to \mathbb{R}^2 \text{ is Lip. continuous.}$$

RNA-Protein model (P)

$$
\begin{aligned}
&\partial_t \boldsymbol{\varphi} - \Delta \boldsymbol{\mu} = \mathrm{S}_{\boldsymbol{\varphi}} && \text{in } Q,\\
&\boldsymbol{\mu} = -\Delta \boldsymbol{\varphi} \quad \underbrace{+\Psi^{(1)}_{\boldsymbol{\varphi}}(\boldsymbol{\varphi})}_{\text{grad. of the singular and convex part}} \quad \underbrace{+\Psi^{(2)}_{\boldsymbol{\varphi}}(\boldsymbol{\varphi})}_{\text{grad. of the quadratic perturbation}} && \text{in } Q,\\
&\partial_t P - \Delta P = S_P && \text{in } Q,\\
&\partial_t \mathrm{R} - \Delta \mathrm{R} = \mathrm{S}_{\mathrm{R}} && \text{in } Q,\\
&\partial_{\mathrm{n}} \boldsymbol{\varphi} = \partial_{\mathrm{n}} \boldsymbol{\mu} = \partial_{\mathrm{n}} \mathrm{R} = 0, \quad \partial_{\mathrm{n}} P = 0 && \text{on } \Sigma,\\
&\boxed{\boldsymbol{\varphi}(0) = 0,} \quad \mathrm{R}(0) = \left(\tfrac{1-P_0}{2}\right)\mathbf{1}, \quad P(0) = P_0 \in (0,1) && \text{in } \Omega,
\end{aligned}
$$

with source terms defined by

$$
\underbrace{\min\{c_1, c_3\} \gg c_2 + c_4}_{\texttt{Biological fact}} \qquad
\begin{cases}
\mathrm{S}_{\boldsymbol{\varphi}} = -\mathrm{S}_{\mathrm{R}} = (c_1 P R_1 - c_2 \varphi_1, c_3 P R_2 - c_4 \varphi_2),\\
S_P = -c_1 P R_1 + c_2 \varphi_1 - c_3 P R_2 + c_4 \varphi_2.
\end{cases}
$$

Existence of global weak solutions

Suppose that

$$\boxed{\varphi_0 := 0,} \qquad P_0 \in L^2, \qquad \mathrm{R}_0 = (R_0^1, R_0^2) := \left(\frac{1-P_0}{2}\right)\mathbf{1},$$

$$0 \le P_0(x) \le 1 \quad \text{for a.a. } x \in \Omega, \qquad \left\| P_0 - \frac{1}{2} \right\|_{L^\infty(\Omega)} \le \frac{1}{2}\left(1 - \frac{c_2 + c_4}{\min\{c_1, c_3\}}\right).$$

Then, there exists $(\varphi, \boldsymbol{\mu}, P, \mathrm{R})$ such that

$$\varphi \in H^1(0,T;(\mathrm{H}^1)^*) \cap L^\infty(0,T;\mathrm{H}^1) \cap L^2(0,T;\mathrm{H}^2_{\mathrm{n}}), \quad \varphi \in \mathrm{L}^\infty(Q): \quad \varphi \in \Delta_\circ \quad \text{a.e. in } Q,$$

$$\boxed{\boldsymbol{\mu} \in L^p(0,T;\mathrm{H}^1) \cap L^2(\sigma,T;\mathrm{H}^1) \quad \forall p \in (1,2) \quad \forall \sigma \in (0,T),} \quad \nabla\boldsymbol{\mu} \in L^2(0,T;\mathrm{L}^2),$$

$$P \in H^1(0,T;(H^1)^*) \cap L^2(0,T;H^1) \cap L^\infty(Q),$$

$$\mathrm{R} \in H^1(0,T;(\mathrm{H}^1)^*) \cap L^2(0,T;\mathrm{H}^1) \cap \mathrm{L}^\infty(Q),$$

$$\boxed{\exists\, c_* > 0: \quad c_* < P(x,t) \le 1, \quad c_* < R_i(x,t) \le 1 \quad \text{for a.a. } (x,t) \in Q, \quad i = 1,2.}$$

