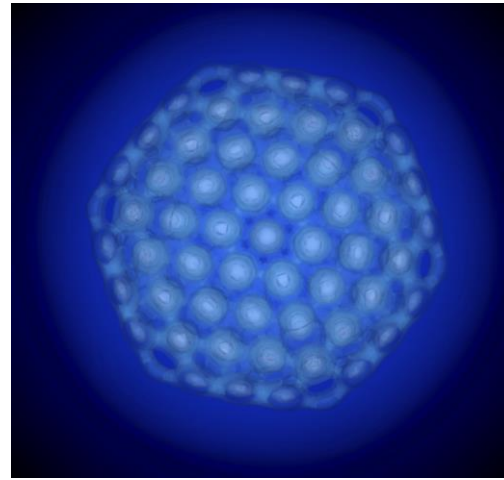# Understanding crystallization using density functional theory and fluctuating hydrodynamics
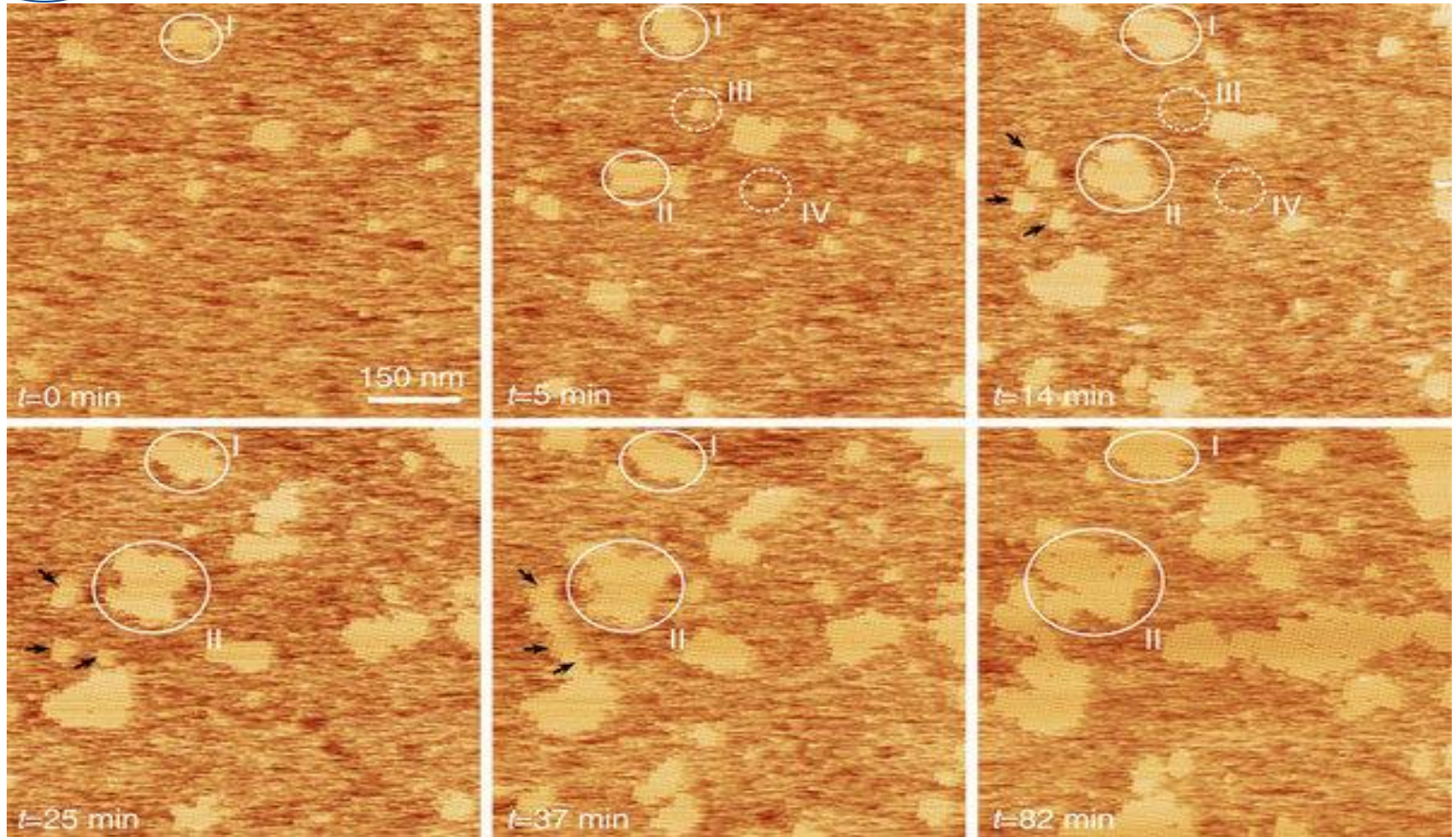

James F. Lutsko
Center for Nonlinear Phenomena and Complex Systems
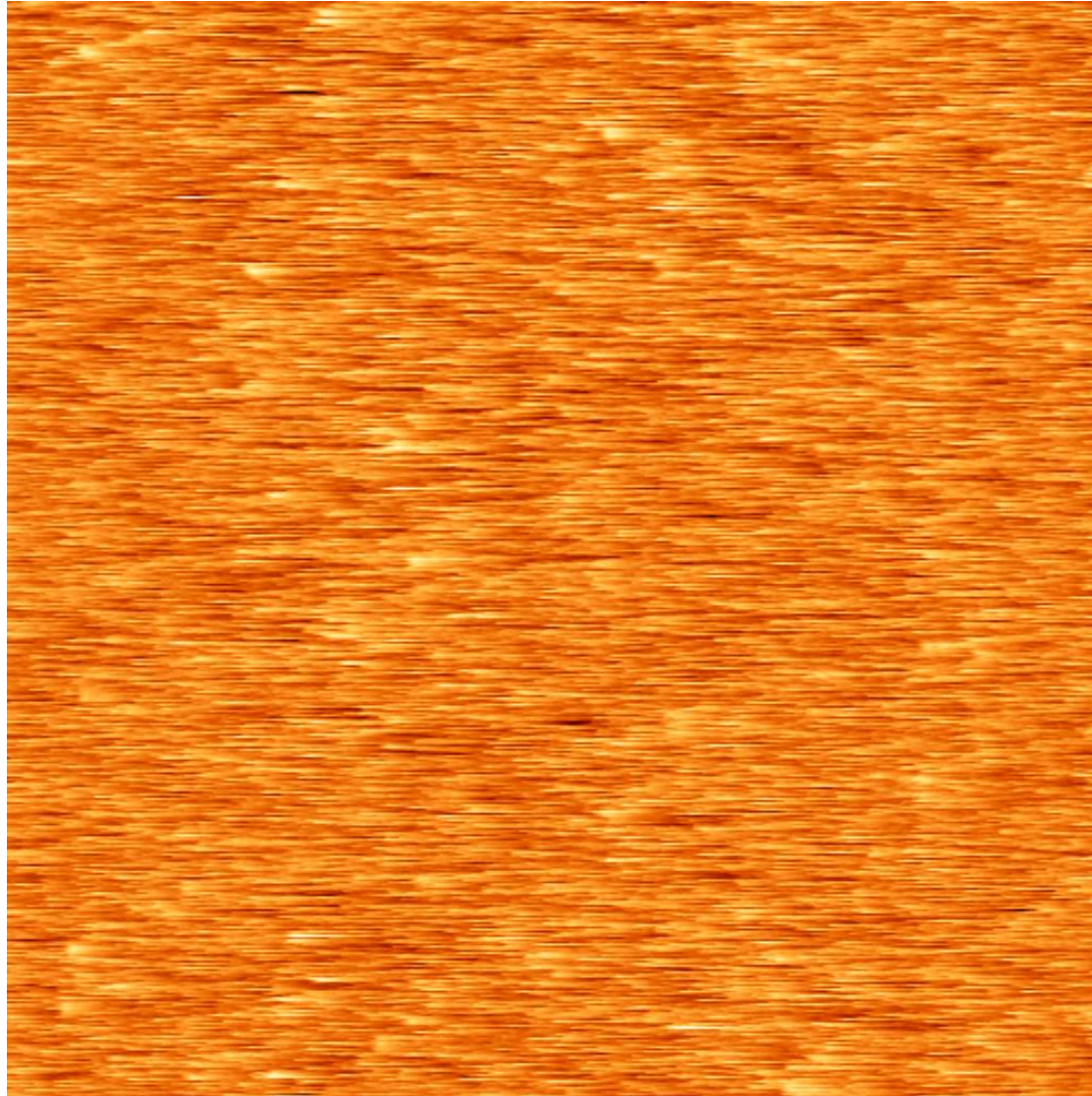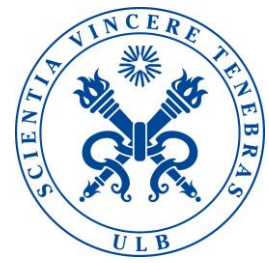Universite Libre de Bruxelles

Example of direct observation of crystal nucleation

M. Sleutel, JFL, A. E. S. Van Driessche, M. A. Durán-Olivencia, and D. Maes. *Observing classical nucleation theory at work by monitoring phase transitions with molecular precision*. Nature Communications, 5:5598, 2014.

Example of direct observation of nucleation

M. Sleutel, JFL, A. E. S. Van Driessche, M. A. Durán-Olivencia, and D. Maes. *Observing classical nucleation theory at work by monitoring phase transitions with molecular precision*. Nature Communications, 5:5598, 2014.

Crystallization is a hot topic ...Why?

Lots of applications

Crystallization

- … occurs throughout physics: snow flakes, the interior of white dwarfs, dirty plasmas, colloids, determination of the structure of molecules;

- … is of importance in human health: e.g. it plays a role in several pathologies such as malaria and of amyloid aggregation leading to Alzheimer's;

- … is important in chemistry and materials science as a means of purification from solution;

- … is critical in the production of pharmaceuticals where polymorphism is a pressing issue;

Why is this problem hard?

