Diffuse and sharp interfaces in Biology and Mechanics

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Plan of the Lecture

- Diffuse interface models in **Biology: tumor growth models**

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  Sharp interfaces $\Longrightarrow$ narrow transition layers - differential adhesive forces among cell-species

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- Ongoing projects and open problems

Part 1 - Diffuse Interfaces in Biology - Multispecies Model

DFRSS: The model

Typical structure of tumors grown in vitro:

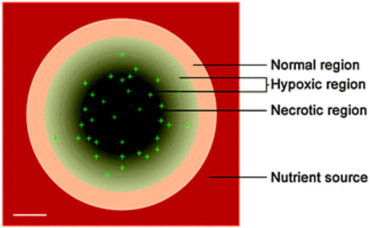

Figure: Zhang et al. Integr. Biol., 2012, 4, 1072–1080. Scale bar $100\mu m = 0{:}1mm$

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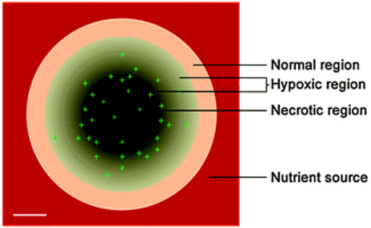

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A continuum thermodynamically consistent model is introduced with the ansatz:

- sharp interfaces are replaced by narrow transition layers arising due to adhesive forces among the cell species: a diffuse interface separates tumor and healthy cell regions
- proliferating and dead tumor cells and healthy cells are present, along with a nutrient (e.g. glucose or oxigene)

DFRSS: The state variables

- $\phi_i, i = 1, 2, 3$: the volume fractions of the cells:
  - $\phi_1 = P$: **proliferating tumor cell fraction**
  - $\phi_2 = \phi_D$: dead tumor cell fraction
  - $\phi_3 = \phi_H$: healthy cell fraction

  The variables above are naturally constrained by the relation $\sum_{i=1}^{3} \phi_i = \phi_H + \Phi = 1$

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- $\Phi = \phi_D + P$: **the volume fraction of the tumor cells** split into the sum of the dead tumor cells and of the proliferating cells
- n: **the nutrient concentration**
- $\mathbf{u}$:=$\mathbf{u}_i, i = 1, 2, 3$: **the tissue velocity field**. We treat the tumor and host cells as inertial-less fluids and assume that the cells are tightly packed and they march together
- Π: the cell-to-cell **pressure**

DFRSS: Mass conservation and choice of the energy

The volume fractions obey the mass conservation (advection-reaction-diffusion) equations:

$$\partial_t \phi_i + \mathrm{div}_x(\mathbf{u}\phi_i) = -\mathrm{div}_x \mathbf{J}_i + \Phi S_i$$

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The total energy adhesion has the form

$$E = \int_\Omega \left(\mathcal{F}(\Phi) + \frac{1}{2}|\nabla_x \Phi|^2 \right) \, \mathrm{d}x$$

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The fluxes $\mathbf{J}_\Phi$ and $\mathbf{J}_H$ that account for mechanical interactions among the species are as follows:

$$\mathbf{J}_\Phi = \mathbf{J}_1 + \mathbf{J}_2 := -\nabla_x \left(\frac{\delta E}{\delta \Phi} \right) = -\nabla_x \left(\mathcal{F}'(\Phi) - \Delta\Phi \right) := -\nabla_x \mu$$

$$\mathbf{J}_H = \mathbf{J}_3 := -\nabla_x \left(\frac{\delta E}{\delta \phi_H} \right) = \nabla_x \left(\frac{\delta E}{\delta \Phi} \right)$$

where we have used in the last equality the fact that $\phi_H = 1 - \Phi$ and where μ is the chemical potential of the system

DFRSS: The convective Cahn-Hilliard equation for the tumor cells fraction

For the source of mass in the host tissue, accounting for gains due to proliferation of cells and loss due to cell death, we have the following relations:

