A Continuum Variational Approach to Vesicle Membrane Modeling

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Ultimate Goal: Modeling Shape Changes in Membranes

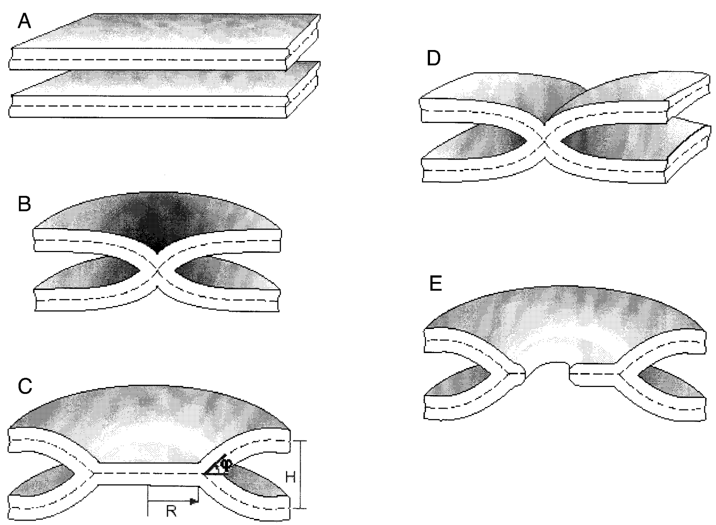
fusion ★ changes in topology ★

rafts ★ adhesion ★

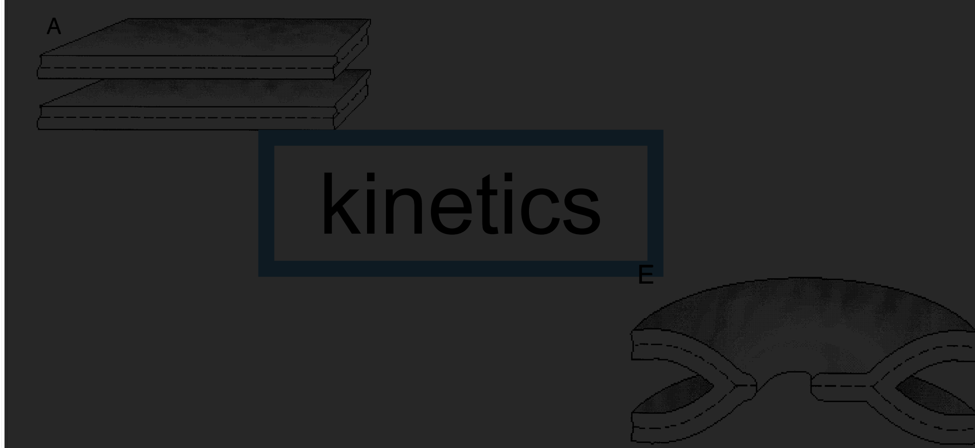
Derive kinetics explicitly--don’t assume intermediates. Intermediate shapes and states are an <u>output</u> of the model.

Ultimate Goal: Modeling Shape Changes in Membranes

Assume Intermediates	Calculate Intermediatates



Kozlovsky, Chernomordik, Koslov, Biophys. J. 2002



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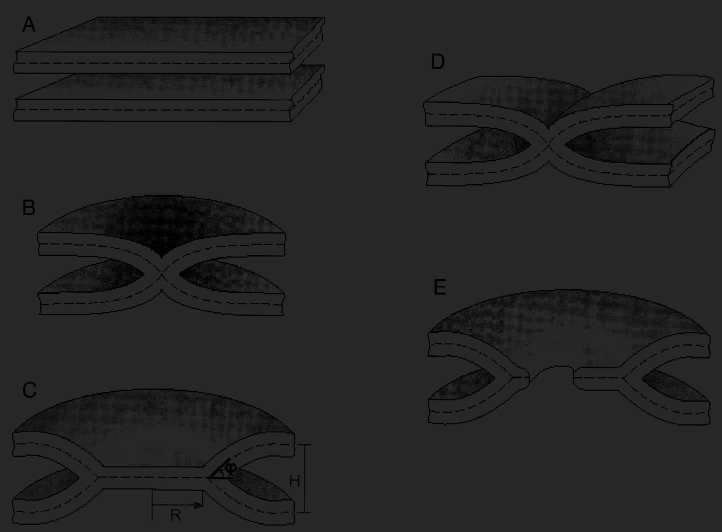

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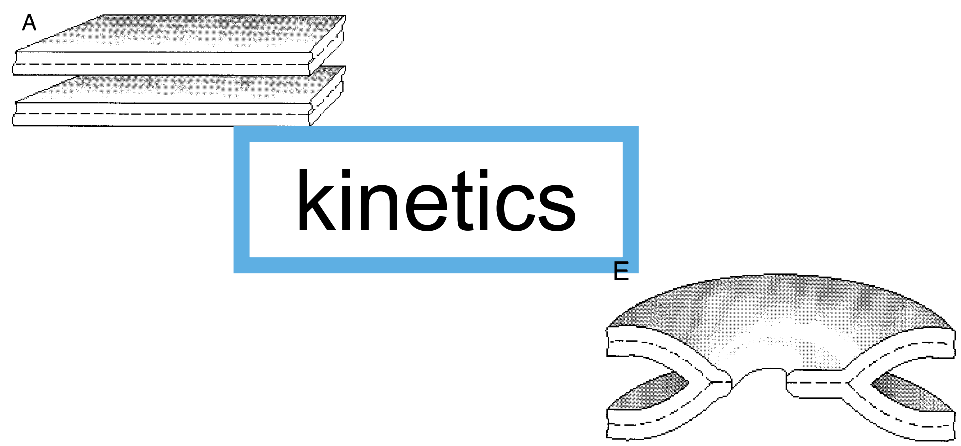
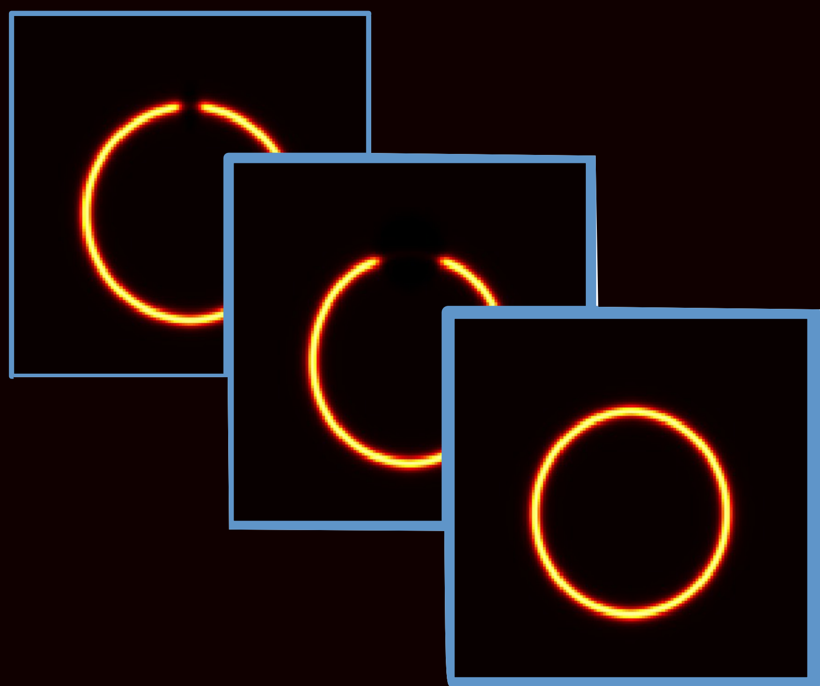


Intermediate Goal:

Verification for a Simpler Problem

★ Growth and Shrinkage of a Lipidic Pore in a Single Bilayer from Osmotic Pressure ★



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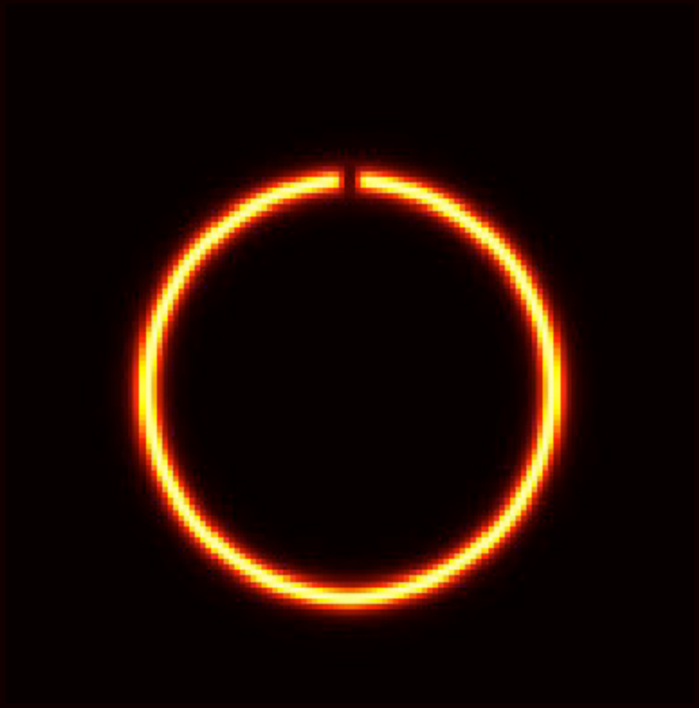
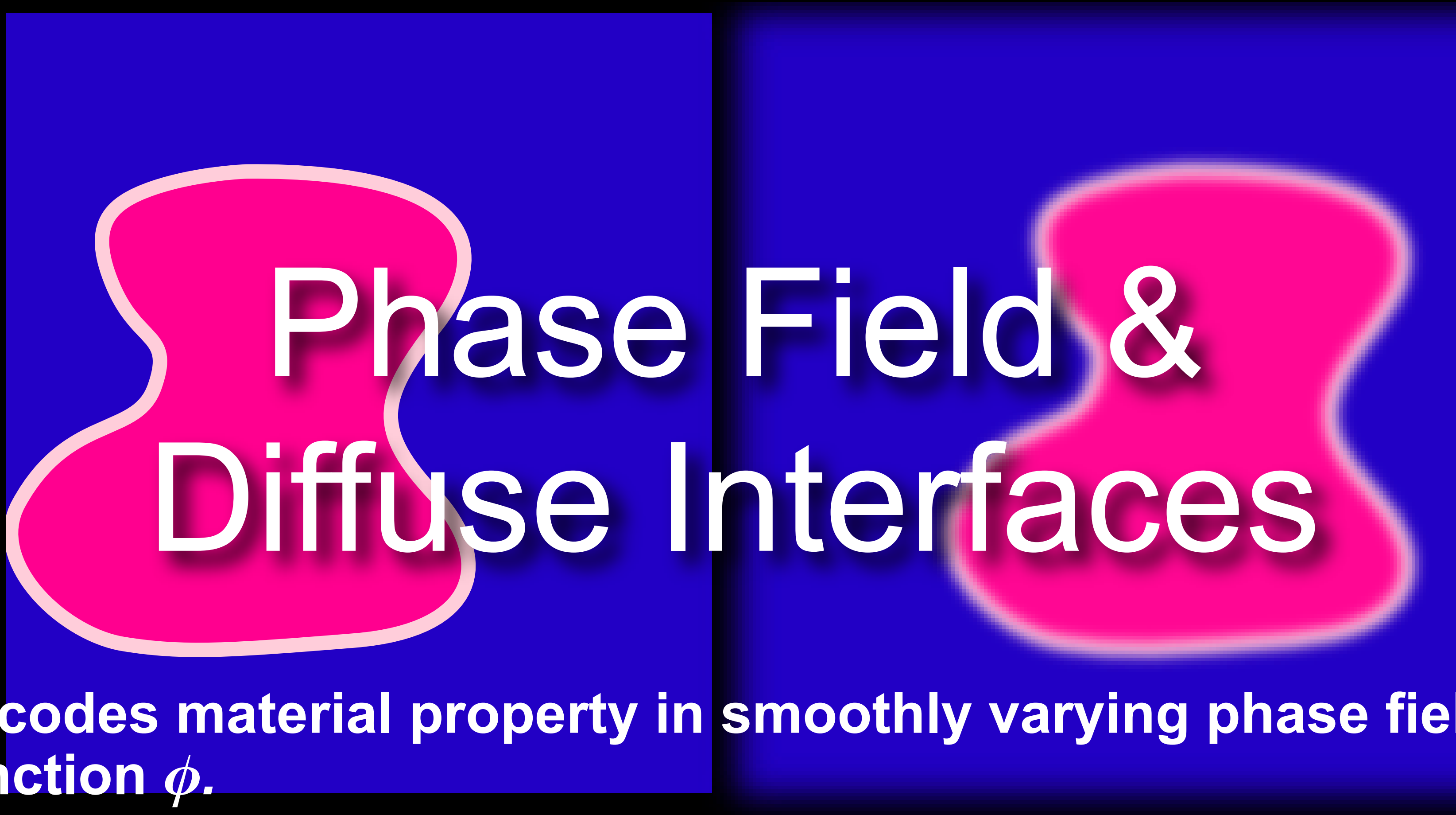