The Cahn–Hilliard–Oono equation

This extends the state of art concerning the Cahn-Hilliard-Oono equation!

$$
\begin{aligned}
&\partial_t \varphi - \Delta \mu = S(\varphi) := m(h - \varphi) && \text{in } Q, \quad m > 0, \quad h \in (-1,1),\\
&\mu = -\Delta \varphi + F'_{\log}(\varphi) && \text{in } Q,\\
&\partial_{\mathrm{n}} \varphi = \partial_{\mathrm{n}} \mu = 0 && \text{on } \Sigma,\\
&\varphi(0) = \varphi_0 = -1 && \text{in } \Omega.
\end{aligned}
$$

Roughly speaking, for T_0 “small":

$$
\underbrace{\mu \in L^2(0,T;H^1)}_{\texttt{Previously:}\ (\varphi_0)_\Omega \in (-1,1)} \qquad \text{vs} \qquad \underbrace{\mu \in \bigcap_{\sigma \in (0,T),\, p \in (1,2)} L^2(\sigma,T;H^1) \cap L^p(0,T_0;H^1)}_{\texttt{Our setting:}\ (\varphi_0)_\Omega = (-1)_\Omega = -1 \notin (-1,1)}.
$$

First energy estimate: first eq. by $\mu \Rightarrow$ $\int_\Omega S(\varphi)\mu \sim \int_\Omega |\nabla \mu| \mathrm{dx} + |\mu_\Omega|.$

$(\varphi_0)_\Omega \in (-1,1)$ + MZ inequality $\Rightarrow$ $F'_{\log}(\varphi) \in L^2(0,T;L^1) \overset{comparison}{\Rightarrow} \mu_\Omega \in L^2(0,T) \overset{\text{Poincaré}}{\Rightarrow} \mu \in L^2(0,T;H^1)$

- A. Miranville and R. Temam: 2016.
- A. Miranville: 2011, 2013, 2017.
- A. Giorgini, M. Grasselli, and A. Miranville: 2017.
- J. He: 2021.
- P. Colli, G. Gilardi, E. Rocca, and J. Sprekels: 2022.

The Flory–Huggins potential

Property (1) (Miranville–Zelik, Kenmochi...)

For every compact subset $K \subset \Delta_\circ$, *there exist constants* $c_\Psi, C_\Psi > 0$ *such that, for every* $\phi \in \Delta_\circ$, $\boxed{\phi_\Omega \in K}$ *it holds that*

$$\boxed{c_\Psi \int_\Omega |\Psi_\varphi^{(1)}(\phi)| \leq \int_\Omega \Psi_\varphi^{(1)}(\phi) \cdot (\phi - \phi_\Omega) + C_\Psi.}$$

Property ($\star$) (Grasselli-Scarpa-S. '22)

There exist constants $c_\Psi, C_\Psi > 0$, $R \in (0, 1/2)$, $q \in (2, +\infty)$, *and a decreasing positive function* $F \in L^q(0,R) \cap C^0(0,R)$ *such that, for every measurable* $\phi = (\phi^1, \phi^2) : \Omega \to \Delta_\circ$ *satisfying*

$$0 < \min\{\phi_\Omega^1, \phi_\Omega^2\} < \phi_\Omega^1 + \phi_\Omega^2 \leq R,$$

it holds that

$$\boxed{c_\Psi \min\{\phi_\Omega^1, \phi_\Omega^2\} \int_\Omega |\Psi_\varphi^{(1)}(\phi)| \leq \int_\Omega \Psi_\varphi^{(1)}(\phi) \cdot (\phi - \phi_\Omega) + C_\Psi(\phi_\Omega^1 + \phi_\Omega^2)\Big(1 + F(\min\{\phi_\Omega^1, \phi_\Omega^2\})\Big).}$$