- $S_T = S_D + S_P := S_2 + S_1$
- $\Phi S_H := \Phi S_3 := \phi_H S_T = (1 - \Phi) S_T$

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Assuming the mobility of the system to be constant, then the tumor volume fraction Φ and the host tissue volume fraction ϕ_H obey the following mass conservation equations

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Using now the fact that $S_T = S_1 + S_2$ and recalling that $\phi_H + \Phi = 1$, $\mathbf{J}_\Phi = -\nabla_x \mu$, we can forget of the equation for ϕ_H and we recover the equation for Φ in the form

$$\boxed{\partial_t \Phi + \mathrm{div}_x(\mathbf{u}\Phi) - \mathrm{div}_x(\nabla_x \mu) = \Phi S_T, \ \mu = \mathcal{F}'(\Phi) - \Delta\Phi}$$

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Suppose the net source of tumor cells S_T to be given by

$$S_T = S_T(n, P, \Phi) = \lambda_M n P - \lambda_L(\Phi - P)$$

where $\lambda_M \geq 0$ is the mitotic rate and $\lambda_L \geq 0$ is the lysing rate of dead cells

DFRSS: The transport equation for the proliferating cells fraction

The volume fraction of dead tumor cells ϕ_D would satisfy an equation similar to the one of Φ. However, we prefer to couple the equation for Φ with the one for $P = \Phi - \phi_D$ which then reads

$$\boxed{\partial_t P + \mathrm{div}_x(\mathbf{u}P) = \Phi(S_T - S_D)}$$

where the source of dead cells is taken as

$$S_D = S_D(n, P, \Phi) = (\lambda_A + \lambda_N H(n_N - n))\, P - \lambda_L(\Phi - P)$$

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Here

- $\lambda_A P$ describes the death of cells due to apoptosis with rate $\lambda_A \geq 0$ and the term $\lambda_N H(n_N - n)P$ models the death of cells due to necrosis with rate $\lambda_N \geq 0$
- for mathematical reasons, we choose H to be a regular and nonnegative function of n
- the term n_N represents the necrotic limit, at which the tumor tissue dies due to lack of nutrients

DFRSS: The Darcy law for the velocity field

The tumor velocity field **u** (given by the mass-averaged velocity of all the components) is assumed to fulfill Darcy's law:

$$\mathbf{u} = -\nabla_x \Pi + \mu \nabla_x \Phi$$

where, for simplicity, the motility has been taken constant and equal to 1

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Summing up the mass balance equations

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$$\partial_t \phi_H + \mathrm{div}_x(\mathbf{u}\phi_H) = -\mathrm{div}_x \mathbf{J}_H + (1-\Phi) S_T$$

and using $\Phi + \phi_H = 1$ and $\mathbf{J}_H = -\mathbf{J}_\Phi$, we end up with the following constraint for the velocity field:

$$\boxed{\mathrm{div}_x \mathbf{u} = S_T = \lambda_M n P - \lambda_L(\Phi - P)}$$

DFRSS: The quasistatic reaction diffusion equation for the nutrient

Since the time scale for nutrient diffusion is much faster than the rate of cell proliferation, the nutrient is assumed to evolve quasi-statically:

$$\boxed{-\Delta n + \nu_U n P = T_c(n, \Phi)}$$

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Here

- ν_U represents the nutrient uptake rate by the viable tumor cells
- ν_1, ν_2 denote the nutrient transfer rates for preexisting vascularization in the tumor and host domains
- n_c is the nutrient level of capillaries
- the function $Q(\Phi)$ is regular and satisfies $\nu_1(1 - Q(\Phi)) + \nu_2 Q(\Phi) \geq 0$