Phase Field & Diffuse Interfaces

- ★ **Encodes material property in smoothly varying phase field function ϕ.**
- ★ **Translates Helfrich energy of membrane into a Hamiltonian in terms of ϕ.**
- ★ **Does not assume a particular shape**
- ★ **Treats membrane as a <u>bulk material</u> (versus a mathematical interface)**

Phase Field Hamiltonian

$$E = \frac{B}{2}\int \epsilon(\tanh(\bar{\phi})+1)\left(\Delta\phi - \frac{1}{\epsilon^2}F'(\phi)\right)\,dx$$
$$+\frac{J}{2}\int\left(\frac{\epsilon}{2}|\nabla\phi|^2+\frac{1}{\epsilon}F(\phi)\right)\left(\frac{\epsilon}{2}|\nabla\bar{\phi}|^2+\frac{1}{\epsilon}F(\bar{\phi})\right)\,dx$$
$$+\frac{S}{2A_0}\left(\int(\tanh(\bar{\phi})+1)\left(\frac{\epsilon}{2}|\nabla\phi|^2+\frac{1}{\epsilon}F(\phi)\right)\,dx - A_0\right)^2$$

Q. Du, C. Liu, X. Wang, *A phase field approach in the numerical study of the elastic bending energy for vesicle membranes*, J. Comp. Phys. 2004

Q. Du, C. Liu, R. Ryham, X. Wang, *Energetic variational approaches in modeling vesicle and fluid interactions*, Phys. D. 2009

X. Wang, Q. Du, *Modelling and simulations of multi-component lipid membranes and open membranes via diffuse interface approaches*, J. Math. Bio. 2008

Equations of Motion

Navier Stokes Equations

$$\rho(\mathbf{u}_t + \mathbf{u} \cdot \nabla \mathbf{u}) + \nabla p = \nu \Delta \mathbf{u} + \mathbf{f}, \qquad \text{(force balance)}$$

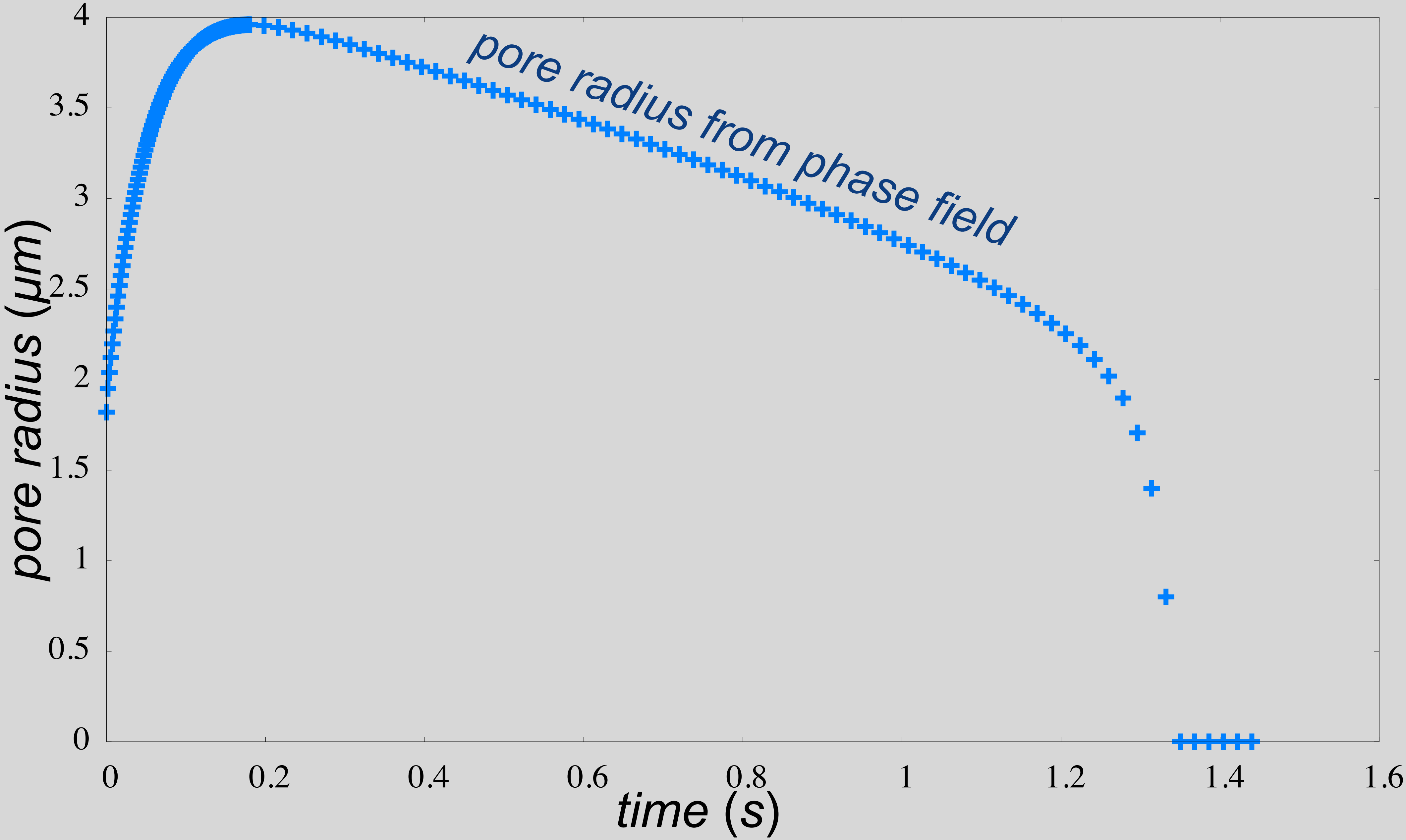
$$\nabla \cdot u = 0, \qquad \text{(incompressibility)}$$

$$\phi_t + \mathbf{u} \cdot \nabla \phi = 0, \qquad \text{(membrane moves with fluid)}$$

- ★ **Flexible way to encode classical and new energies**
- ★ **Coupling with water is made easy (vesicle and water are one fluid)**
- ★ **Forces and time dependence, <u>outputs</u>, are strictly based on first principle physics**

Dynamics of a Lipidic Pore

Calculated Pore Radius as a Function of Time



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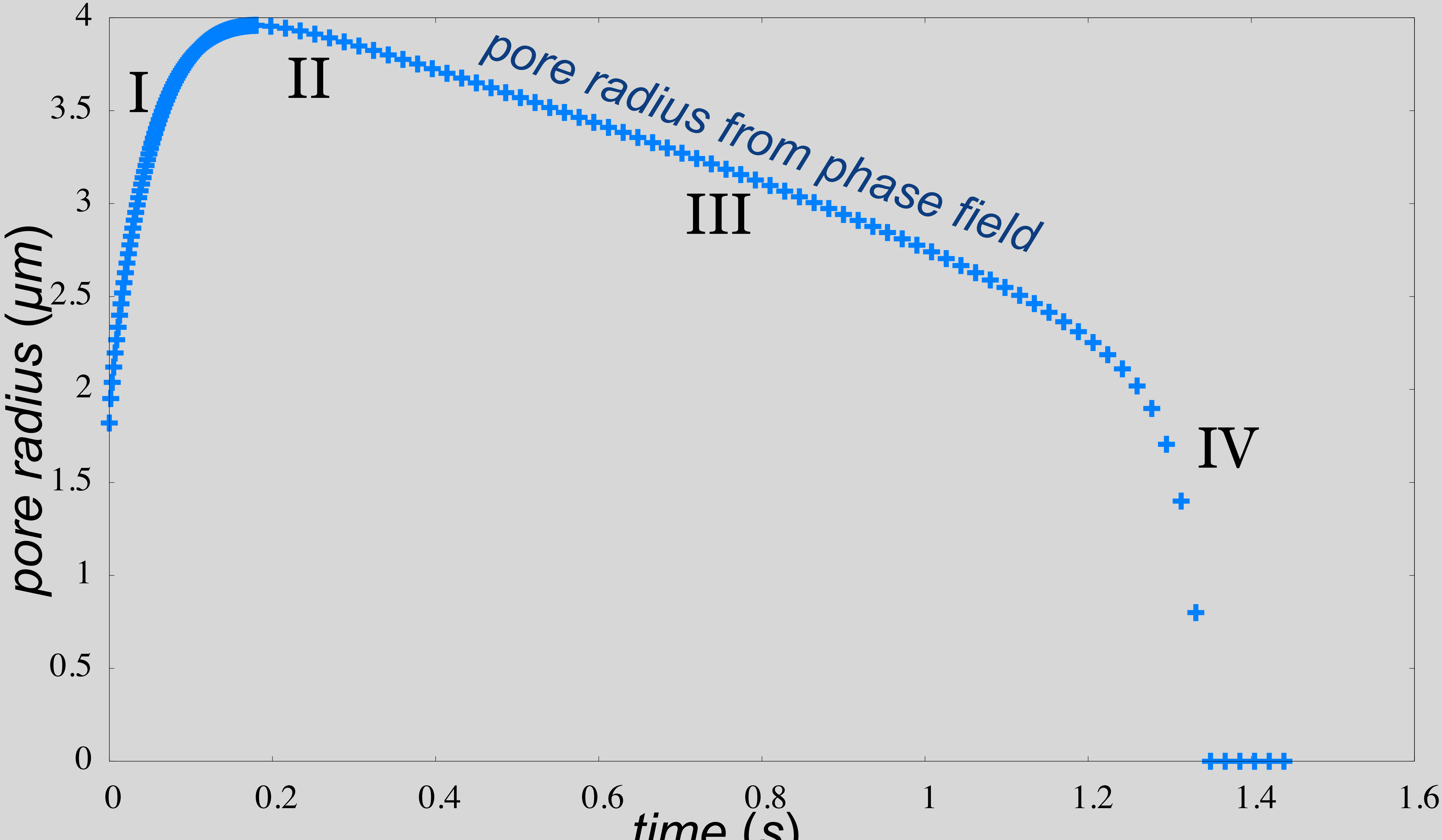