Nucleation begins with the formation of a critical cluster which often consists of only 10's or 100's of molecules ➜ *small objects*

Nucleation is a rare event: protein nucleation experiments often take day or even weeks before a single crystallite is formed ➜ *mixed time scale*

And all of this happens somewhere in a macroscopic, 3D volume ➜ *mixed length scales*

Historically, experiment➜ indirect methods (e.g. light-scattering)

Historically, simulations ➜ small volumes, small time scales

… until …

The development of rare event simulation techniques beginning in the 1980's

Development of new nanoscale observational techniques (AFM, cryo-TEM)

The overwhelming interest in protein nucleation

Nucleation *Precursors*

Experiments and simulations have shown that crystal formation is not as straightforward as once imagined but the details are elusive.

Theory has not kept pace so the process remains poorly understood.
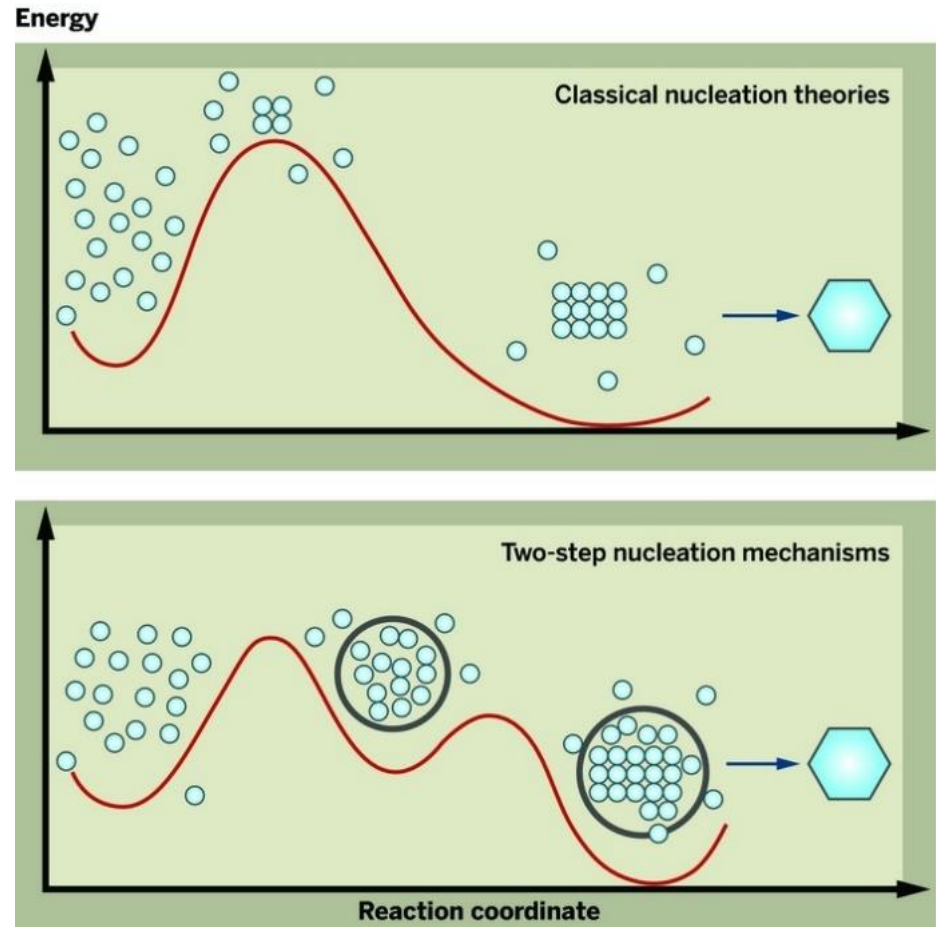
Credit: J. kemsley, Chem. & Eng. News, 93, 28 (2015).

Why nucleation?

Nucleation occurs when there is an extensive free energy barrier between the *homogeneous* states:
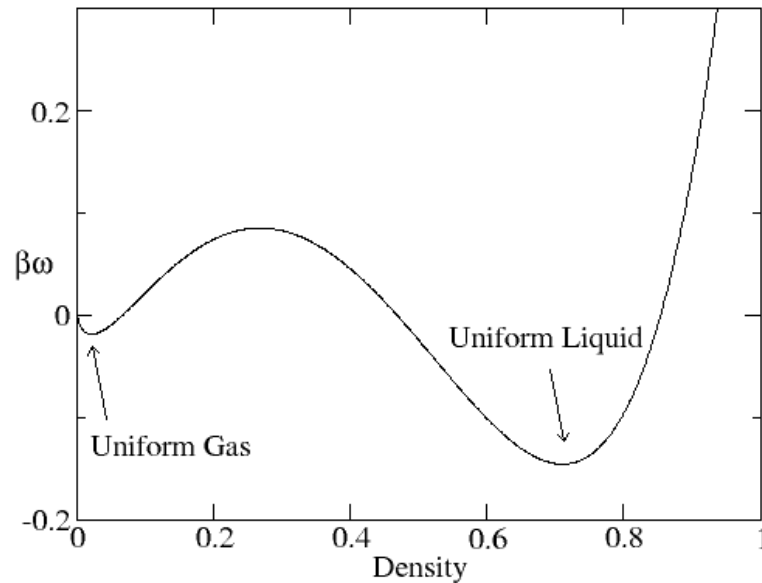
Uniform transition of the entire system requires macroscopic amounts of energy and is effectively impossible. So the only means is a nonuniform, local transition.

Classical Nucleation Theory: 1. Energetics

Local change of phase:
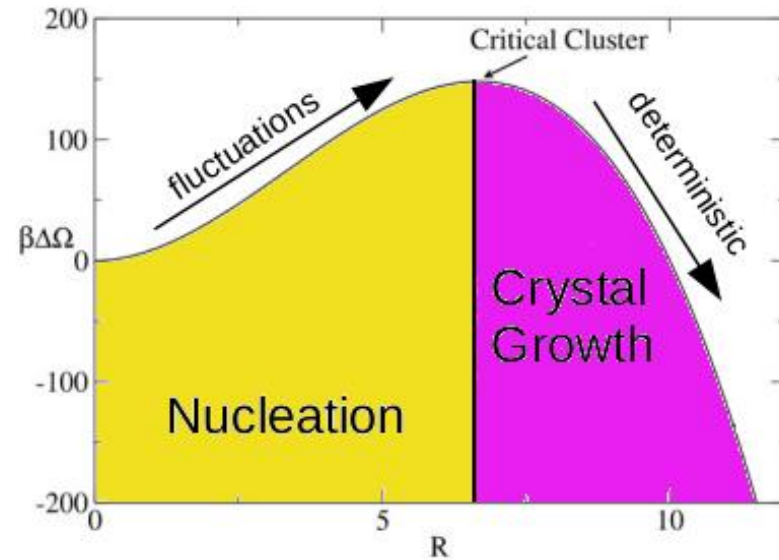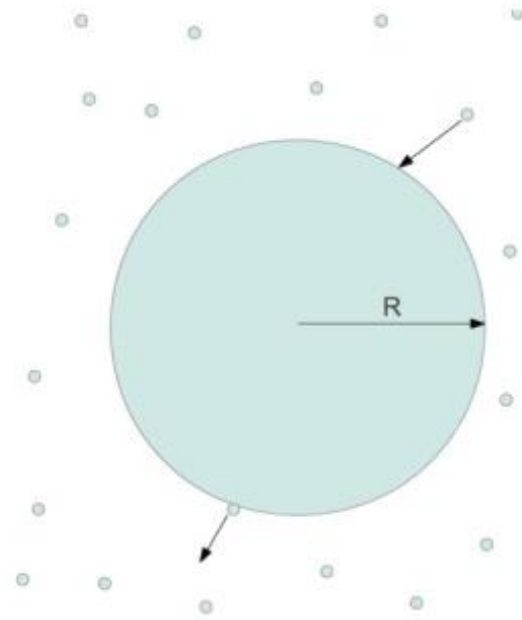
Free energy of cluster: $\Delta\Omega = \Delta\omega V(R) + \gamma S(R)$
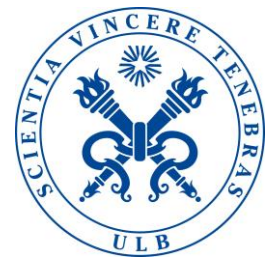
Classical Nucleation Theory: 2. Dynamics
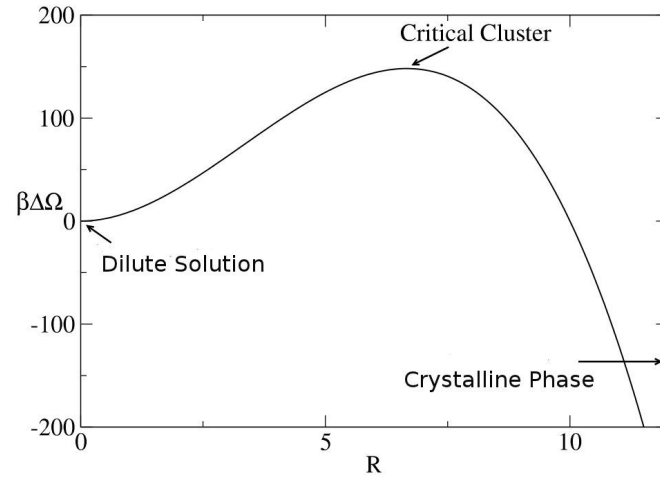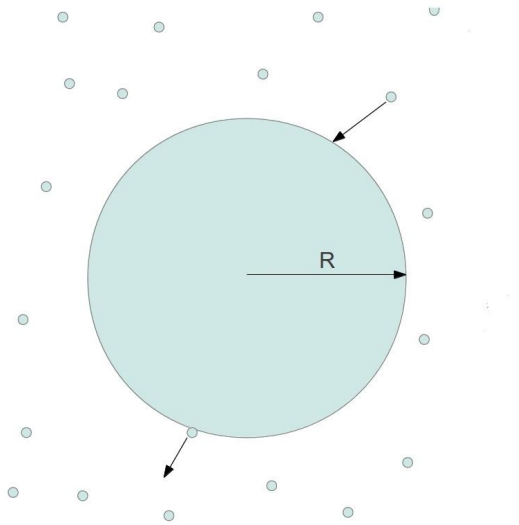
$c_t(n)$ = number of clusters of n molecules (per unit volume) at time t

$$\frac{dc_t(n)}{dt} = \frac{\partial}{\partial n}\left(-f(n)\frac{\partial \beta \Delta \Omega(n)}{\partial n} + f(n)\frac{\partial}{\partial n}\right)c_t(n,t)$$

$f(n)$ = attachment rate

$$J \approx c_1 f(n_c)\sqrt{\frac{1}{2\pi}}\sqrt{|\Delta \beta \Omega''(n_c)|}exp\big(-\Delta \beta \Omega(n_c)\big)$$

Beyond the classical paradigm

CNT is heuristic and was never intended to describe anything except the simplest liquid-vapour nucleation:

Real clusters are not homogeneous and do not have sharp interfaces

Without sharp interfaces, how can one speak of attachment and detachment?