DFRSS: The boundary conditions

- We chose the b.c.s of [**CWSL**: Y. Chen, S.M. Wise, V.B Shenoy, J.S. Lowengrub, Int. J. Numer. Methods Biomed. Eng., 2014] for μ, Π, n, and Φ (ν is the outer normal unit vector to $\partial\Omega$):

$$\mu = \Pi = 0, \quad n = 1, \quad \nabla_x \Phi \cdot \nu = 0$$

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- As $P \geq 0$, the boundary condition $P\mathbf{u} \cdot \nu \geq 0$ means $P = 0$ **whenever** $\mathbf{u} \cdot \nu < 0$ i.e. on the part of the inflow part of the boundary

DFRSS: The PDEs

In summary, let $\Omega \subset \mathbb{R}^3$ be a bounded domain and $T > 0$ the final time of the process. For simplicity, choose $\lambda_M = \nu_U = 1$, $\lambda_A = \lambda_1$, $\lambda_N = \lambda_2$, $\lambda_L = \lambda_3$.

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Then, in $\Omega \times (0, T)$, we have the following system of equations:

$$
\begin{aligned}
&\textbf{(Cahn – Hilliard)} && \partial_t \Phi + \mathrm{div}_x(\mathbf{u}\Phi) - \mathrm{div}_x(\nabla_x \mu) = \Phi S_T, \ \mu = -\Delta\Phi + \mathcal{F}'(\Phi) \\
&\textbf{(Darcy)} && \mathbf{u} = -\nabla_x \Pi + \mu \nabla_x \Phi, \quad \mathrm{div}_x \mathbf{u} = S_T \\
&\textbf{(Transport)} && \partial_t P + \mathrm{div}_x(\mathbf{u}P) = \Phi(S_T - S_D) \\
&\textbf{(Reac – Diff)} && -\Delta n + nP = T_c(n, \Phi)
\end{aligned}
$$

where

$$
\begin{aligned}
&\textbf{(Source – Tumor)} && S_T(n, P, \Phi) = nP - \lambda_3(\Phi - P) \\
&\textbf{(Source – Dead)} && S_D(n, P, \Phi) = (\lambda_1 + \lambda_2 H(n_N - n))\, P - \lambda_3(\Phi - P) \\
&\textbf{(Nutrient – Capill)} && T_c(n, \Phi) = [\nu_1(1 - Q(\Phi)) + \nu_2 Q(\Phi)]\,(n_c - n)
\end{aligned}
$$

coupled with the boundary conditions on $\partial\Omega \times (0, T)$: $\mu = \Pi = 0$, $n = 1$, $\nabla_x \Phi \cdot \nu = 0$, $P\mathbf{u} \cdot \nu \geq 0$ and with the initial conditions $\Phi(0) = \Phi_0$, $P(0) = P_0$ in Ω

DFRSS: Assumptions on the potential $\mathcal{F}$

We suppose that the potential $\mathcal{F}$ supports the natural bounds

$$0 \leq \Phi(t, x) \leq 1$$

To this end, we take $\mathcal{F} = \mathcal{C} + \mathcal{B}$, where $\mathcal{B} \in C^2(\mathbb{R})$ and

$$\mathcal{C} : \mathbb{R} \mapsto [0, \infty] \text{ convex, lower-semi continuous, } \mathcal{C}(\Phi) = \infty \text{ for } \Phi < 0 \text{ or } \Phi > 1$$

Moreover, we ask that

$$\mathcal{C} \in C^1(0,1), \quad \lim_{\Phi \to 0^+} \mathcal{C}'(\Phi) = \lim_{\Phi \to 1^-} \mathcal{C}'(\Phi) = \infty$$

A typical example of such $\mathcal{C}$ is the *logarithmic potential*

$$\mathcal{C}(\Phi) = \begin{cases} \Phi \log(\Phi) + (1 - \Phi) \log(1 - \Phi) \text{ for } \Phi \in [0, 1], \\ \\ \infty \text{ otherwise} \end{cases}$$