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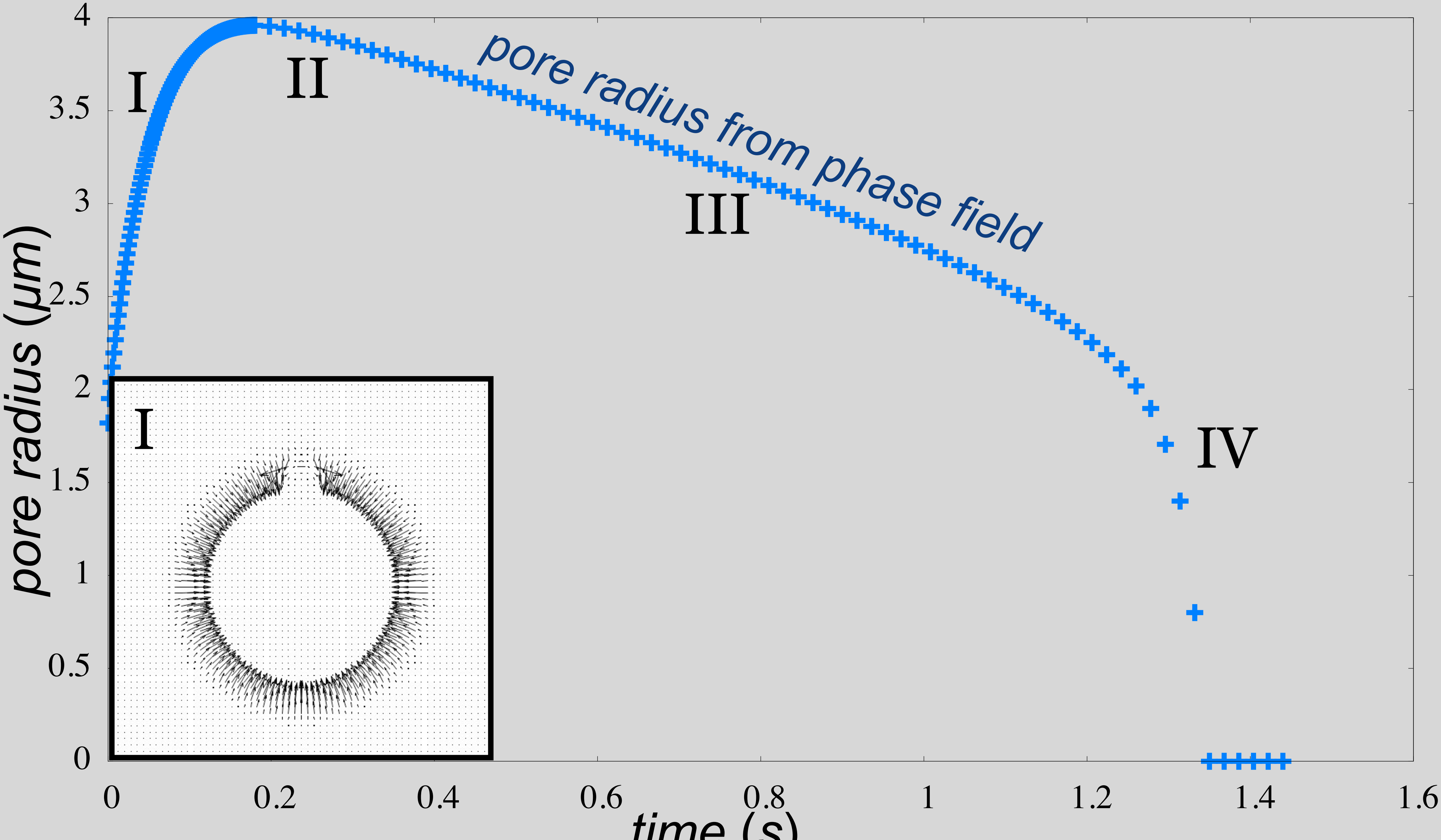

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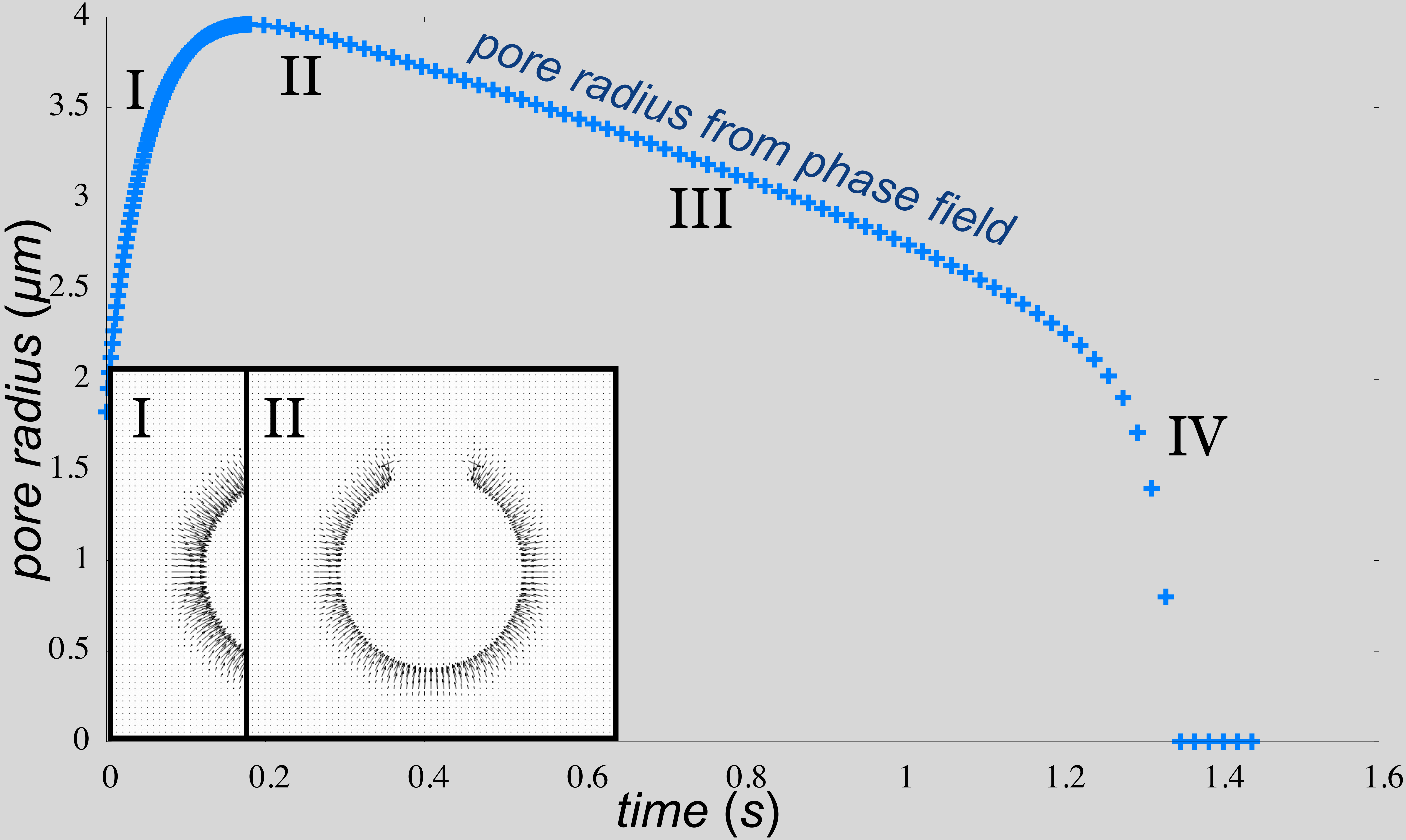

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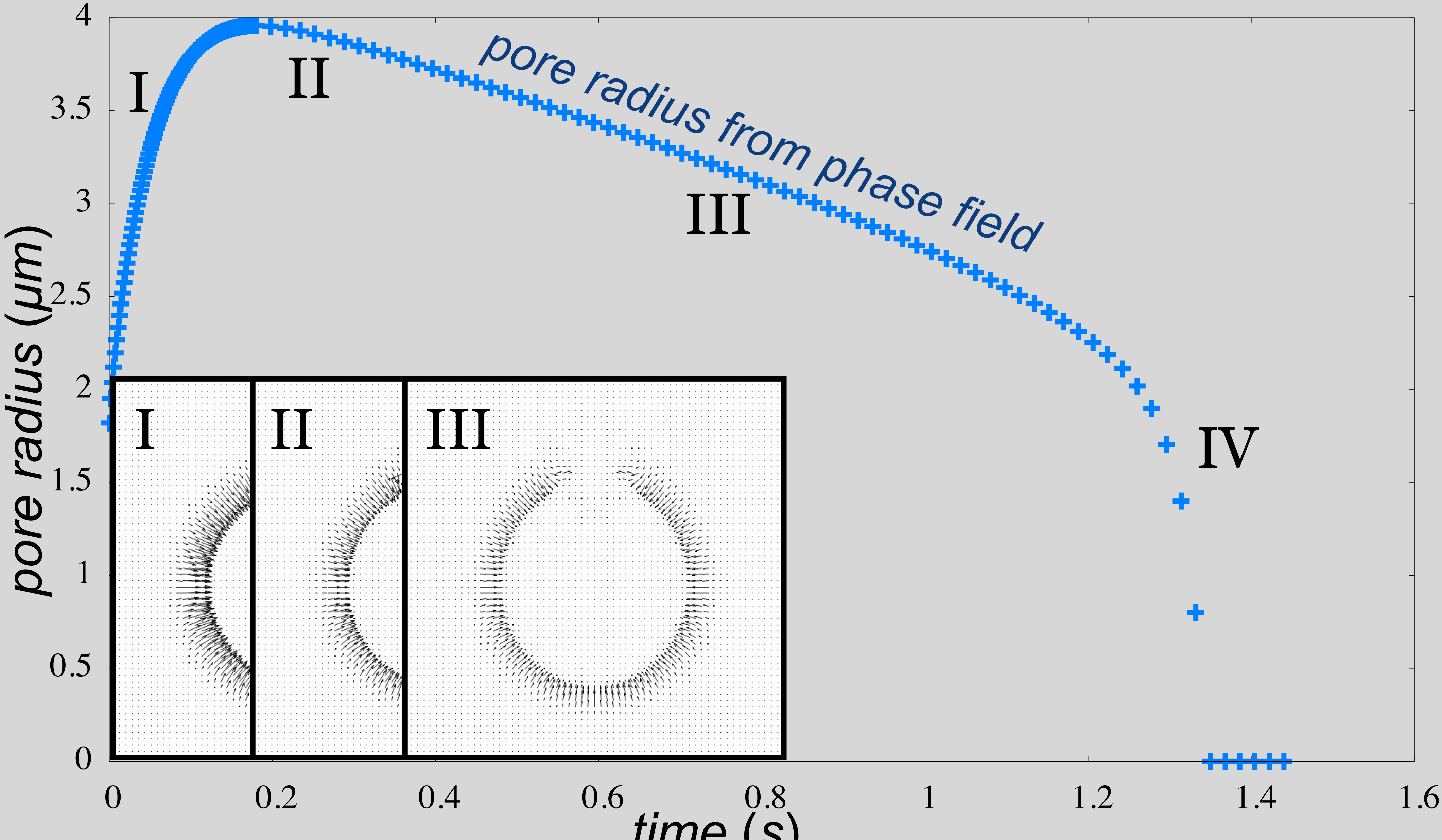