What about multiple order parameters? What replaces the rate dynamics?

Even in liquid-vapour nucleation, what justifies treating bulk transport and cluster growth separately?

The goal of Mesoscopic Nucleation Theory (MNT) is to:

- Treat structure and energetics realistically
- Treat dynamics and fluctuations consistently

classical DFT

Formal structure

Local density $\rho(\mathbf{r})$ (ensemble-averaged but *not* coarse-grained)

External field $\phi(\mathbf{r})$ (walls, electric field, gravity, …)

A functional: $\Lambda[\rho, \phi] = F[\rho] + \displaystyle\int \rho(\mathbf{r})\phi(\mathbf{r})d\mathbf{r}$ (from models: exactly known in a few case

Classic theorems (Hohenberg-Kohn, Mermin) assure us that minimizing wrt density gives equilibrium density and (grand-canonical) free energy

$$\Lambda[\rho] \geq \Lambda[\rho_{equil}] = \Omega$$

Examples:

Ideal gas (exact): $F_{ideal}[\rho] = \displaystyle\int \left(\rho(\mathbf{r})\ln\rho(\mathbf{r}) - \rho(\mathbf{r}) \right) d\mathbf{r}$

Van der Waals: $F_{vdW}[\rho] = \displaystyle\int \left(f(\rho(\mathbf{r})) + K(\nabla\rho(\mathbf{r}))^2 \right) d\mathbf{r}$

Landau, Cahn-Hillard, …

JFL, Adv. Chem. Phys. 144, 1 (2010).

classical DFT
Exact result: hard rods

$$F\left[\rho\right] = \int_{-\infty}^{\infty} \rho_x \left(\ln \rho_x - 1\right) dx - \int_{-\infty}^{\infty} s_x \left[\rho\right] \ln \left(1 - \eta_x \left[\rho\right]\right) dx$$

$$\eta_x \left[\rho\right] = 1 - \int_{x-\frac{\sigma}{2}}^{x+\frac{\sigma}{2}} \rho_y dy$$

$$s_x \left[\rho\right] = \frac{1}{2} \left(\rho_{x-\frac{\sigma}{2}} + \rho_{x+\frac{\sigma}{2}}\right)$$

Percus, J. Stat. Phys. 15, 505–511 (1976).

classical DFT
Fundamental Measure Theory

Helmholtz functional:

$$F_{HS}[\rho; d] = F^{id}[\rho; d] + F_{HS}^{ex}[\rho; d]$$

FMT excess functional:

$$F_{HS}^{FMT}[\rho; d] = \int \left(\frac{1}{\pi d^2} \Phi_1(\mathbf{r}) + \frac{1}{2\pi d} \Phi_2(\mathbf{r}) + \frac{1}{24\pi} \Phi_3(\mathbf{r}) \right) d\mathbf{r}$$

with
$$\Phi_1(\mathbf{r}) = -s(\mathbf{r})\ln(1 - \eta(\mathbf{r})) \qquad \Phi_2(\mathbf{r}) = \frac{s^2(\mathbf{r}) - v^2(\mathbf{r})}{(1 - \eta(\mathbf{r}))} \qquad \Phi_3(\mathbf{r}) = ???$$

Where the fundamental measures are:

$$\eta(\mathbf{r}_1) = \int \Theta\left(\frac{d}{2} - r_{12}\right) \rho(\mathbf{r}_2) d\mathbf{r}_2$$

$$\begin{Bmatrix} s(\mathbf{r}_1) \\ \mathbf{v}(\mathbf{r}_1) \\ \mathbf{T}(\mathbf{r}_1) \end{Bmatrix} = \int \delta\left(\frac{d}{2} - r_{12}\right) \begin{Bmatrix} 1 \\ \hat{\mathbf{r}}_{12} \\ \hat{\mathbf{r}}_{12}\hat{\mathbf{r}}_{12} \end{Bmatrix} \rho(\mathbf{r}_2) d\mathbf{r}_2$$

"volume measure"

"surface measures"
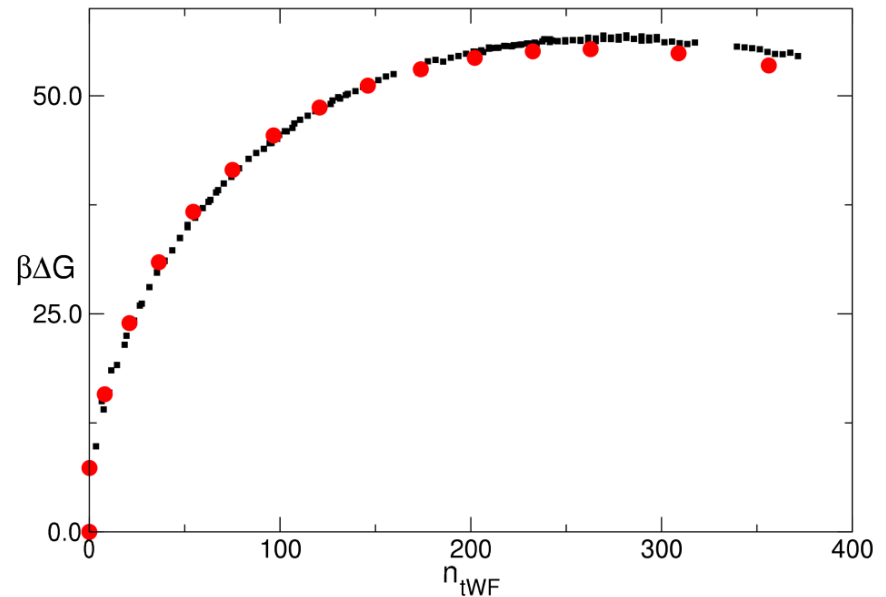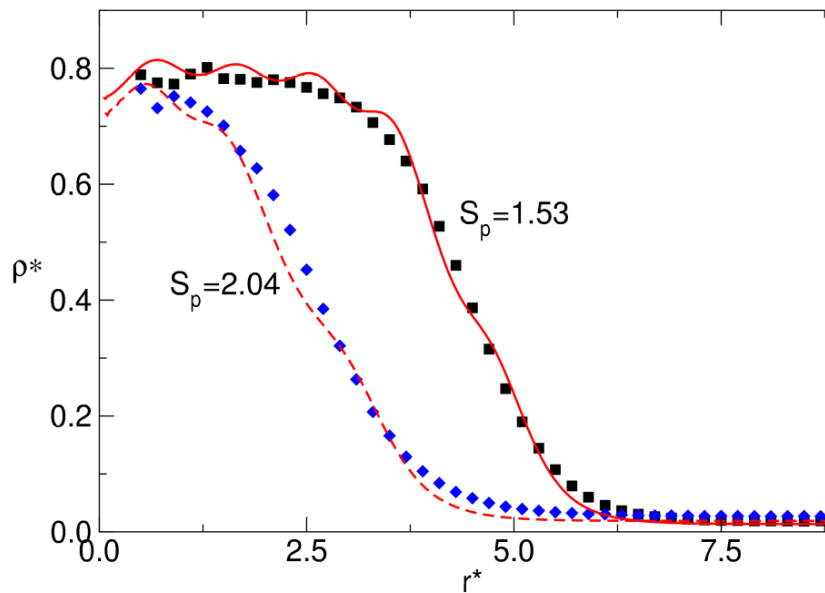
Simulation data: P. ten Wolde and Daan Frenkel, J. Chem. Phys. 109, 9901 (1998).

Calculations: JFL, J. Chem. Phys. 129, 244501 (2008).

Interregnum:

The tools of cDFT are developed in the grand canonical ensemble (open system, number of particles can change). Useful for nucleation because of large density changes (e.g. vapor to solid).

In the open system, the critical cluster is a saddle point ➔ minimizing at constant chemical potential is hard.