DFRSS: Assumptions on the other data

Regarding the functions the constants in the definitions of S_T and S_D, we assume $Q, H \in C^1(\mathbb{R})$ and

$$\lambda_i \geq 0 \text{ for } i = 1, 2, 3, \quad H \geq 0$$

$$[\nu_1(1 - Q(\Phi)) + \nu_2 Q(\Phi)] \geq 0, \quad 0 < n_c < 1$$

Finally, we suppose Ω be a bounded domain with smooth boundary in $\mathbb{R}^3$ and impose the following conditions on the initial data:

$$\Phi_0 \in H^1(\Omega), \quad 0 \leq \Phi_0 \leq 1, \quad \mathcal{C}(\Phi_0) \in L^1(\Omega)$$

$$P_0 \in L^2(\Omega), \quad 0 \leq P_0 \leq 1 \quad \text{a.e. in } \Omega$$

DFRSS: Weak formulation

$(\Phi, \mathbf{u}, P, n)$ is a weak solution to the problem in $(0, T) \times \Omega$ if

(i) these functions belong to the regularity class:

$$\Phi \in C^0([0,T]; H^1(\Omega)) \cap L^2(0,T; W^{2,6}(\Omega))$$

$$\mathcal{C}(\Phi) \in L^\infty(0,T; L^1(\Omega)), \quad \text{hence, in particular, } 0 \le \Phi \le 1 \text{ a.a. in } (0,T)\times\Omega$$

$$\mathbf{u} \in L^2((0,T)\times\Omega; \mathbb{R}^3), \ \mathrm{div}\, \mathbf{u} \in L^\infty((0,T)\times\Omega)$$

$$\Pi \in L^2(0,T; W_0^{1,2}(\Omega)), \quad \mu \in L^2(0,T; W_0^{1,2}(\Omega))$$

$$P \in L^\infty((0,T)\times\Omega), \ 0 \le P \le 1 \ \text{ a.a. in } (0,T)\times\Omega$$

$$n \in L^2(0,T; W^{2,2}(\Omega)), \ 0 \le n \le 1 \ \text{ a.a. in } (0,T)\times\Omega$$

(ii) the following integral relations hold:

$$\int_0^T \int_\Omega [\Phi \partial_t \varphi + \Phi \mathbf{u} \cdot \nabla_x \varphi + \mu \Delta \varphi + \Phi S_T \varphi] \ \mathrm{d}x \ \mathrm{d}t = -\int_\Omega \Phi_0 \varphi(0,\cdot) \ \mathrm{d}x$$

for any $\varphi \in C_c^\infty([0,T)\times\Omega)$, where

$$\mu = -\Delta\Phi + \mathcal{F}'(\Phi), \ \mathbf{u} = -\nabla_x \Pi + \mu \nabla_x \Phi$$

$$\mathrm{div}_x \mathbf{u} = S_T \text{ a.a. in } (0,T)\times\Omega; \quad \nabla_x \Phi \cdot \nu|_{\partial\Omega} = 0$$

$$\int_0^T \int_\Omega [P \partial_t \varphi + P \mathbf{u} \cdot \nabla_x \varphi + \Phi(S_T - S_D)\varphi] \ \mathrm{d}x \ \mathrm{d}t \ge -\int_\Omega P_0 \varphi(0,\cdot) \ \mathrm{d}x$$

for any $\varphi \in C_c^\infty([0,T)\times\overline{\Omega})$, $\varphi|_{\partial\Omega} \ge 0$

$$-\Delta n + nP = T_c(n,\Phi) \text{ a.a. in } (0,T)\times\Omega; \ n|_{\partial\Omega} = 1$$

DFRSS: Existence of weak solutions

Now, we are able to state the main result of **[M. Dai, E. Feireisl, E.R., G. Schimperna, M. Schonbek, Analysis of a diffuse interface model of multispecies tumor growth, preprint arXiv:1507.07683 (2015)]**

Theorem

Let $T > 0$ be given. Under the previous assumptions the variational formulation of our initial-boundary value problem admits **at least one solution** *on the time interval* $[0, T]$