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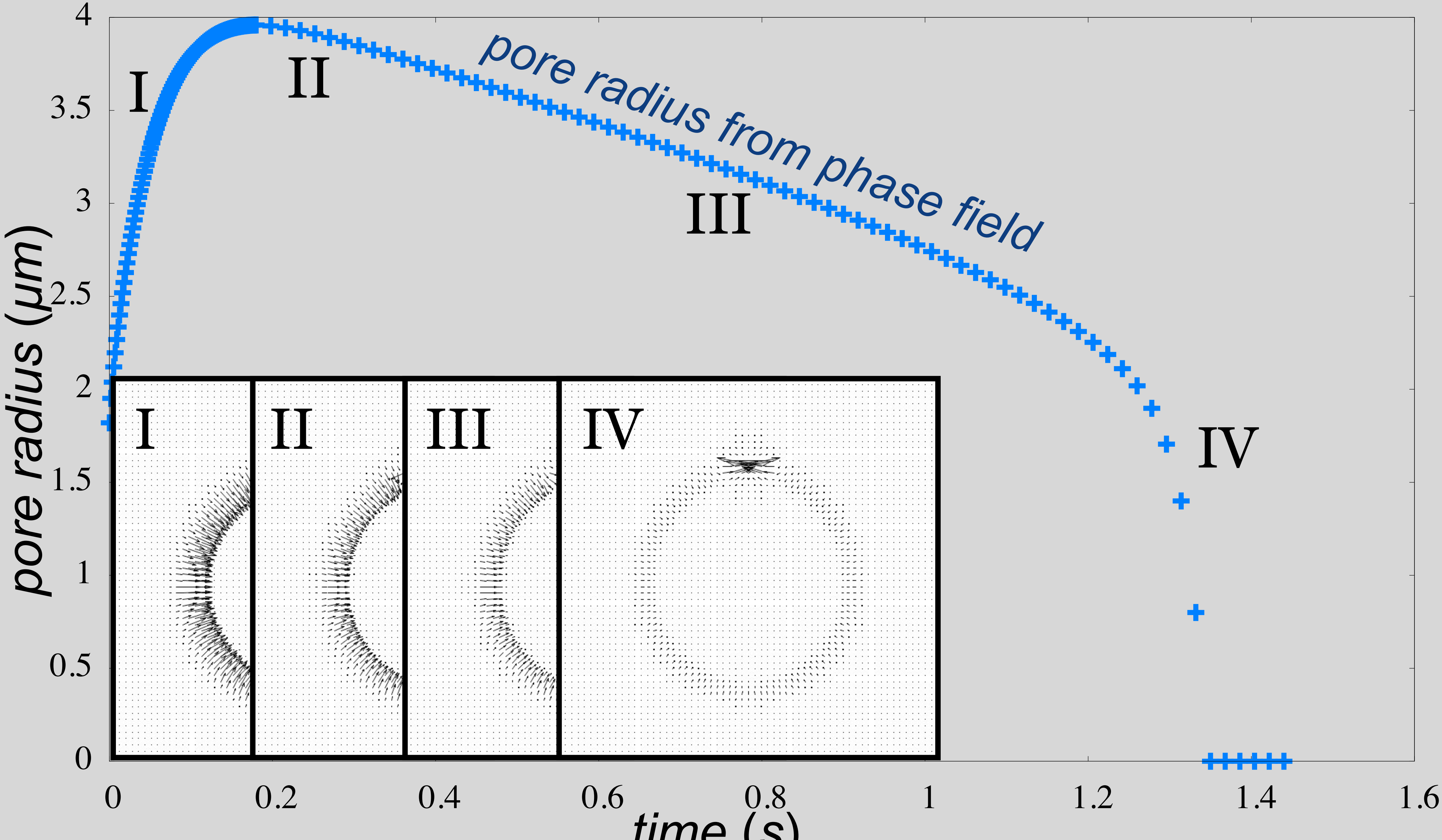

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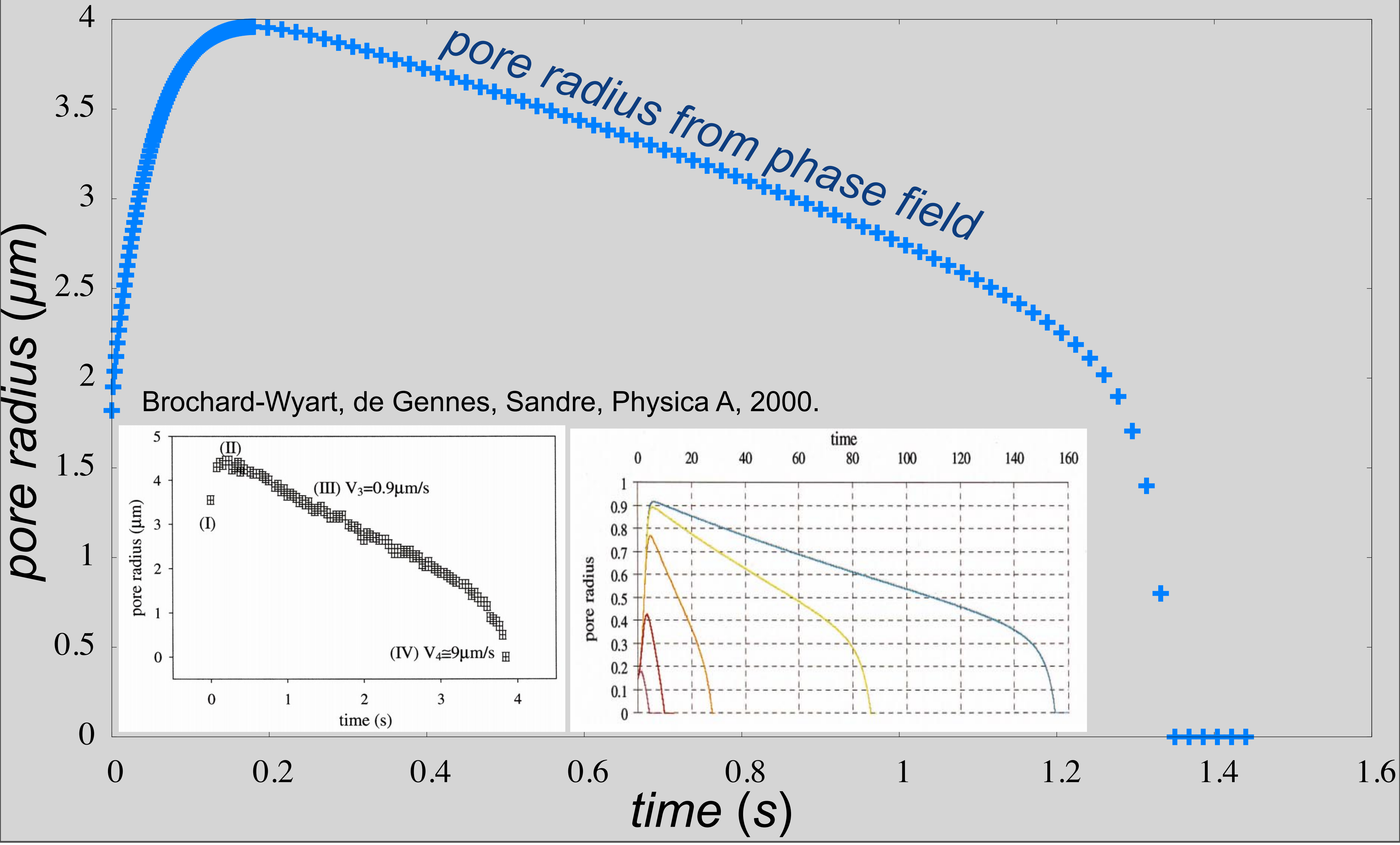
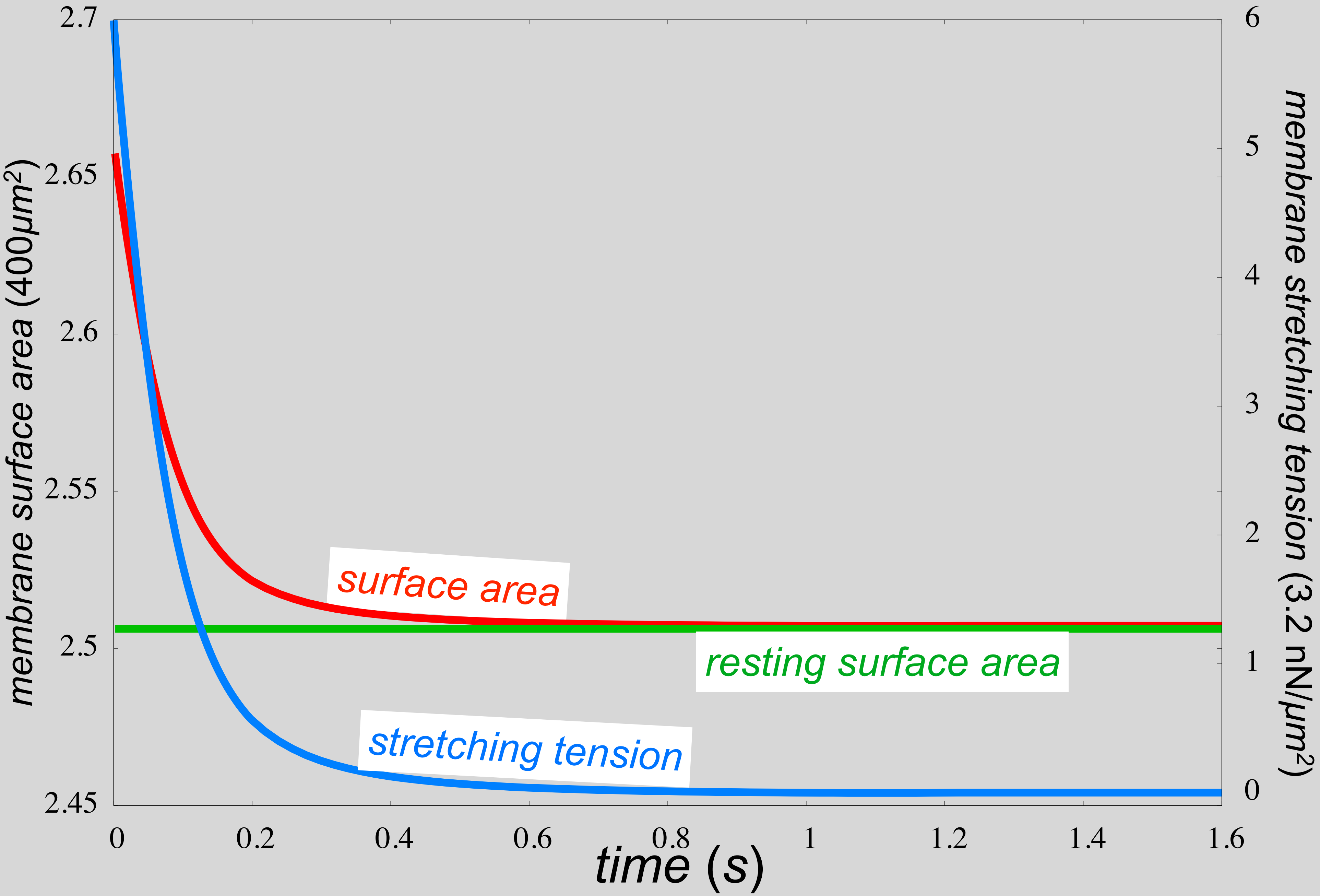