However, it is easy to prove that minimizing at fixed particle number ("canonical ensemble", but not really) gives exactly the same density field and in this case, the gce saddle point becomes a minimum.
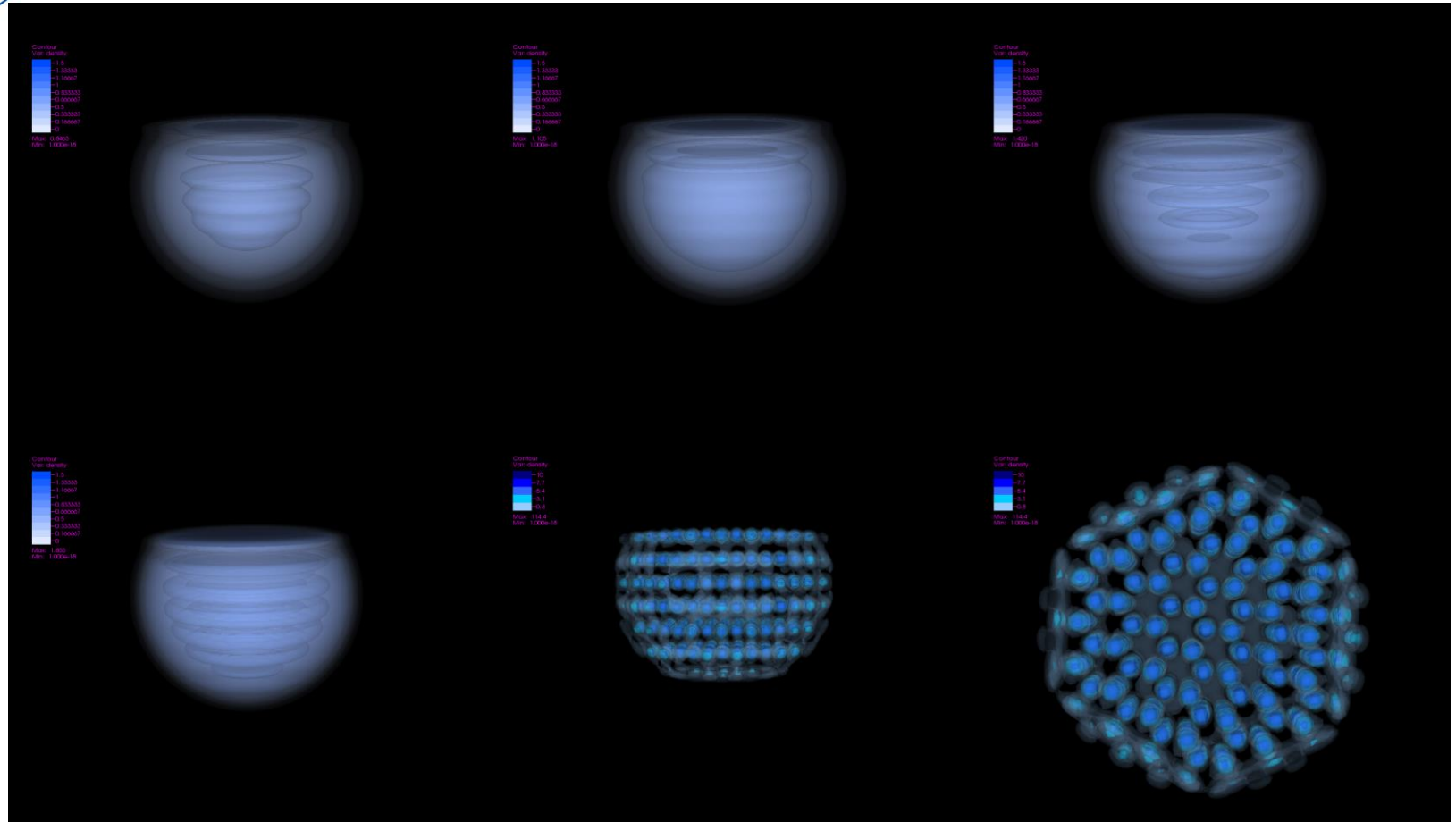
This **"Grand canonical/canonical duality"** is a useful tool
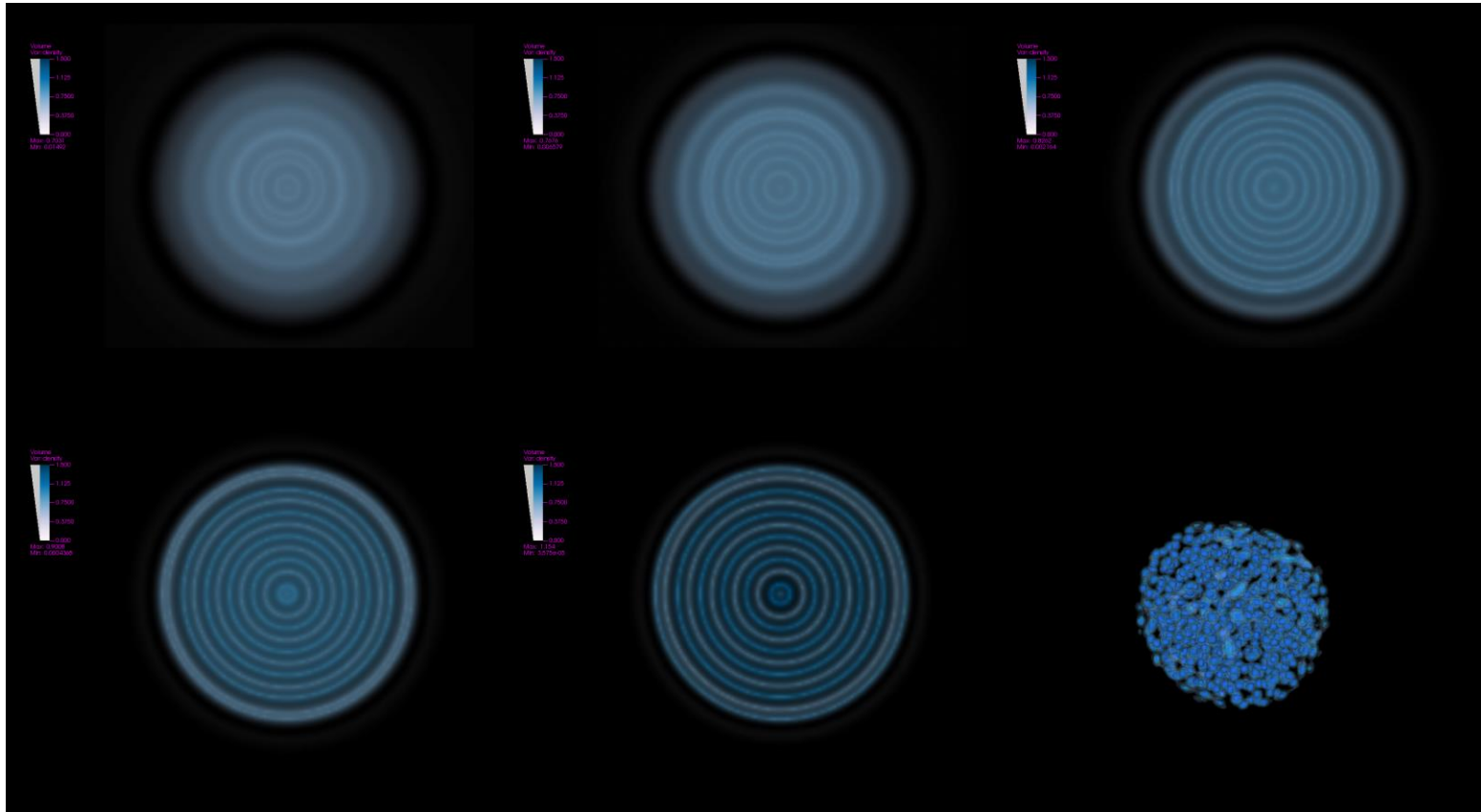
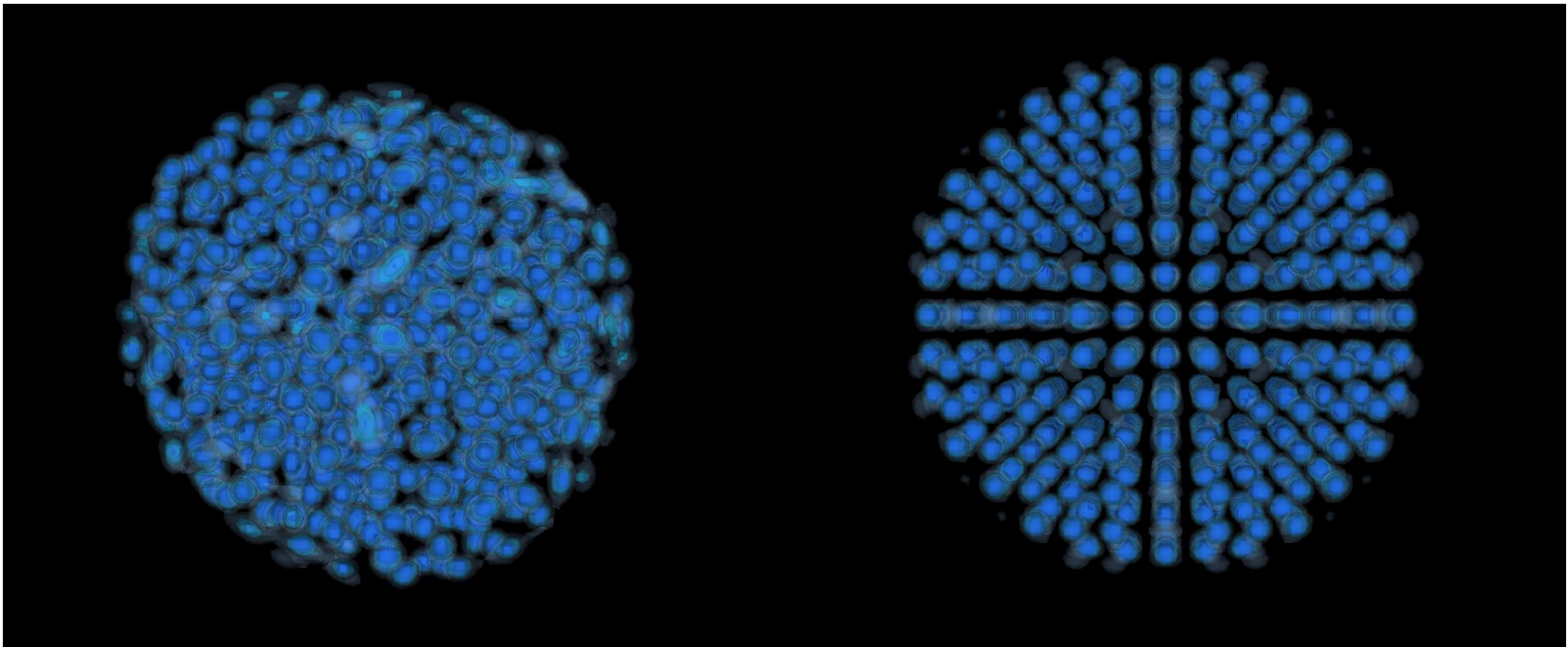# Mesoscopic Nucleation Theory:
1. Energetics and structure: cDFT

JFL and Julien Lam, Phys. Rev. E 98, 12604 (2018).

Mesoscopic Nucleation Theory:
1. Energetics and structure: cDFT

Amorphous and crystalline clusters

Free energy surfaces are not enough!

Gradient descent (« steepest descent », « minimum energy pathway ») is often used to « identify » nucleation pathways (and, in other contexts, chemical reaction pathways)

Gradient descent:
- Choose a starting point, x.
- Draw a circle (with some small radius) around x
- Calculate energy at each point on the circle
- Move to the point with the lowest energy

Problem: to draw a circle, we need a metric and where does this come from?

Naive solution: solve $\dfrac{dx^i}{dt} = -\dfrac{\partial F(x)}{\partial x^i}$

... or $\dfrac{dy^i}{dt} = -\dfrac{\partial F\big(x(y)\big)}{\partial y^i}$?   ... So this is just a way to hide the ambuguity

Free energy surfaces are not enough!