DFRSS: Idea of the proof

- Approximation: regularize the equations
- Perform uniform a priori estimates
- Use compactness arguments in order to pass to the limit

Comparison with some other models including velocities

- **Numerical simulations** of diffuse-interface models for tumor growth have been carried out in several papers (cf., e.g., [Cristini, Lowengrub, Cambridge Univ. Press, 2010] and more recently [Garcke, Lam, Sitka, Styles, arXiv:1508.00437, 2015]). However, a **rigorous mathematical analysis** of the resulting PDEs is still in its beginning and only for **one species models with regular potentials** (cf. [Garcke, Lam, J. Appl. Math and arXiv:1604.00287, 2016])

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  - [J. Jang, H. Wu, S. Zheng, J. Differential Equations, 2015] where S_T is not 0 but it's not depending on the other variables but just on time and space

Perspectives and Open problems

- An ongoing project with S. Frigeri, K.-F. Lam, G. Schimperna: To study the **multispecies model** introduced in **[CWSL]** including **different mobilities** and non-Dirichlet b.c.s on the chemical potential $\Longrightarrow$ the main problems are:

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  - we need the mean values of φ_i (the proliferating and dead cells phases) in the two Cahn-Hilliard equations to be away from the potential bareers $\Longrightarrow$ ad hoc estimate based on ODEs technique
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$$\partial_t \Phi + \mathrm{div}_x(\mathbf{u}\Phi) - \mathrm{div}_x(\nabla_x \mu) = 0, \ \ \mu = -\varepsilon^2 \Delta \Phi + \mathcal{F}'(\Phi)$$

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  - Very partial result in **[DFRSS]** assuming strict convexity of $\mathcal{F}$ and $S_T = S_D = 0$
  - An ongoing project with S. Melchionna: **Varifold solutions** at the limit as $\varepsilon \searrow 0$ in case we just consider the Cahn-Hilliard-Darcy system coupling the Φ equation to the u equation (neglecting the nutrient)

Part 2 - From Diffuse to Sharp Interfaces in a simplified tumor model

One Species Tumor Model

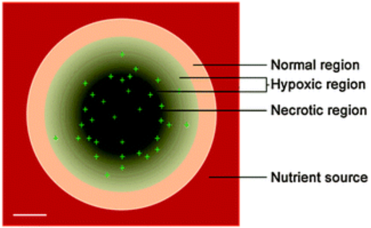

Figure: Zhang et al. Integr. Biol., 2012, 4, 1072–1080. Scale bar 100μm = 0:1mm

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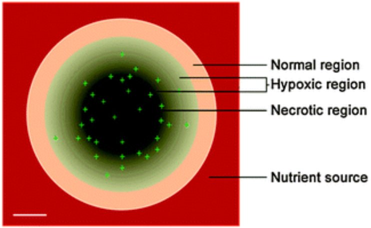

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In **[RS] E. Rocca, R. Scala: A rigorous sharp interface limit of a diffuse interface model related to tumor growth, preprint arXiv:1606.04663 (2016)** we study the case where there are only

- proliferating tumor cells
- surrounded by (healthy) host cells
- and a nutrient (e.g. glucose) is present

and we neglect velocities

RS: The Cahn-Hilliard-Reaction-Diffusion system

The coupled Cahn-Hilliard-Reaction-Diffusion system with sources is

$$\varphi_t - \Delta\mu = \mathcal{R}, \qquad \mu = \frac{1}{\varepsilon}\Psi'(\varphi) - \varepsilon\Delta\varphi$$

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$$\varphi(x) \simeq 1 \Rightarrow \text{ tumor cell at } x$$
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For $\varepsilon \sim 0$ we will obtain a **sharp interface model!**