Schematics of the Proof

1. λ-Approximation: smoothing of Ψ and truncation of $\mathrm{S}_\varphi, \mathrm{S}_\mathrm{R}$, and S_P;
2. Preliminary estimate on φ_λ: parabolic-type estimate for $t \sim 0$;
3. Dual estimate: L^1-control of $\Psi_\lambda^{(1)}$ and of the convex conjugate $(\Psi_\lambda^{(1)})^*$;
4. Energy estimate: control of $\nabla\boldsymbol{\mu}_\lambda \in L^2(0,T;\mathrm{L}^2)$;
5. Mean value property for φ_λ; mean value behaviour as $t \sim 0$;
6. Estimate of $\boldsymbol{\mu}_\lambda$: understand the behaviour as $t \sim 0$;
7. Passing to the limit $\lambda \to 0$.

Step I: Approximation

Idea: $\Psi^{(1)} \rightsquigarrow \Psi^{(1)}_\lambda$ `Lip.`, $S_\varphi \rightsquigarrow S^\lambda_\varphi \in L^\infty$, $S_R \rightsquigarrow S^\lambda_R \in L^\infty$, and $S_P \rightsquigarrow S^\lambda_P \in L^\infty$.

$$\text{For any } \lambda \in (0,1), \quad \underbrace{\Psi^{(1)}_\lambda : \mathbb{R}^2 \to \mathbb{R},}_{\text{Yosida reg.}} \quad \underbrace{J_\lambda := (I_{\mathbb{R}^2} + \lambda \Psi^{(1)}_\varphi)^{-1},}_{\text{Resolvent operator}}$$

and suitable truncations $S^\lambda_\varphi, S^\lambda_P$, and S^λ_R for the source terms. Then, $(P)_\lambda$ can be solved and

$$\varphi_\lambda \in H^1(0,T;(H^1)^*) \cap L^\infty(0,T;H^1) \cap L^2(0,T;H^3), \quad \mu_\lambda \in L^2(0,T;H^1),$$
$$P_\lambda \in H^1(0,T;(H^1)^*) \cap L^2(0,T;H^1), \quad R_\lambda \in H^1(0,T;(H^1)^*) \cap L^2(0,T;H^1).$$

Lemma (Approximated max-min principle)

There exists a threshold $c_* > 0$ independent of λ such that

$$c_* \le P_\lambda(t) \le 1, \quad c_* \le R_{\lambda,i}(t) \le 1 \quad \text{a.e. in } \Omega, \quad i = 1,2, \quad \forall t \in [0,T].$$

`Remark`: the threshold is `explicit` as $0 < c_* \le (c_2 + c_4)(8\min\{c_1, c_3\})^{-1}$.

56.25%

Step II: Preliminary estimate on φ_λ

We test the first equation by φ_λ and the second by $-\Delta\varphi_\lambda$:

$$\frac{1}{2}\|\varphi_\lambda(t)\|^2 + \int_{Q_t} |\Delta\varphi_\lambda|^2 + \underbrace{\int_{Q_t} \Psi^{(1)}_{\lambda,\varphi}(\varphi_\lambda)\cdot(-\Delta\varphi_\lambda)}_{\geq 0 \quad \texttt{by convexity}} = \int_{Q_t} \mathsf{S}^\lambda_\varphi \cdot \varphi_\lambda - \underbrace{\int_{Q_t} \Psi^{(2)}_\varphi(\varphi_\lambda)\cdot(-\Delta\varphi_\lambda)}_{\texttt{Young ineq.}}.$$

The `Gronwall` lemma (+ `elliptic regularity`) yields

$$\|\varphi_\lambda\|_{L^\infty(0,T;\mathrm{L}^2)\cap L^2(0,T;\mathrm{H}^2_{\mathbf{n}})} \leq C.$$

Plugging this estimate into the above lines, produces

$$\|\varphi_\lambda\|_{L^\infty(0,t;\mathrm{L}^2)\cap L^2(0,t;\mathrm{H}^2_{\mathbf{n}})} \leq Ct^{1/2} \qquad \forall\, t \in [0,T].$$