Gradient descent (« steepest descent », « minimum energy pathway ») is often used to « identify » nucleation pathways (and, in other contexts, chemical reaction pathways)

Gradient descent:
- Choose a starting point, x.
- Draw a circle (with some small radius) around x
- Calculate energy at each point on the circle
- Move to the point with the lowest energy

Problem: to draw a circle, we need a metric and where does this come from?

Solution: some additional physics is needed ... problem-specific dynamics.

Mesoscopic Nucleation Theory:
2. Dynamics

Specialized to: large molecules or colloidal particles moving in a fluid of small molecules (Brownian dynamics, over-damped limit).

Continuity equation (conservation of mass)

$$\frac{\partial \rho(\mathbf{r}, t)}{\partial t} + \nabla \cdot j(\mathbf{r}, t) = 0 \qquad \text{where} \qquad j = \rho v$$

Momentum equation

$$\frac{\partial j}{\partial t} + \nabla \cdot \frac{jj}{\rho} + \nabla p + \nabla \cdot \Pi = -\gamma j + \sqrt{2\gamma k_B T \rho}\ \xi_t$$

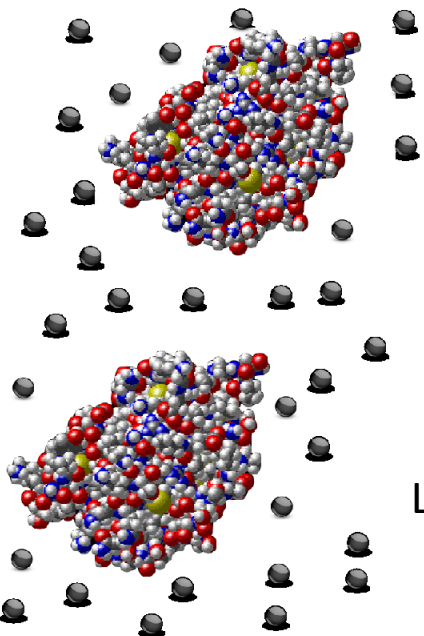convective   pressure   Dissipitive stress   friction   White noise

Gibbs-Duhem relation

$$dp(\mathbf{r}, t) = \rho(\mathbf{r}, t) d\mu(\mathbf{r}; t) = \rho(\mathbf{r}, t) d \frac{\delta F[\rho]}{\delta \rho(\mathbf{r}, t)}$$

JFL, J. Chem. Phys. 135, 161101 (2011); 136, 34509 (2012)

Over-damped limit:

$$\frac{\partial \rho(\mathbf{r},t)}{\partial t} = \underbrace{\gamma k_B T \nabla \cdot \rho(\mathbf{r},t) \nabla \frac{\delta \beta F}{\delta \rho(\mathbf{r},t)}}_{\text{deterministic}} - \underbrace{\nabla \cdot \sqrt{2\gamma k_B T \rho(\mathbf{r},t)} \xi(\mathbf{r},t)}_{\text{fluctuating}}$$
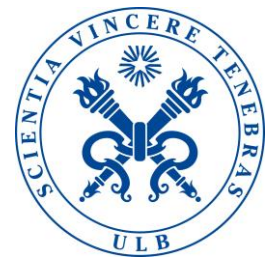
$F[\rho]$ Microscopic DFT model

"Dean-Kawasaki model"

Low density (ideal gas) limit: $$F_{ideal}[\rho] = \int \big(\rho(\mathbf{r}) \ln \rho(\mathbf{r}) - \rho(\mathbf{r})\big) d\mathbf{r}$$

$$\frac{\partial \rho(\mathbf{r},t)}{\partial t} = \gamma k_B T \nabla^2 \rho(\mathbf{r},t) - \nabla \cdot \sqrt{2D\rho(\mathbf{r},t)} \xi(\mathbf{r},t)$$

Coeff of (tracer) diffusion $\gamma k_B T = D$

Mesoscopic Nucleation Theory:
2. Dynamics

$$\frac{\partial \rho(\mathbf{r},t)}{\partial t} = \underbrace{D\nabla \cdot \rho(\mathbf{r},t)\nabla \frac{\delta \beta F}{\delta \rho(\mathbf{r},t)}}_{\text{deterministic}} - \underbrace{\nabla \cdot \sqrt{2D\rho(\mathbf{r},t)}\xi(\mathbf{r},t)}_{\text{fluctuating}}$$

Discretized equation:

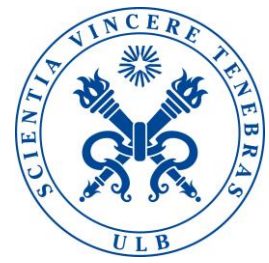$$\rho(\mathbf{r},t) \rightarrow \rho(I,t) \rightarrow x_t^I$$

$$D\nabla \cdot \rho(\mathbf{r}) \rightarrow g^{IJ}(x) \qquad \nabla \cdot \sqrt{2D\rho(\mathbf{r})} \rightarrow q_a^I(x)$$

$$\frac{\delta \beta F}{\delta \rho(\mathbf{r})} \rightarrow \frac{\partial F(x)}{\partial x^J}$$

$$\frac{dx^i}{dt} = -g^{ij}(x)\frac{\partial F(x)}{\partial x^j} + 2\epsilon q_a^i(x)\xi^a(t), \qquad g^{ij}(x) = q_a^i(x)q_a^j(x)$$

Mesoscopic Nucleation Theory:
2. Dynamics

$$\frac{dx^i}{dt} = -g^{ij}(x)\frac{\partial F(x)}{\partial x^j} + 2\epsilon q_a^i(x)\xi^a(t), g^{ij}(x) = q_a^i(x)q_a^j(x)$$

For nucleation, we want to know how a system that begins in one homogeneous state,   ,
transforms into a final inhomogeneous state, $\rho_A(r)$, which has a critical cluster. $\rho_B(r)$

For diffusive, stochastic processes, the probability that the system follows a particular pathway
x(t) from the initial state x(0)=x$_A$ to the final state x(T)=x$_B$ is known **exactly** and can be
expressed in the form

$$P(x) = N \times exp\left(-\frac{1}{2}\epsilon^{-2}\int_0^T L\,[x_t]dt\right)$$

In the weak noise limit, the Lagrangian is simply

$$L[x] = \left(\frac{dx^i}{dt} + g^{ij}\frac{\partial F}{\partial x^j}\right)g_{jk}\left(\frac{dx^k}{dt} + g^{kl}\frac{\partial F}{\partial x^l}\right)$$

This is equivalent to the Freidlin-Wentzell-Graham theory of large deviations

Mesoscopic Nucleation Theory:
2. Dynamics

$$\frac{dx^i}{dt} = -g^{ij}(x)\frac{\partial F(x)}{\partial x^j} + 2\epsilon q_a^i(x)\xi^a(t), \, g^{ij}(x) = q_a^i(x)q_a^j(x)$$

In the weak noise limit, here is a simple fluctuation theorem concerning going from a metastable basin to a saddle point:

$$\frac{P[x_t]}{P[x_{-t}]} = exp\left(-\beta\big(F(x^*) - F(x_A)\big)\right)$$
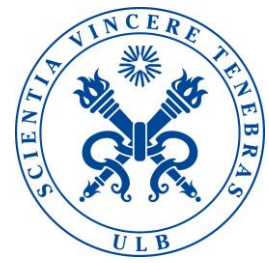
Using this, it is easy to show that the most likely path (MLP) passes through the critical cluster and is determined by solving

$$\frac{dx^i}{dt} = \pm g^{ij}(x)\frac{\partial F(x)}{\partial x^j}$$

i.e. by gradient descent with a metric, g , **dictated by the dynamics**

- Gradient descent is not exact (weak noise limit)
- In general, metric is far from Euclidean:

$$g_{r_1 r_2}[\rho] = \left(\nabla_1\rho(\boldsymbol{r_1})\nabla_1\delta(\boldsymbol{r_1} - \boldsymbol{r_2})\right)^{-1}$$

Bridging length scales: Order Parameters

Reduced description in terms of one or more order parameters

$$\rho(r,t) = \rho\big(r; x^1(t), x^2(t), \dots\big) = \rho\big(r; \mathbf{x}(t)\big)$$

$$\frac{dx^i}{dt} = -D \sum_j g^{ij}\big(\mathbf{x}(t)\big) \frac{\partial \beta F\big(\mathbf{x}(t)\big)}{\partial x^j(t)} + \frac{1}{\sqrt{detg}} \frac{\partial g^{ij}\sqrt{detg}}{\partial x^j} + \sqrt{2D} \sum_a \underbrace{q^{ia}\big(\mathbf{x}(t)\big)}_{\mathbf{qq=g}} \underbrace{\xi_a(t)}_{white\ noise}$$

"Kinetic coefficients"

State-dependent noise
(Stratonovich interpretation)

with $\qquad F[\rho] \to F(\mathbf{x}) \qquad\qquad m(r; \mathrm{x}) = \int_0^r 4\,\pi r'^2 \rho(r'; \mathbf{x})dr'$

$$g_{ij}(\mathbf{x}) = \int \frac{1}{4\pi r^2 \rho(r; \mathbf{x})} \frac{\partial m(r; \mathbf{x})}{\partial x^i} \frac{\partial m(r; \mathbf{x})}{\partial x^j} dr \qquad\qquad g^{ij}g_{jk} = \delta_k^i$$

$\rho(r; R) = \rho_0 + (\rho_1 - \rho_0)\Theta(R - r)$ ➜ reproduces CNT
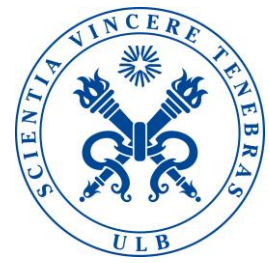
Spherical Symmetry

If the mass within a ball of radius R is

$$m(R) = \int \Theta(R - r)\rho(\boldsymbol{r})d\boldsymbol{r}$$

Then one can show that

$$\frac{\partial m_t(R)}{\partial t} = -D\frac{\partial m_t(R)}{\partial R}\frac{\delta\beta F[\rho_t]}{\delta m_t(R)} - \sqrt{2D\frac{\partial m_t(R)}{\partial R}}\xi_t(R)$$

The exact expression for distance in density-space can be shown to be

$$d[\rho_1, \rho_2] = \sqrt{\int \left(R(m; [\rho_1]) - R(m; [\rho_2])\right)^2 dm}$$

with

$$m(R; [\rho]) \Leftrightarrow R(m; [\rho])$$

and not the Euclidean

$$d[\rho_1, \rho_2] = \sqrt{\int_0^\infty \left(\rho_1(r) - \rho_2(r)\right)^2 4\pi r^2 dr}$$

Note: changing variables from *m(R)* to *R(m)* gives a SDE with state independent noise ...