RS: The Gradient Flow system

We now want to write the system

$$\begin{cases} \varphi_t - \Delta\mu = 2\sigma + \varphi - \mu \\ \sigma_t - \Delta\sigma = -2\sigma - \varphi + \mu \\ \mu = \frac{1}{\varepsilon}\Psi'(\varphi) - \varepsilon\Delta\varphi \end{cases}$$

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Then we recognize as a **gradient flow** of the energy

$$E^{\varepsilon}(u,\sigma) := \frac{1}{\varepsilon}\int_{\Omega}\Psi(u-\sigma)dx + \varepsilon\int_{\Omega}|\nabla(u-\sigma)|^2dx + \frac{1}{2}\|\sigma\|^2_{H^1} + \int_{\Omega}u\sigma dx$$

with respect to the space $\mathcal{V}' \times L^2(\Omega)$, where $\mathcal{V}' := \left\{\zeta \in H^1(\Omega)' : \frac{1}{|\Omega|}\langle\zeta, 1\rangle = 0\right\}$

Gamma convergence of gradient flows

$X_\varepsilon \subset Y$ Hilbert spaces, E_ε C^1-functionals on X_ε, $u^\varepsilon : [0,T] \to X_\varepsilon$ solutions of

$$u_t^\varepsilon = -\nabla_{X_\varepsilon} E_\varepsilon(u^\varepsilon) \text{ with energy balance } E_\varepsilon(u^\varepsilon(0)) - E_\varepsilon(u^\varepsilon(t)) = \int_0^t \|u_t^\varepsilon\|_{X_\varepsilon}^2 \, ds.$$

Assume that $u^\varepsilon \xrightarrow{S} u$ in some sense (to be specified from case to case) and

(i) (Gamma liminf) There exists a C^1 functional F on a Hilbert space $X \subset Y$ such that for all sequences $v^\varepsilon \xrightarrow{S} v$ it holds
$$\liminf_{\varepsilon\to 0} E_\varepsilon(v^\varepsilon) \geq F(v).$$

(ii) (Lower bound on the velocities) If $u^\varepsilon(t) \xrightarrow{S} u(t)$ for all $t \in [0,T]$ then
$$\liminf_{\varepsilon\to 0} \int_0^s \|u_t^\varepsilon(t)\|_{X_\varepsilon}^2 \, dt \geq \int_0^s \|u_t(t)\|_X^2 \, dt.$$

(iii) (Lower bound on the slopes) If $v^\varepsilon \xrightarrow{S} v$ then $\liminf_{\varepsilon\to 0} \|\nabla_{X_\varepsilon} E_\varepsilon(v^\varepsilon)\|_{X_\varepsilon} \geq \|\nabla_X F(v)\|_X$.

(iv) The initial data are well prepared, in the sense that $E_\varepsilon(u^\varepsilon(0)) \to F(u(0))$.

Theorem (Sandier-Serfaty)

Then $u_t = -\nabla_X F(u)$

RS: The sharp interface limit (i)

We aim to apply the Sandier-Serfaty technique introduced so far (with few modifications) to the **gradient flow** of the energy

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First, we have by the well-known Modica-Mortola Theorem

Theorem

The functionals E^ε Γ-converge in $L^1 \times L^1$ to

$$E^0(u,\sigma) = c_\Psi \mathcal{H}^2(\Gamma) + \frac{1}{2}\|\sigma\|^2_{H^1} + \int_\Omega u\sigma dx$$

when $u-\sigma \in \{\pm 1\}$ and where Γ denotes the interface between the two open sets Ω^+ and Ω^- where φ takes values ± 1, and $c_\Psi = \int_{-1}^{1}\Psi(s)\,ds$

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when $u - \sigma \in \{\pm 1\}$ and where Γ denotes the interface between the two open sets Ω^+ and Ω^- where φ takes values ± 1, and $c_\Psi = \int_{-1}^{1} \Psi(s)\, ds$

This implies condition (i) with $F = E^0$ (Gamma liminf).