Iterating: $\forall\, \alpha \in [0,1), \quad \exists\, C_\alpha > 0 : \quad \|\varphi_\lambda\|_{L^\infty(0,t;\mathrm{L}^2)\cap L^2(0,t;\mathrm{H}^2_{\mathbf{n}})} \leq C_\alpha t^\alpha \qquad \forall\, t \in [0,T].$

Step III: Dual estimate

Consider $\int_0^t (1) \times \boldsymbol{\mu}_\lambda + (2) \times \varphi_\lambda$:

$$\int_0^t \int_{Q_s := \Omega \times [0,s]} |\nabla \boldsymbol{\mu}_\lambda|^2 \,\mathrm{d}s + \int_{Q_t} |\nabla \varphi_\lambda|^2 + \underbrace{\int_{Q_t} \Psi^{(1)}_{\lambda,\varphi}(\varphi_\lambda) \cdot \varphi_\lambda}_{= \int_{Q_t} \Psi^{(1)}_\lambda(\varphi_\lambda) + \int_{Q_t} (\Psi^{(1)}_\lambda)^*(\Psi^{(1)}_{\lambda,\varphi}(\varphi_\lambda))} = \int_0^t \int_{Q_s} \mathsf{S}^\lambda_\varphi \cdot \boldsymbol{\mu}_\lambda \,\mathrm{d}s - \underbrace{\int_{Q_t} \Psi^{(2)}_\varphi(\varphi_\lambda) \cdot \varphi_\lambda}_{\texttt{prev. est.}},$$

where $(\Psi^{(1)}_\lambda)^*$ stands for the convex conjugate of $\Psi^{(1)}_\lambda$. After some computations, we obtain

$$\int_0^t \int_{Q_s} |\nabla \boldsymbol{\mu}_\lambda|^2 \,\mathrm{d}s + \int_{Q_t} |\nabla \varphi_\lambda|^2 + \int_{Q_t} \Psi^{(1)}_\lambda(\varphi_\lambda) + \int_{Q_t} \left|(\Psi^{(1)}_\lambda)^*(\Psi^{(1)}_{\lambda,\varphi}(\varphi_\lambda))\right| \\ \leq C \int_0^t \int_{Q_s} \left|(\Psi^{(1)}_\lambda)^*(\Psi^{(1)}_{\lambda,\varphi}(\varphi_\lambda))\right| \,\mathrm{d}s + C.$$

Then Gronwall's lemma yields that

$$\left\|\Psi^{(1)}_\lambda(\varphi_\lambda)\right\|_{L^1(Q)} + \left\|(\Psi^{(1)}_\lambda)^*(\Psi^{(1)}_{\lambda,\varphi}(\varphi_\lambda))\right\|_{L^1(Q)} \leq C.$$

Furthermore, Yosida + convex analysis produce

$$\lambda^{1/2} \left\|\Psi_{\lambda,\varphi}(\varphi_\lambda)\right\|_{L^2(0,T;\mathbf{L}^2)} \leq C.$$

Step IV: Energy estimate

Consider $(1) \times \boldsymbol{\mu}_\lambda + (2) \times \partial_t \varphi_\lambda$:

$$\frac{1}{2}\int_\Omega |\nabla \varphi_\lambda(t)|^2 + \int_\Omega \Psi_\lambda^{(1)}(\varphi_\lambda(t)) + \int_{Q_t} |\nabla \boldsymbol{\mu}_\lambda|^2 = \underbrace{\int_\Omega \Psi_\lambda(\varphi_0) - \int_\Omega \Psi_\lambda^{(2)}(\varphi_\lambda(t))}_{\leq C} + \int_{Q_t} \mathrm{S}_\varphi^\lambda \cdot \boldsymbol{\mu}_\lambda.$$