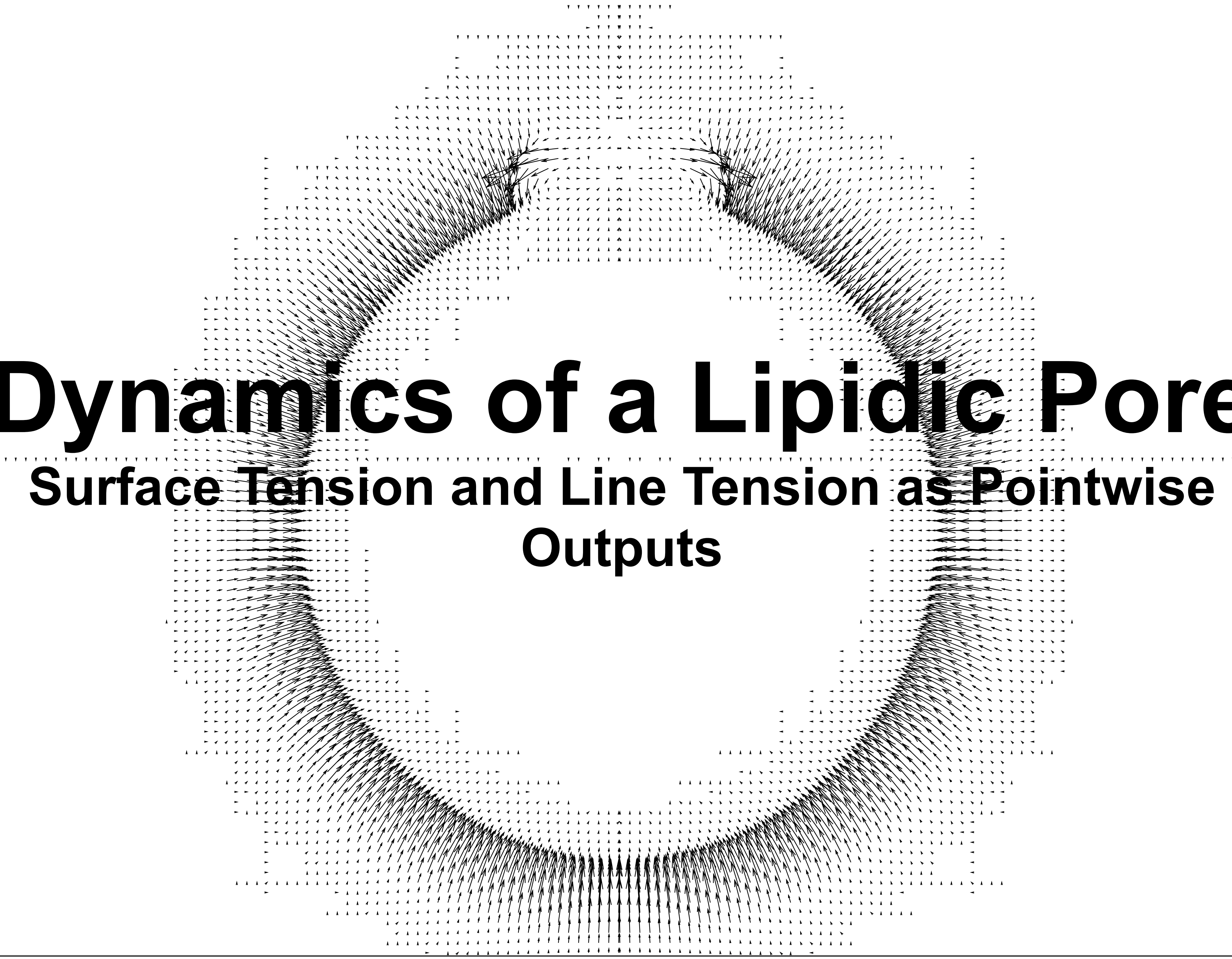
Dynamics of a Lipidic Pore

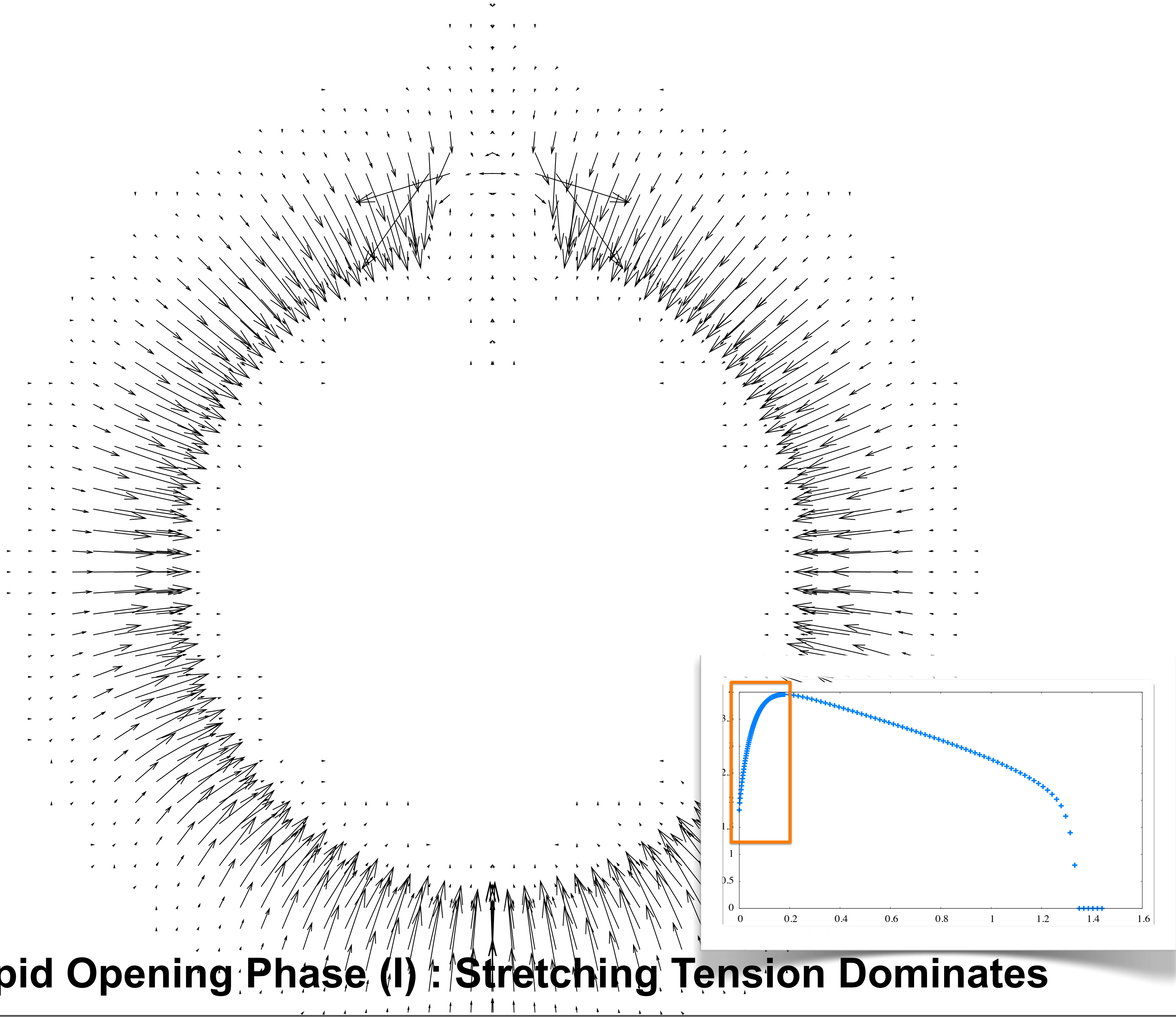
Calculated Surface Areas as a Function of Time