RS: The sharp interface limit (iii)

It is easy to obtain the following a-priori estimates

$$\begin{aligned}
\|u^\varepsilon\|_{H^1(0,T;\mathcal{V}')\cap L^\infty(0,T;L^4(\Omega))} &\le M \\
\|\sigma^\varepsilon\|_{H^1(0,T;L^2(\Omega))\cap L^\infty(0,T;H^1(\Omega))} &\le M \\
\|\mu^\varepsilon\|_{L^2(0,T;H^1(\Omega))} &\le M \\
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from which follows condition (iii) (Lower bound on the slope).

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Lemma

For a subsequence, we have

$$\varphi^\varepsilon \rightharpoonup \varphi \qquad \textit{weakly in } L^4(\Omega \times [0, T]).$$

Moreover, following [N.Q. Le, Calc. Var. (2008)], we have:
for all $t \in [0, T]$, $\varphi(t) \in BV(\Omega; \{-1, 1\})$ *and*

$$
\begin{aligned}
\varphi^\varepsilon(t) &\rightharpoonup \varphi(t) && \textit{weakly in } L^4(\Omega) \\
\varphi^\varepsilon(t) &\to \varphi(t) && \textit{strongly in } L^1(\Omega) \\
\varphi^\varepsilon(t) &\rightharpoonup \varphi(t) && \textit{weakly* in } BV(\Omega).
\end{aligned}
$$

The sharp interface limit (ii)

If we assume that the limit interface Γ is smooth (at least C^3), then we have:

Lemma

Let $\cup_{t\in[0,T]}\Gamma(t)\times\{t\}\subset\Omega\times[0,T]$ *be a* C^3 *hypersurface with* $\Gamma(t)$ *closed for all* $t\in[0,T]$. *Let* $\varphi(t):=\chi_{\Omega^+(t)}-\chi_{\Omega^-(t)}$ *for all* $t\in[0,T]$, *and assume* $\varphi\in L^\infty(0,T;L^2(\Omega))\cap H^1(0,T;\mathcal{V}')$ *and* $\sigma\in L^\infty(0,T;H^1(\Omega))\cap L^2(0,T;H^2(\Omega))\cap H^1(0,T;L^2(\Omega))$. *Then for all* $t\in[0,T]$

$$
\begin{aligned}
\frac{d}{dt}E^0(\varphi(t)+\sigma(t),\sigma(t)) = & -2c_\Psi\langle V(t),k(t)\rangle_{L^2(\Gamma)}+2\langle V(t),\sigma(t)\rangle_{L^2(\Gamma)} \\
& +\langle\sigma_t(t),-\Delta\sigma(t)+\varphi(t)+3\sigma(t)\rangle,
\end{aligned}
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where $V(t)$ *is the normal velocity of the surface* $\Gamma(t)$, *and* $k(t)$ *is its mean curvature.*

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where $V(t)$ *is the normal velocity of the surface* $\Gamma(t)$*, and* $k(t)$ *is its mean curvature.*

We are now ready to prove the lower bound on the velocities, (ii):
For all $t\in[0,T]$ there holds

$$\liminf_{\varepsilon\to 0}\int_0^t \|u_t^\varepsilon(s)\|_{H_n^{-1}(\Omega)}ds \ge \int_0^t \|2\partial_t\Gamma(s)+\sigma_t(s)\|_{H_n^{-1}(\Omega)}ds.$$

This follows from the fact that $u_t^\varepsilon=\varphi_t^\varepsilon+\sigma_t^\varepsilon$ and from the Gradient Flow structure of the problem

RS: The main result

Finally we need the following lemma:

Lemma (Equipartition of Energy)

The functions $\mu^\varepsilon \rightharpoonup \mu$ *weakly in* $L^2(0, T; H^1(\Omega))$ *and* μ *satisfies for a.e.* $t \in [0, T]$

$$\mu(t) = -c_\Psi k(t) \quad \text{on } \Gamma(t),$$

where $k(t) \in H^{1/2}(\Gamma(t))$ *is the mean curvature of the smooth surface* $\Gamma(t)$ *at time* t.