Results

LJ pair potential

$$v_{\mathsf{LJ}}(r) = \left(v_{\mathsf{LJ}}(r) - v_{\mathsf{min}}\right)\Theta\left(r_{\mathsf{min}} - r\right) + w_{\mathsf{att}}(r)$$

Effective HS radius

$$d = \int e^{-\beta v(r)}\, dr$$

vDW DFT model

$$F[\rho] = F_{FMT}[\rho] + \int \rho\left(\boldsymbol{r_1}\right)\rho\left(\boldsymbol{r_2}\right)w_{\mathsf{att}}(r_{12})d\boldsymbol{r_1}d\boldsymbol{r_2}$$
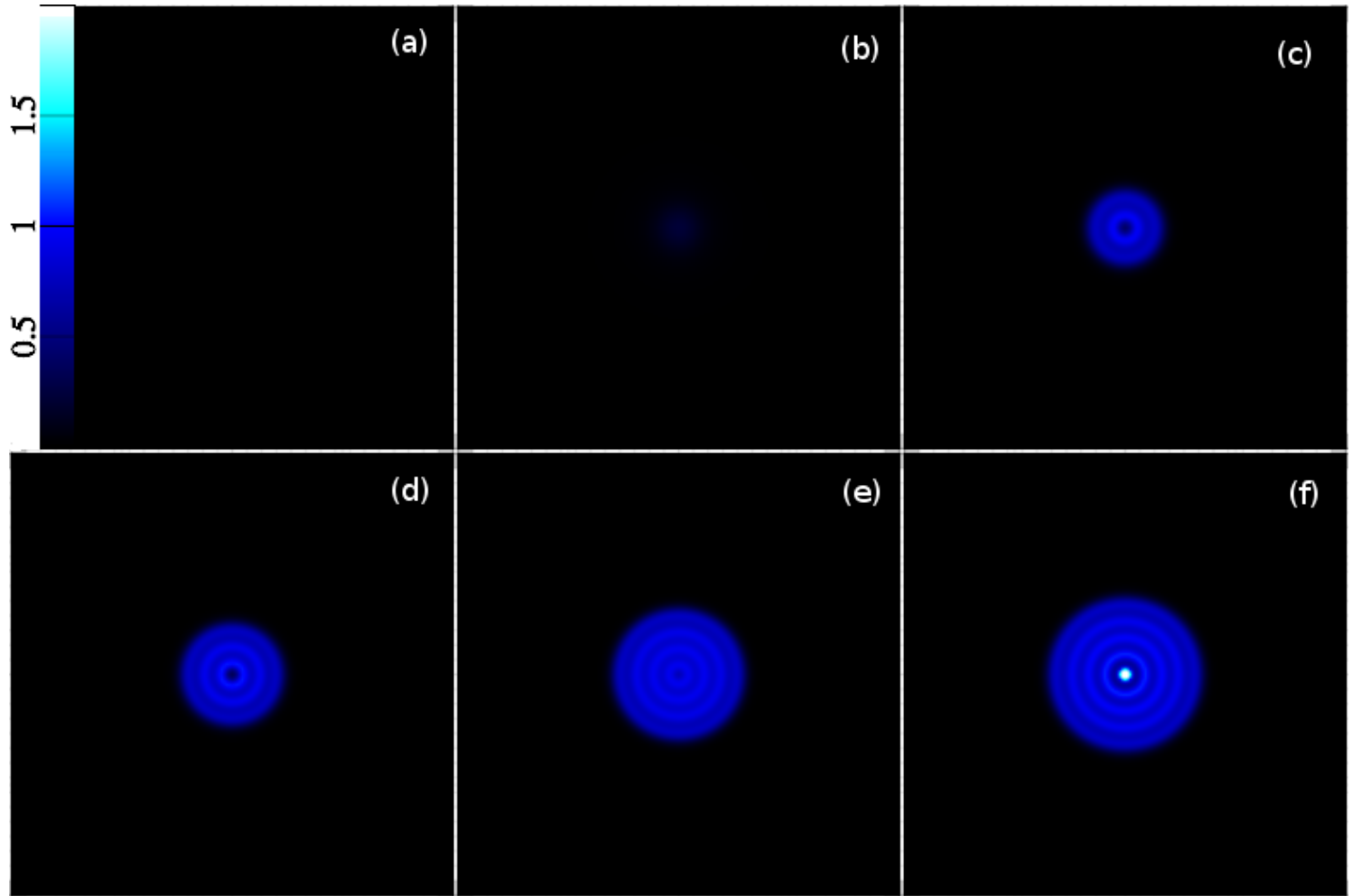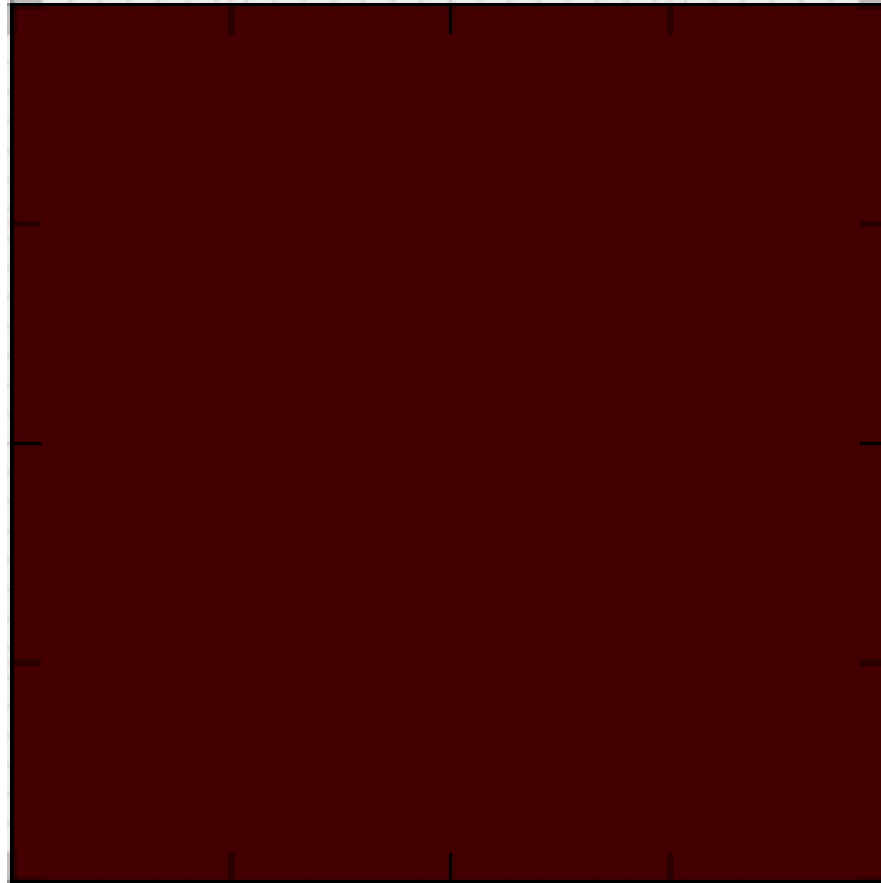
Liquid-vapor nucleation
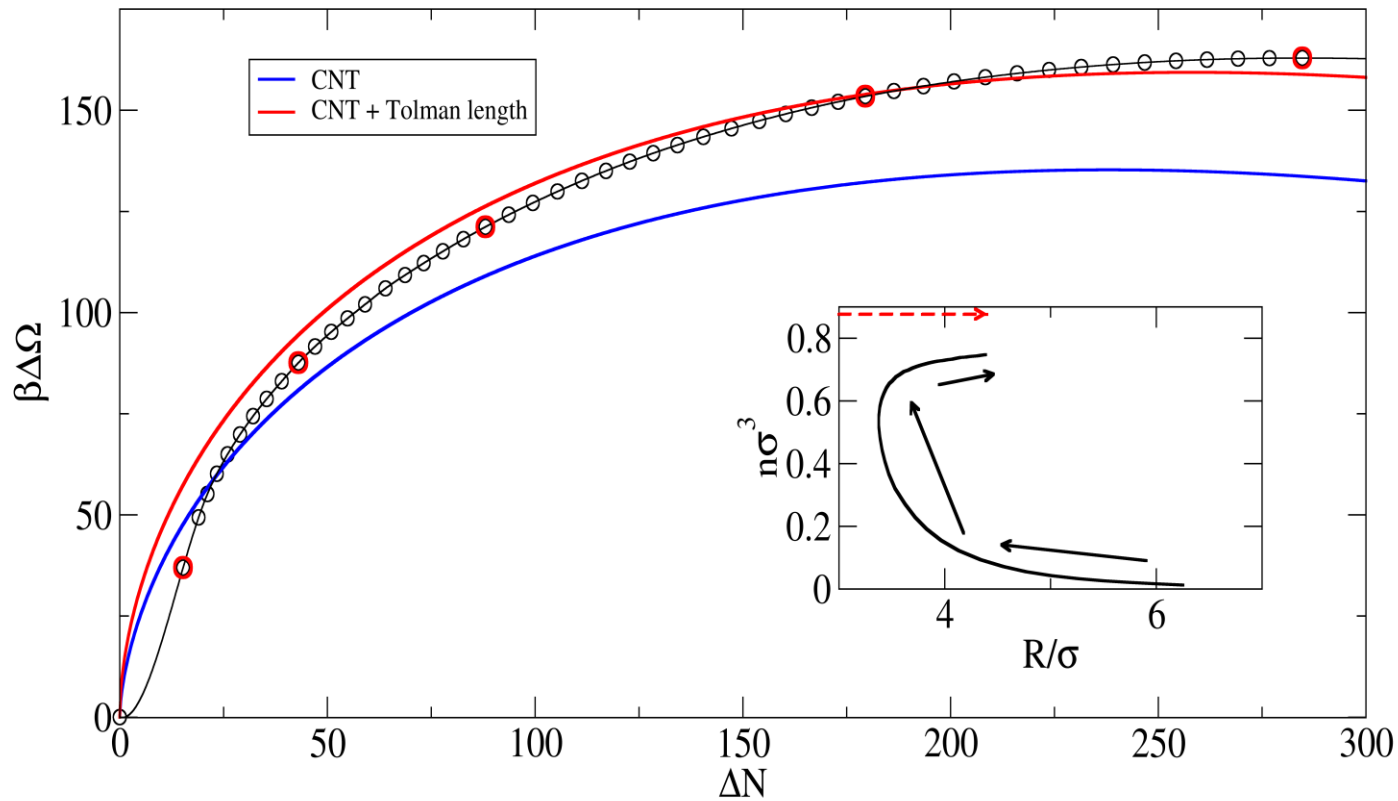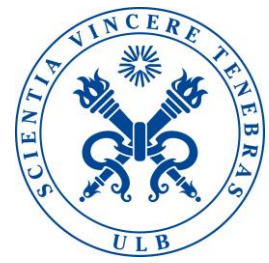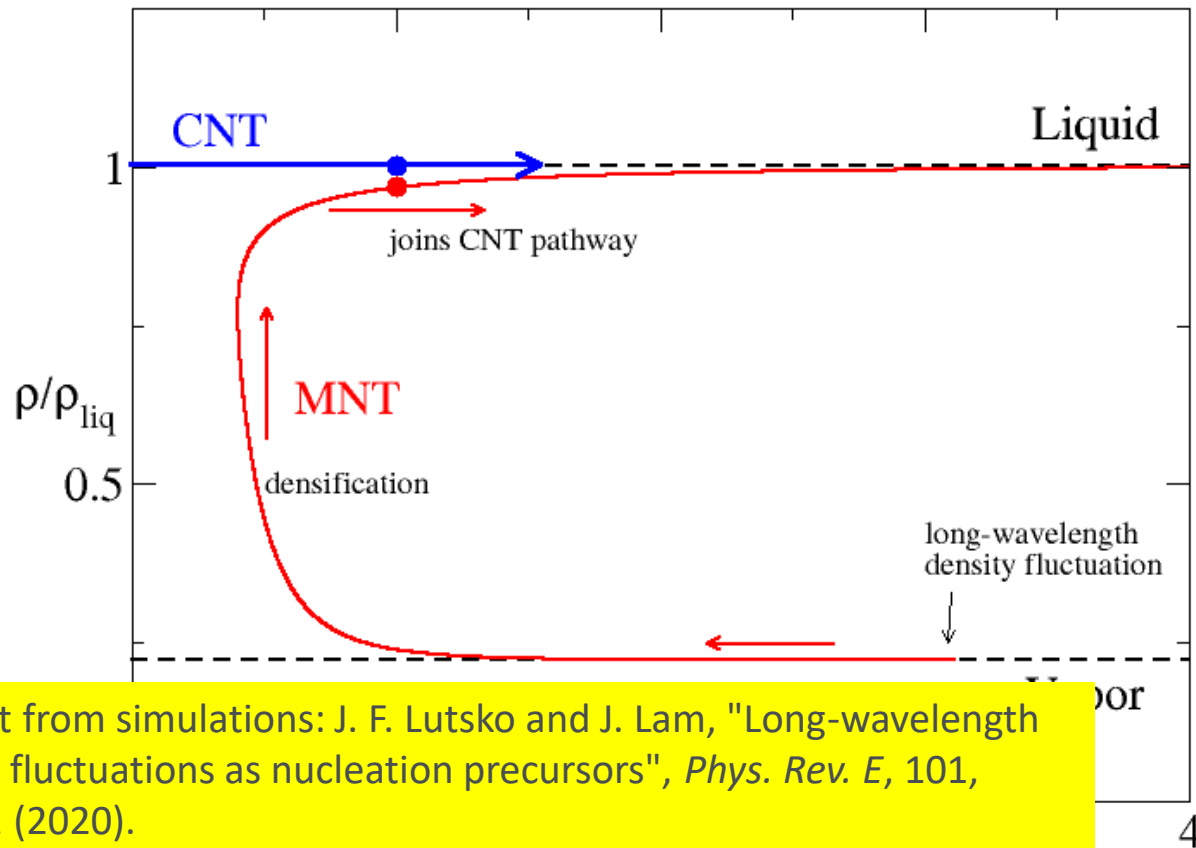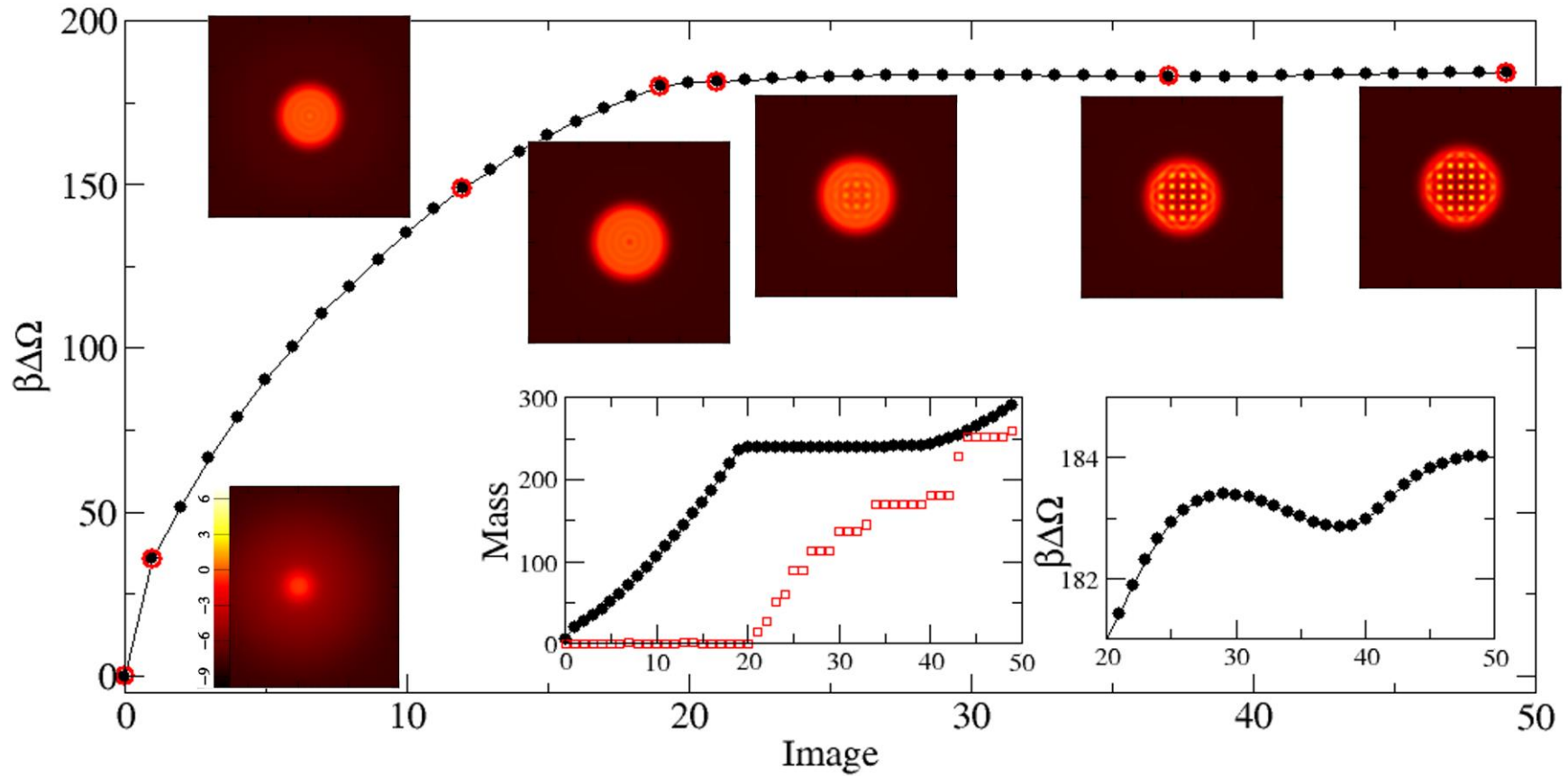
Liquid-vapor nucleation
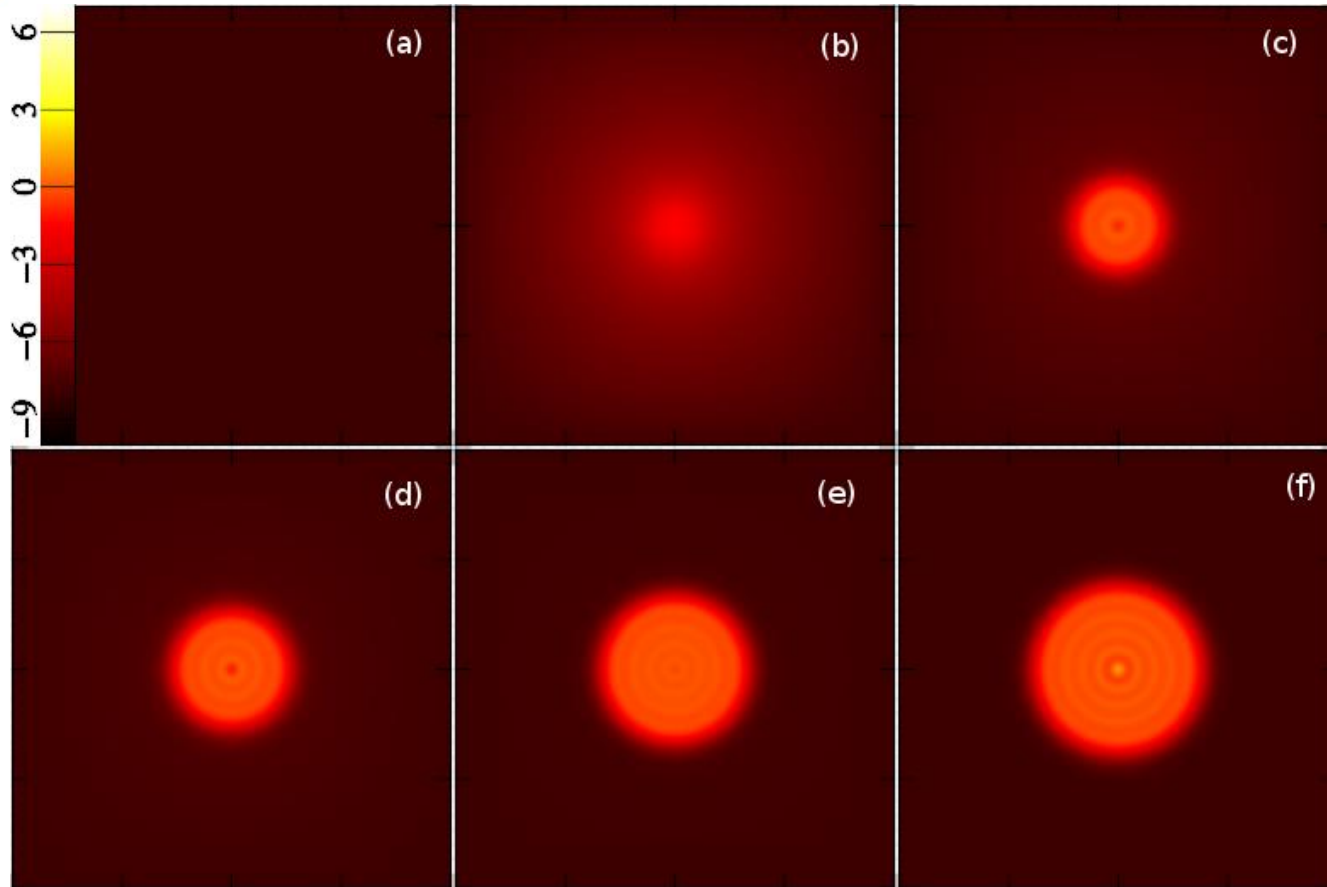
Liquid-vapor nucleation