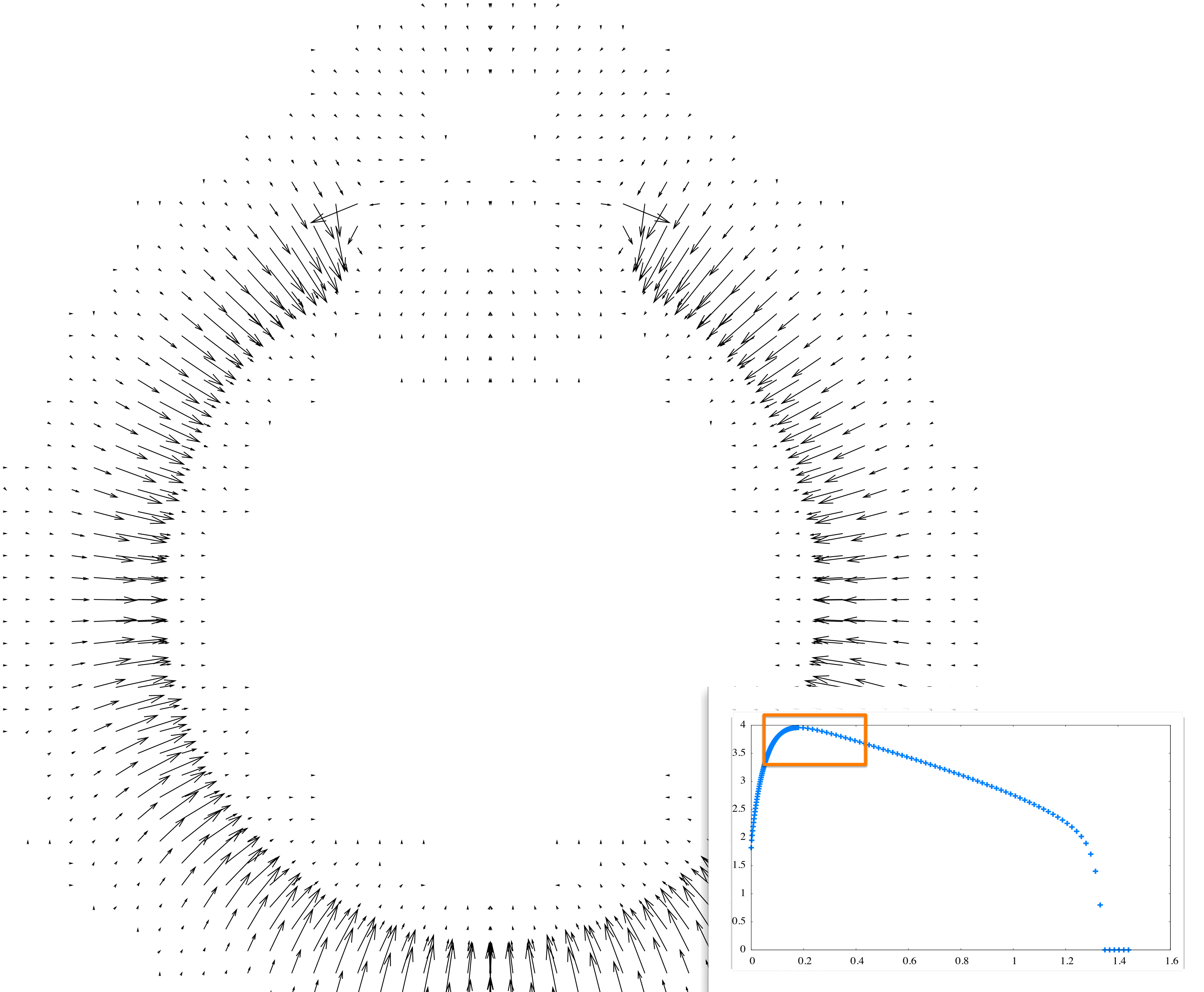
Dynamics of a Lipidic Pore

Surface Tension and Line Tension as Pointwise Outputs

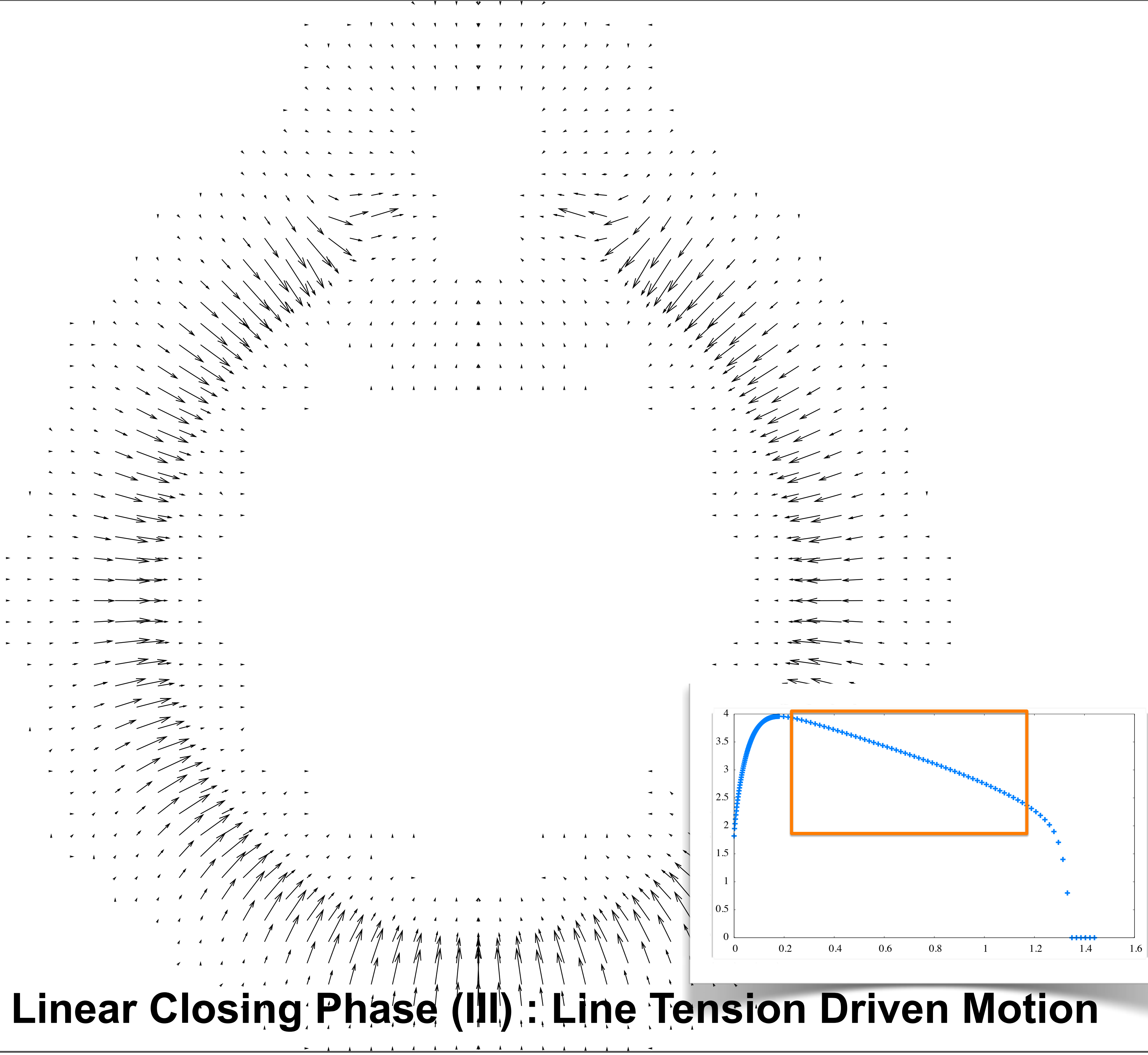




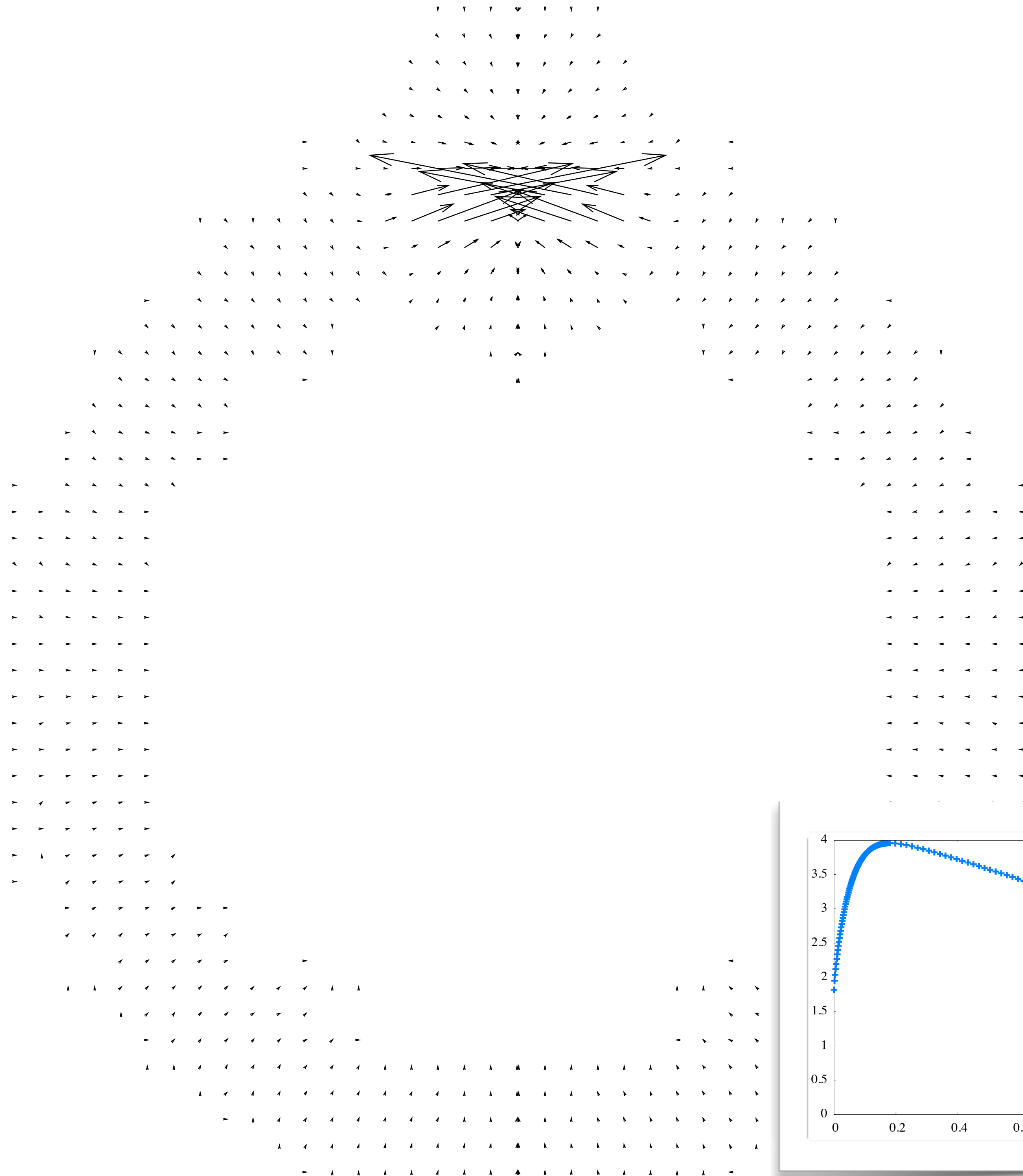
Rapid Opening Phase (I) : Stretching Tension Dominates