After some computations, we obtain

$$\|\varphi_\lambda\|_{L^\infty(0,T;\mathrm{H}^1)} + \left\|\Psi_\lambda^{(1)}(\varphi_\lambda)\right\|_{L^\infty(0,T;\mathrm{L}^1)} + \|\nabla \boldsymbol{\mu}_\lambda\|_{L^2(0,T;\mathrm{L}^2)} \leq C.$$

Next, comparison in the first eq. yield

$$\|\varphi_\lambda\|_{H^1(0,T;(\mathrm{H}^1)^*)} \leq C.$$

Finally, by the properties of the `Yosida` regularisation, we derive that

$$\lambda^{1/2} \|\Psi_{\lambda,\varphi}(\varphi_\lambda)\|_{L^\infty(0,T;\mathrm{L}^2)} \leq C.$$

Step V: Mean value property

Goal: passing from "$\nabla \boldsymbol{\mu} \in L^2(0,T;\mathrm{L}^2)$" to "$\boldsymbol{\mu} \in L^p(0,T;\mathrm{H}^1)$" $\forall p \in (1,2)$.

$$\texttt{(MVP)} + (\star) \Longrightarrow \quad \Psi^{(1)}_{\lambda,\boldsymbol{\varphi}}(\varphi) \in L^p(0,T;\mathrm{L}^1) \overset{comparison}{\Longrightarrow} \quad \boldsymbol{\mu}_\Omega \in L^p(0,T) \overset{\text{Poincaré}}{\Longrightarrow} \boldsymbol{\mu} \in L^p(0,T;\mathrm{H}^1)$$

Lemma (Mean value properties (MVP))

Set $\alpha_0 := (P_0)_\Omega \in (0,1)$. *Then*

$$(\varphi_{\lambda,1}(t))_\Omega + (\varphi_{\lambda,2}(t))_\Omega \le \min\{\alpha_0 - c_*, 1-\alpha_0-2c_*\} < 1 \qquad \forall\, t \in [0,T],$$

$$(\varphi_{\lambda,i}(t))_\Omega \le \frac{1-\alpha_0}{2} - c_* < 1 \quad \forall\, t \in [0,T], \qquad \textit{for } i = 1,2,$$

$$\exists \lambda_0 \in (0,1), c_0 > 0: \quad c_0(1-e^{-c_{2i}t}) \le (\varphi_{\lambda,i}(t))_\Omega \le c_{2i-1}t \qquad \forall\, t \in [0,T], \forall \lambda \in (0,\lambda_0).$$

Step VI: Estimate of $\boldsymbol{\mu}$

- Case $t \in (\sigma, T)$, for every $\sigma \in (0, T)$: standard method ✓
- What happen when $t \sim 0$? By the (MVP) $\exists T_0 \in (0, T), c_0' \in (0, 1)$:

$$0 < c_0' t \leq \min\{(\varphi_{\lambda,1}(t))_\Omega, (\varphi_{\lambda,2}(t))_\Omega\} < (\varphi_{\lambda,1}(t))_\Omega + (\varphi_{\lambda,2}(t))_\Omega \leq (c_1 + c_3)t \leq \frac{R}{2}, \quad \forall t \in (0, T_0),$$

where $R \in (0, 1/2)$ is given by Property $(\star)$.
Property $(\star)$ with $\phi = \boldsymbol{J}_\lambda(\boldsymbol{\varphi}_\lambda(t))$ and $t \in (T_\lambda, T_0)$ implies

$$c_\Psi(c_0' t - C\lambda^{1/2}) \int_\Omega |\Psi^{(1)}_{\lambda,\varphi}(\boldsymbol{\varphi}_\lambda(t))| \leq \int_\Omega \Psi^{(1)}_{\lambda,\varphi}(\boldsymbol{\varphi}_\lambda(t)) \cdot (\boldsymbol{J}_\lambda(\boldsymbol{\varphi}_\lambda(t)) - (\boldsymbol{J}_\lambda(\boldsymbol{\varphi}_\lambda(t)))_\Omega) + C_\Psi\left((c_1 + c_3)t + 2C\lambda^{1/2}\right)\left(1 + F(c_0' t - C\lambda^{1/2})\right).$$