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Lemma (Equipartition of Energy)

The functions $\mu^\varepsilon \rightharpoonup \mu$ weakly in $L^2(0, T; H^1(\Omega))$ and μ satisfies for a.e. $t \in [0, T]$

$$\mu(t) = -c_\Psi k(t) \quad \text{on } \Gamma(t),$$

where $k(t) \in H^{1/2}(\Gamma(t))$ is the mean curvature of the smooth surface $\Gamma(t)$ at time t.

We then obtain the following statements:

Theorem

If the initial data are well prepared, i.e., $E^\varepsilon(\varphi^\varepsilon(0), \sigma^\varepsilon(0)) \to E(\varphi(0), \sigma(0))$, then it holds

$$\begin{aligned} -\Delta\mu &= u + \sigma - \mu \quad \text{on } \Omega^+ \cup \Omega^- \\ \sigma_t &= -\Delta\sigma + \mu - u - \sigma \quad \text{on } \Omega \\ \mu &= -c_\Psi k \quad \text{and} \quad \left[\frac{\partial\mu}{\partial n}\right] = -2V \quad \text{a.e. on } \Gamma \end{aligned}$$

almost everywhere on $[0, T]$.

Remarks and Open Problems

We tacitly made some hypotheses:

- One is on the regularity of the limit interface. As a consequence there will be a death time T^* until the evolution is regular. After the death time the evolution is undetermined!

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$$\frac{\varepsilon}{2}|\nabla u^\varepsilon|^2 + \frac{W(u^\varepsilon)}{\varepsilon} \rightharpoonup 2c_\Psi d\mathcal{H}^2 \llcorner \Gamma$$

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- To obtain higher regularity it is possible regularize the gradient flow by introduce a suitable s-power of the Laplacian replacing Δ both in the ϕ and the σ equations. Unfortunately in such a case it is nontrivial (and out of reach) to prove the analogous of the interface property $[\frac{\partial \mu}{\partial n}] = -2V$ unless $s = 2$

Diffuse Interface models in other applications: Liquid Crystals

Consider the following 2D hydrodynamical model for the flow of nematic liquid crystals (cf. [F.-H. Lin, Nonlinear theory of defects in nematic liquid crystals: Phase transitions and flow phenomena, Comm. Pure Appl. Math. (1989)]):

$$\partial_t \mathbf{v} + \mathbf{v} \cdot \nabla \mathbf{v} - \nu \Delta \mathbf{v} + \nabla P = -\lambda \nabla \cdot (\nabla \mathbf{d} \odot \nabla \mathbf{d})$$

$$\nabla \cdot \mathbf{v} = 0$$

$$\partial_t \mathbf{d} + \mathbf{v} \cdot \nabla \mathbf{d} = \Delta \mathbf{d} - \frac{1}{\epsilon^2}(|\mathbf{d}|^2 - 1)\mathbf{d}$$

where **v** is the velocity field of the flow and **d** represents the averaged macroscopic/continuum molecular orientations.

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Possible applications of the results we have seen in the biological models and a big open issue is:

- **The sharp interface limit as $\epsilon \searrow 0$:** the potential $F(\mathbf{d}) = \frac{1}{4\epsilon^2}(|\mathbf{d}|^2 - 1)^2$ was introduced to relax the nonlinear constraint $|\mathbf{d}| = 1$ on molecule length. Can the Gamma-Convergence technique be applied at least for the $\mathbf{d}$-equation without velocities? This is - up to my knowledge - a very open problem!

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- Only very recently in [Fei et al., SIMA, 2015] the sharp interface dynamic for a tensorial model of LCs has been obtained by means of matched asymptotic expansion method, but a **rigorous analysis is still missing**

Many thanks to all of you for the attention!

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