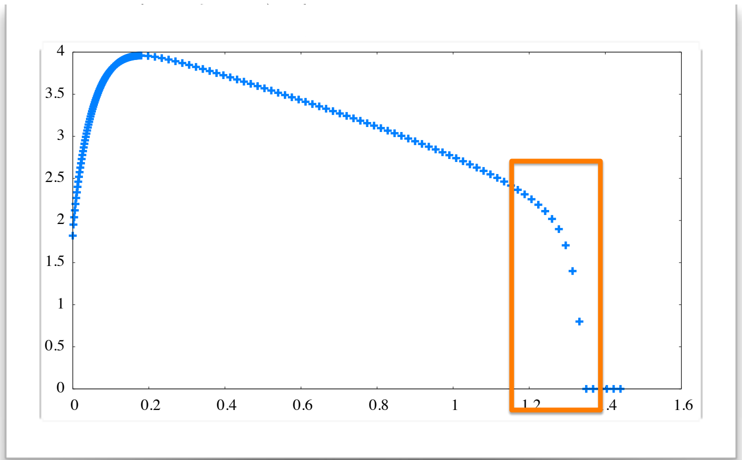


Reversal Phase (II) : Surface Area Equilibrates

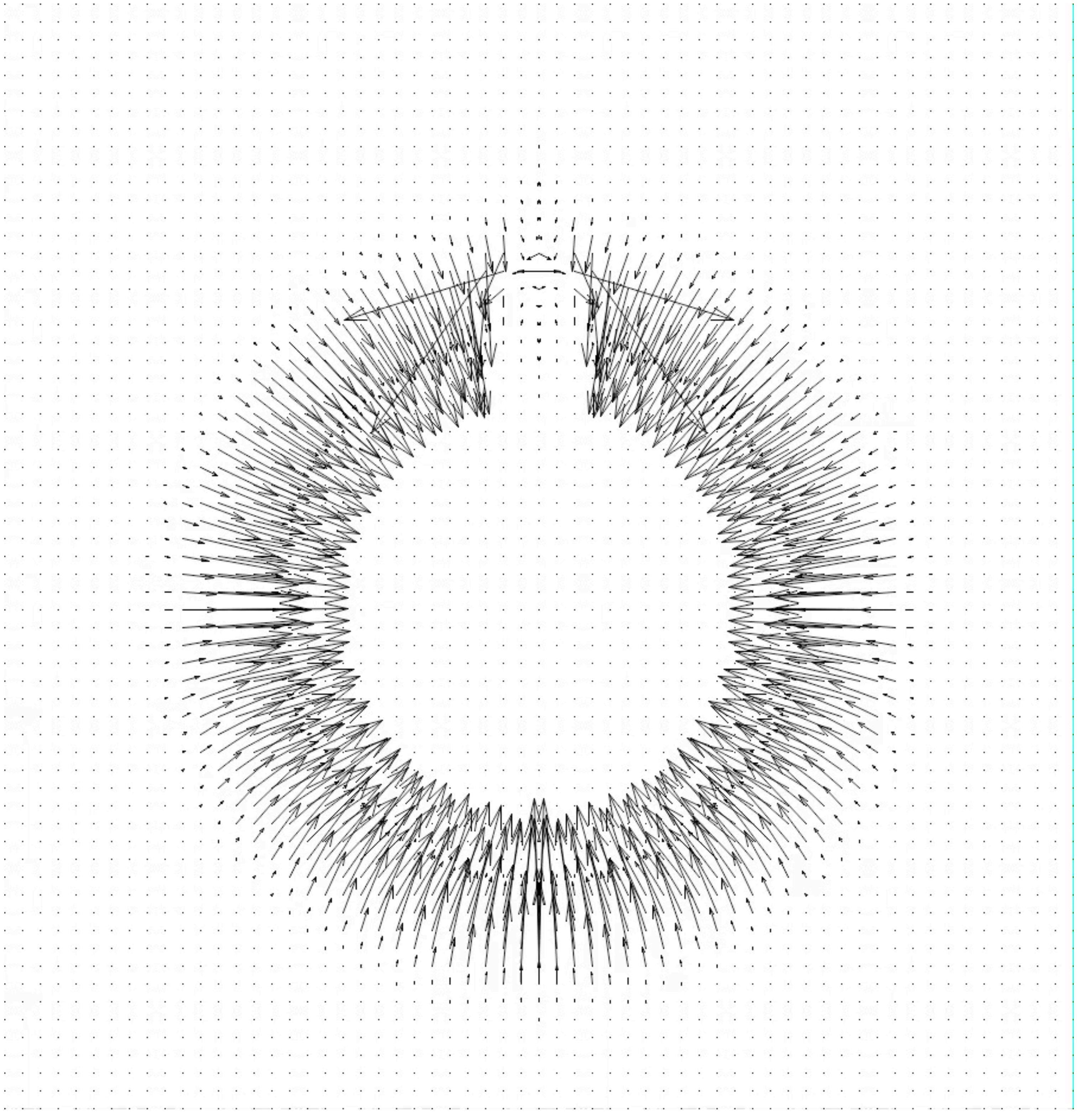


Slower Linear Closing Phase (III) : Line Tension Driven Motion



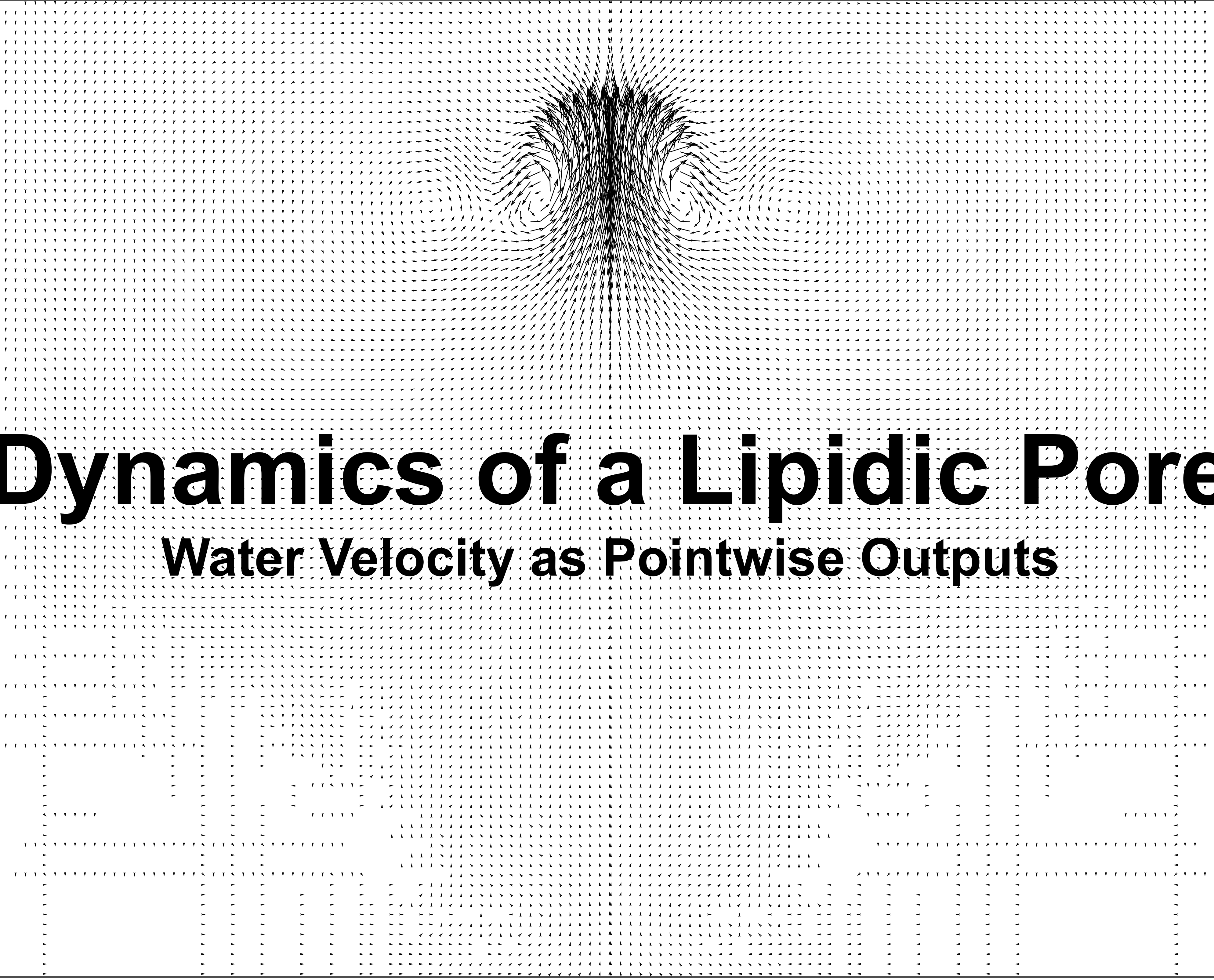


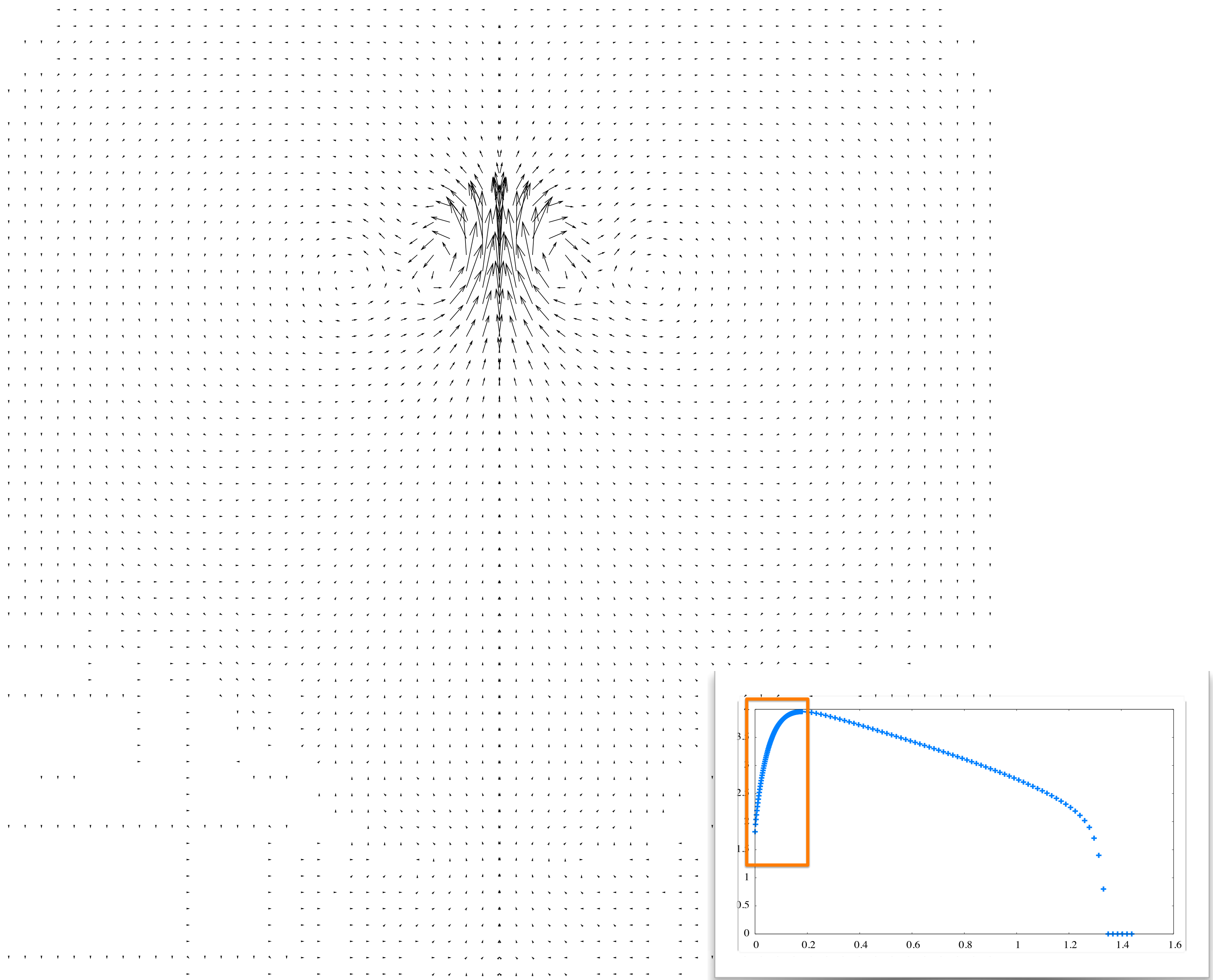
Rapid Closing Phase (IV) : Line Tension Dominates