We test the second eq. by $\boldsymbol{J}_\lambda(\boldsymbol{\varphi}_\lambda) - (\boldsymbol{J}_\lambda(\boldsymbol{\varphi}_\lambda))_\Omega$ and $\forall\, \alpha \in [0, 1)$ $\|\boldsymbol{\varphi}_\lambda\|_{L^\infty(0,t;\mathbf{L}^2)} \leq C_\alpha t^\alpha \Rightarrow$

Step VI: Estimate of $\boldsymbol{\mu}$

$$c_\Psi(c_0' t - C\lambda^{1/2}) \int_\Omega |\Psi^{(1)}_{\lambda,\varphi}(\varphi_\lambda(t))| \le C_\Psi\left((c_1+c_3)t + 2C\lambda^{1/2}\right)\left(1 + F(c_0't - C\lambda^{1/2})\right)$$
$$+ C_\alpha\,(1 + \|\nabla \boldsymbol{\mu}_\lambda(t)\| + \|\varphi_\lambda(t)\|)\,(t^\alpha + \lambda^{1/2}) \quad \forall t \in (T_\lambda, T_0), \alpha \in (0,1).$$

Equivalently, for $t \in (T_\lambda, T_0)$, $T_\lambda := 2C(c_0')^{-1}\lambda^{1/2}$,

$$c_\Psi \int_\Omega |\Psi^{(1)}_{\lambda,\varphi}(\varphi_\lambda(t))| \le \underbrace{C_\Psi \frac{(c_1+c_3)t + 2C\lambda^{1/2}}{c_0't - C\lambda^{1/2}}}_{\le C}\left(1 + F(c_0't - C\lambda^{1/2})\right) + C_\alpha \underbrace{\frac{t^\alpha + \lambda^{1/2}}{c_0't - C\lambda^{1/2}}}_{\le \frac{2}{c_0'}\frac{1}{t^{1-\alpha}}}(1 + \|\nabla \boldsymbol{\mu}_\lambda(t)\| + \|\varphi_\lambda(t)\|)$$

Therefore, for $a.e$ $t \in (T_\lambda, T_0)$,

$$\int_\Omega |\Psi^{(1)}_{\lambda,\varphi}(\varphi_\lambda(t))| \le \underbrace{C\left(1 + F(c_0't - C\lambda^{1/2})\right)}_{\text{OK: } L^{2+}(T_\lambda,\, T_0)} + C_\alpha \underbrace{\left(1 + \frac{1}{t^{1-\alpha}}\right)}_{\in L^\bullet(T_\lambda, T_0)?} \underbrace{(1 + \|\nabla \boldsymbol{\mu}_\lambda(t)\| + \|\varphi_\lambda(t)\|)}_{L^2(T_\lambda, T_0)}.$$

$$\forall \ell \in (1,+\infty)\, \exists \alpha \in (0,1), C_\ell > 0 : \quad \left\| t \mapsto \frac{1}{t^{1-\alpha}} \right\|_{L^\ell(T_\lambda, T_0)} \le C_\ell$$

Step VI: Estimate of $\boldsymbol{\mu}$

Therefore, by the Hölder inequality we get

$$\forall\, p \in (1,2), \quad \exists\, C_p > 0 : \quad \left\| \Psi^{(1)}_{\lambda,\varphi}(\varphi_\lambda) \right\|_{L^p(T_\lambda, T_0; \mathrm{L}^1)} \leq C_p.$$

Setting $\quad \chi_\lambda : [0, T] \to [0,1]\,, \qquad \chi_\lambda(t) := \begin{cases} 0 & \text{if } t \in [0, T_\lambda], \\ 1 & \text{if } t \in (T_\lambda, T], \end{cases}$

the above can reduces to

$$\forall\, p \in (1,2), \quad \exists\, C_p > 0 : \quad \left\| \chi_\lambda \Psi^{(1)}_{\lambda,\varphi}(\varphi_\lambda) \right\|_{L^p(0, T_0; \mathrm{L}^1)} \leq C_p.$$

Comparison in the second eq. then leads us to

$$\forall\, p \in (1,2), \quad \exists\, C_p > 0 : \quad \| \chi_\lambda (\boldsymbol{\mu}_\lambda)_\Omega \|_{L^p(0, T_0)} \leq C_p \overset{\text{Poincaré}}{\Longrightarrow} \| \chi_\lambda \boldsymbol{\mu}_\lambda \|_{L^p(0, T_0; \mathrm{H}^1)} \leq C_p.$$

`Step VII: Pass to the limit` $\lambda \to 0$.

Conclusion:

Existence of weak solutions for a system of PDEs related to RNA-Protein dynamics.

Design of a new strategy to generalize existence results for Cahn-Hilliard type systems when the initial datum is a pure phase
(work in progress: cover more general source terms and nonlocal models).

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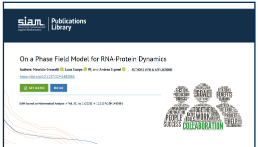
Recap (continues)

Slide 1

Slide 2



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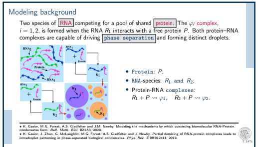

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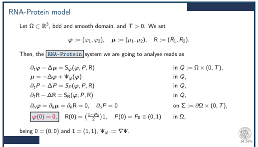
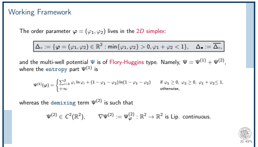
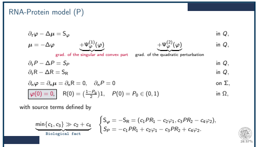


Slide 5



Slide 6



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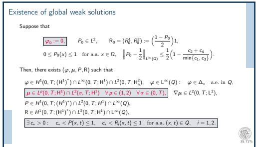

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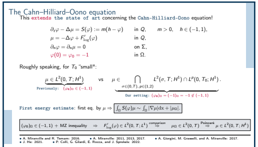

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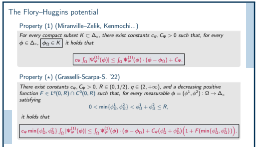

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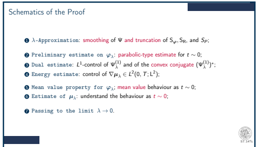

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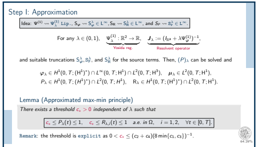
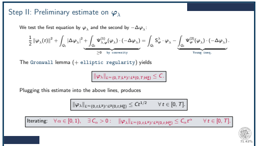


Slide 12

Recap (continues)



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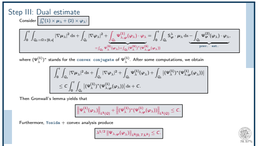

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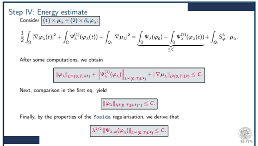
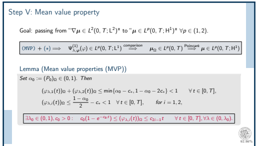


Slide 15



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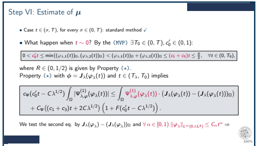

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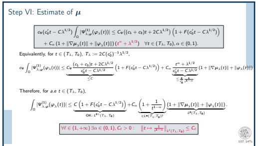

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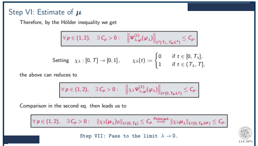

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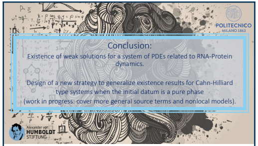

Slide 20