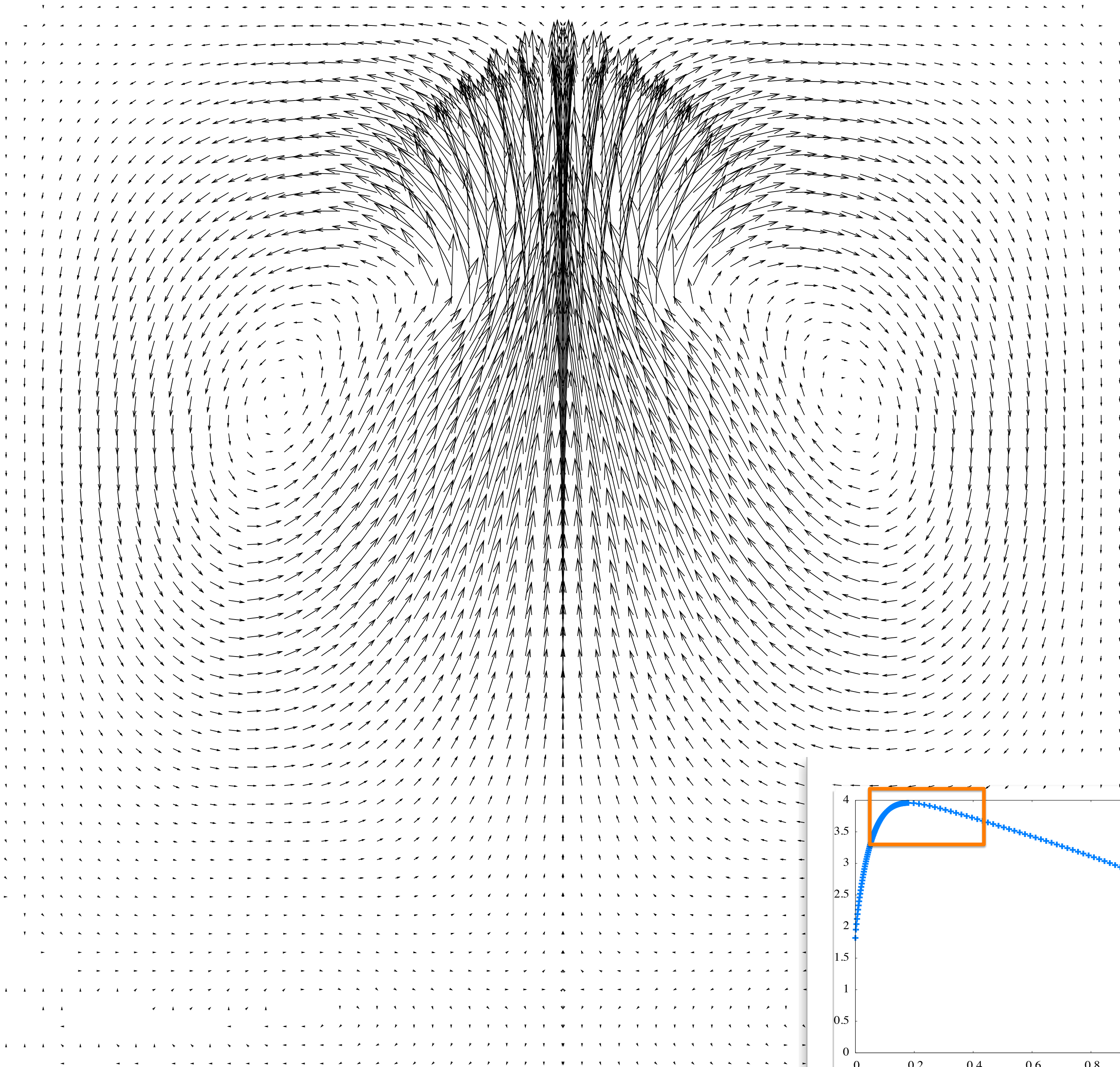
Dynamics of a Lipidic Pore

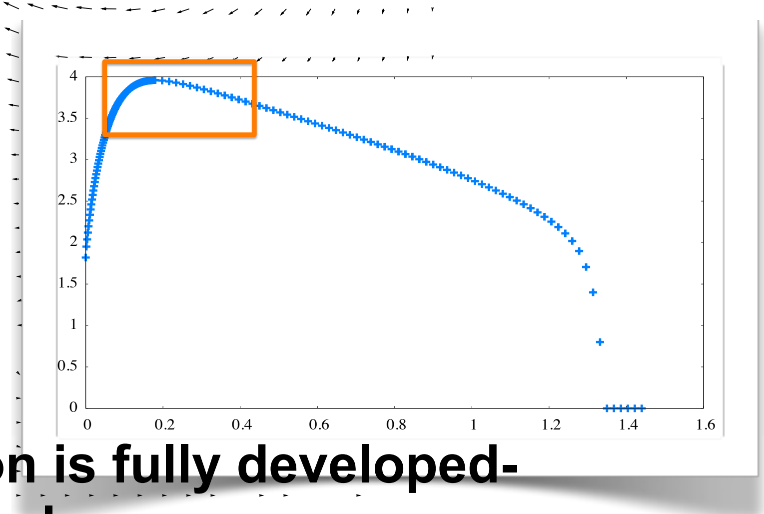
Water Velocity as Pointwise Outputs



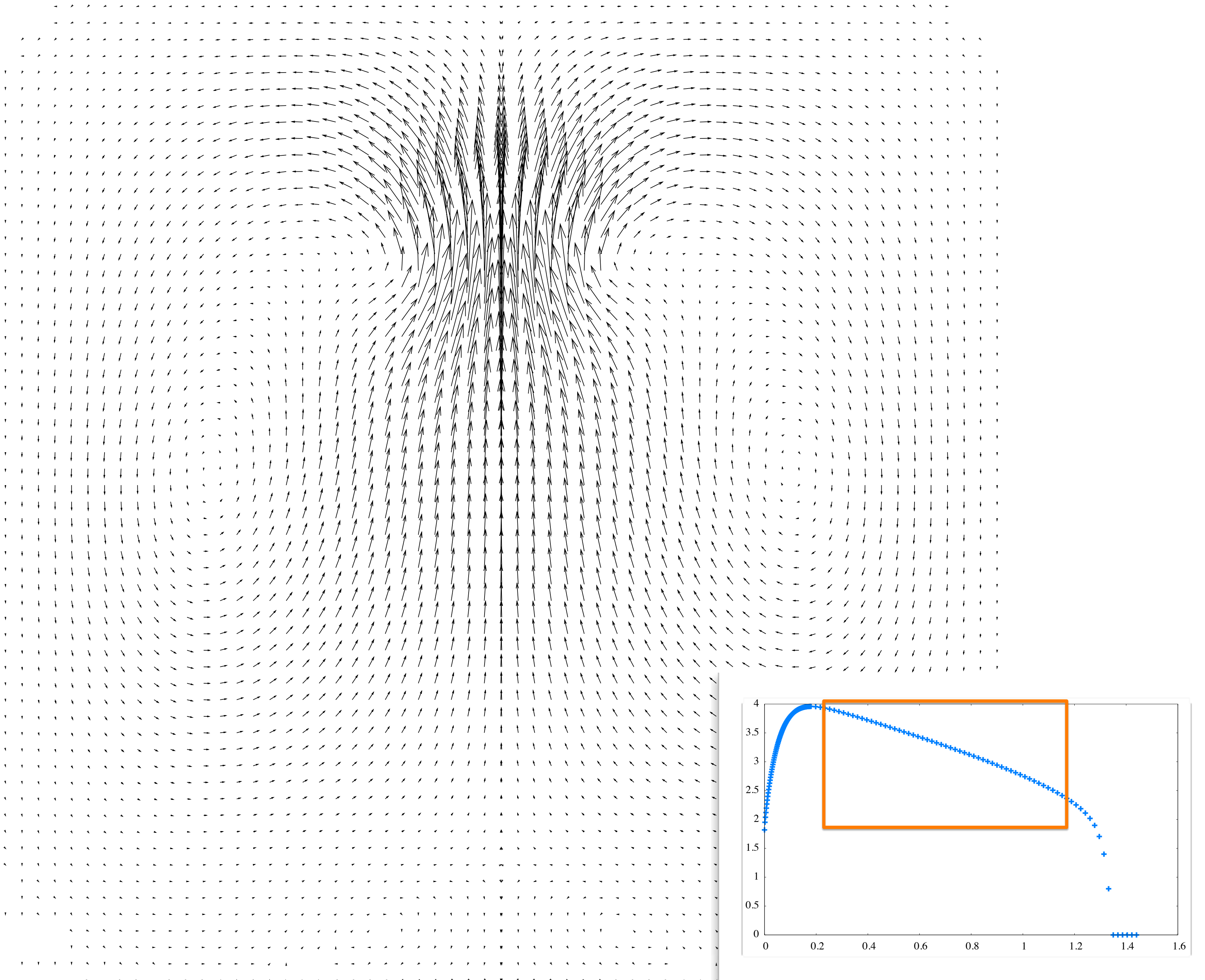


Rapid Opening Phase (I) : pressure drives water near hole

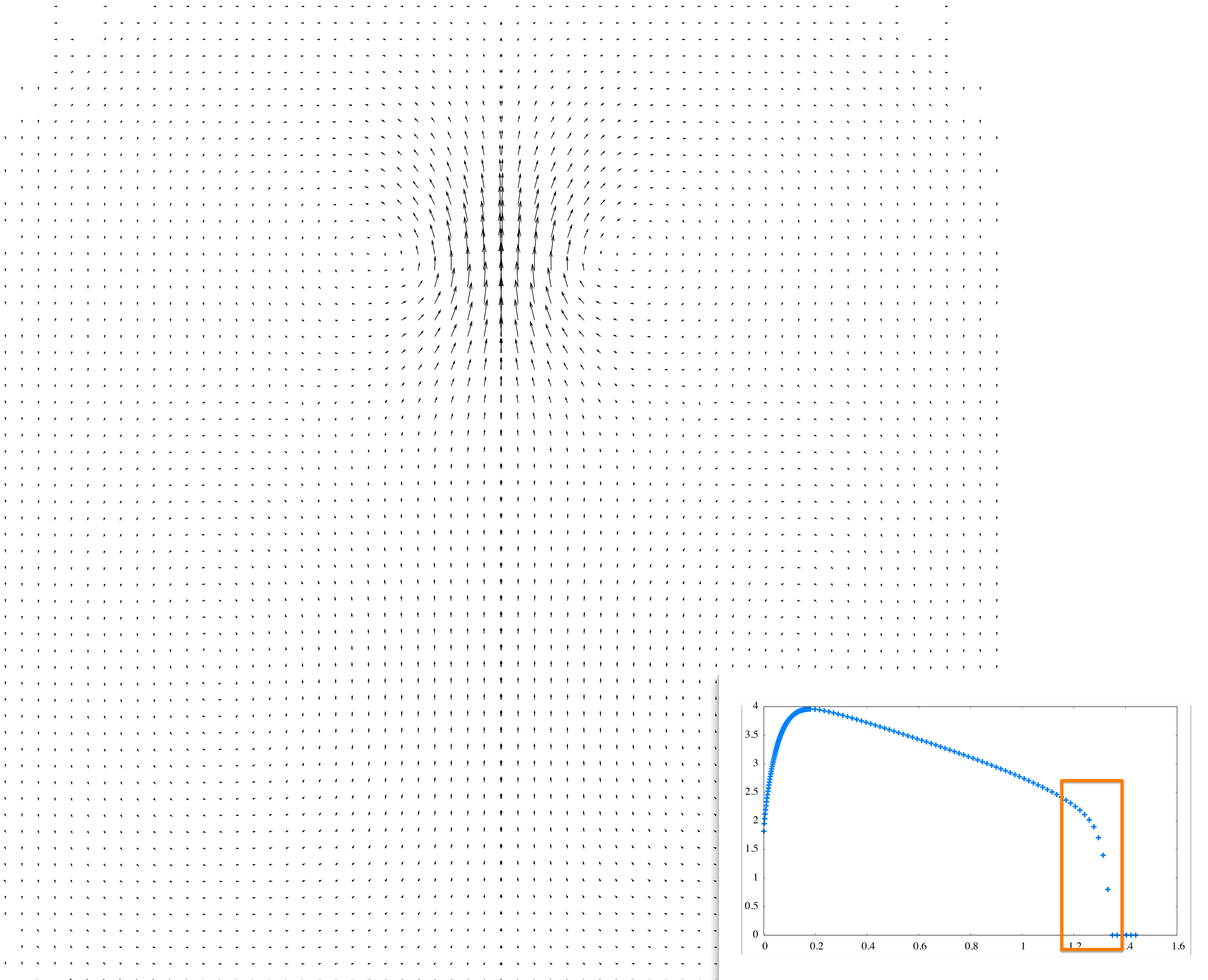




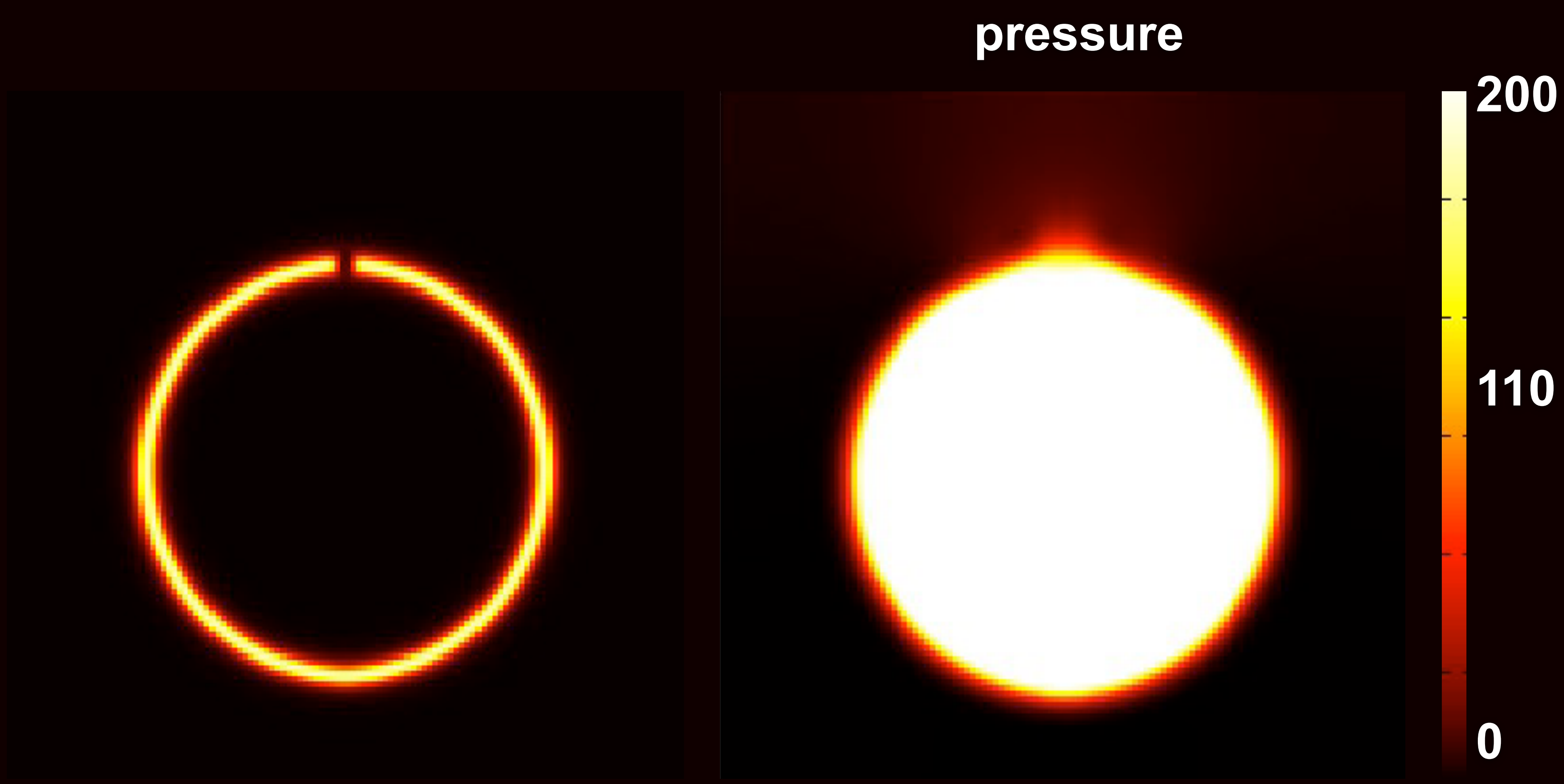
Reversal Phase (II) : stretching driven motion is fully developed- vesicle becomes aspherical



Slower Linear Closing Phase (III) : motion of water not effected by vesicle



Rapid Closing Phase (IV) : out flow during closure is quite small


pressure
200
110
0