Liquid-vapor nucleation

Image = 0 Omega = -5.28 N = 5.30

A Microscopic Theory of Crystallization
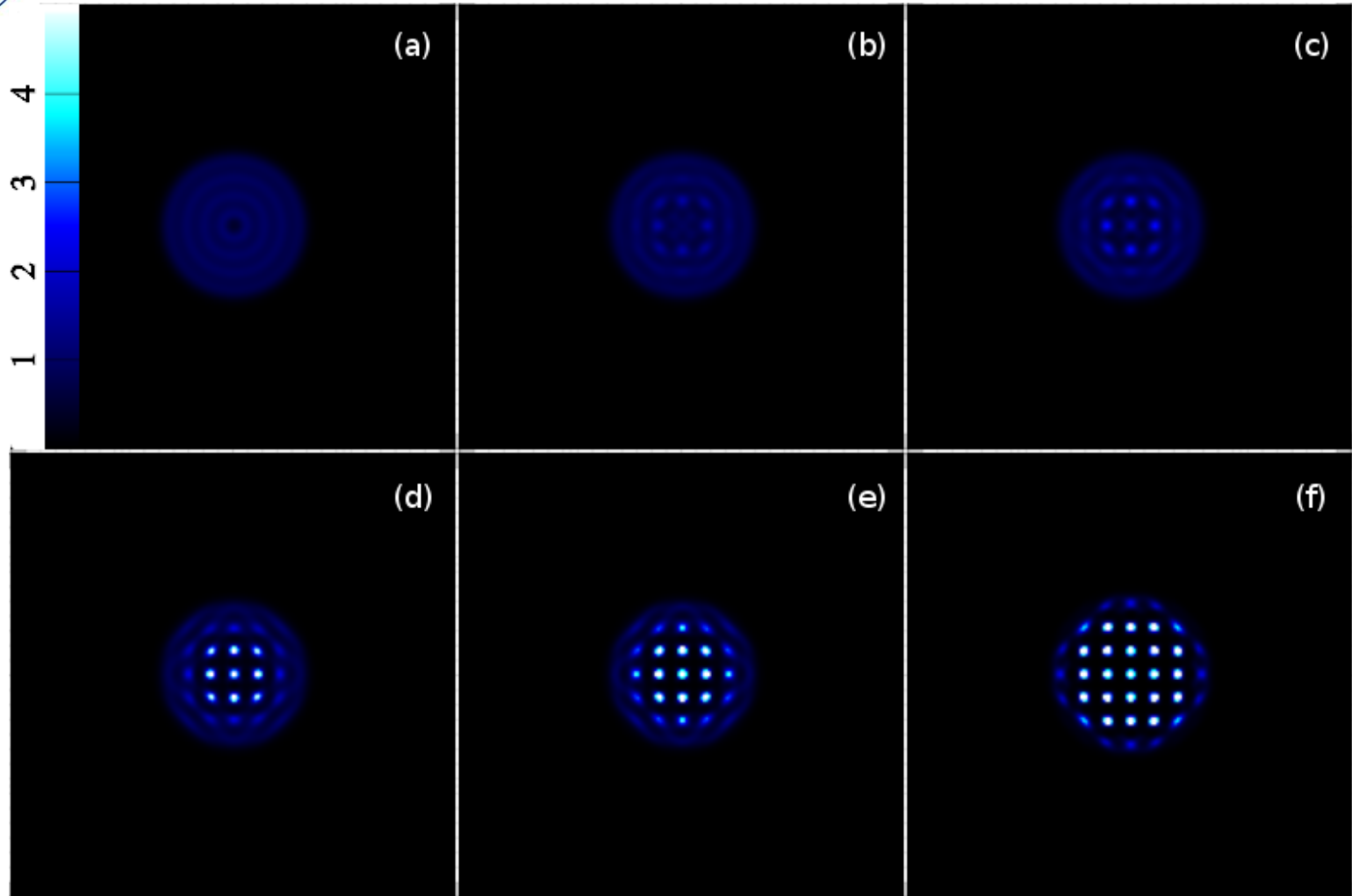
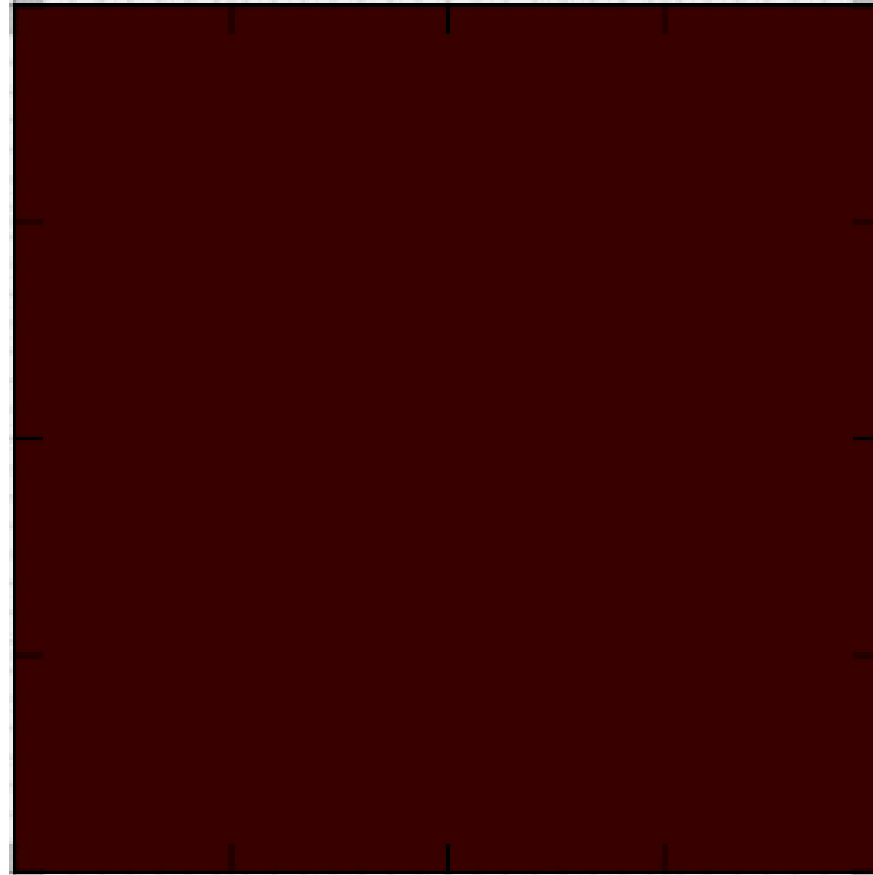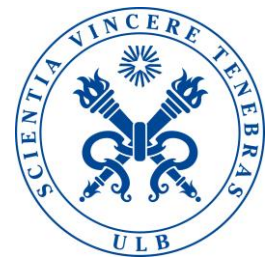# A Microscopic Theory of Crystallization

Image = 0 Omega = -4.85 N = 4.87

Remarks

- Classical Nucleation Theory can be derived from this framework.

- The dynamics could be extended to inertial systems (e.g. hydrodynamics rather than diffusive dynamics.

- The metric is not a meaningless technicality: in spherically symmetric systems, the Euclidean distance between two density fields:

$$d[\rho_1, \rho_2] = \sqrt{\int_0^\infty \left(\rho_1(r) - \rho_2(r)\right)^2 4\pi r^2 dr}$$

is incorrect. The one dictated by the dynamics can be worked out explicitly:

$$m(R; [\rho]) = \int \Theta\,(R - r)\rho(r)4\pi r^2 dr \qquad m(R; [\rho]) \Leftrightarrow R(m; [\rho])$$

$$d[\rho_1, \rho_2] = \sqrt{\int \left(R(m; [\rho_1]) - R(m; [\rho_2])\right)^2 dm}$$

so in terms of this variable, the sde has state independent noise …

References

JFL, "How crystals form: A theory of nucleation pathways", Science Advances, 5, eaav7399 (2019)

JFL and Julien Lam, "Classical density functional theory, unconstrained crystallization, and polymorphic behavior", Phys. Rev. E, 98, 12604 (2018)

JFL, "Systematically extending classical nucleation theory", New Journal of Physics, 20, 103015 (2018)

JFL and Miguel A. Durán-Olivencia, "A Two-parameter Extension of Classical Nucleation Theory", J. Phys. Cond. Matt., 27, 235101 (2015)

JFL, "Nucleation of colloids and macromolecules in a finite volume", J. of Chemical Physics, 137, 154903 (2012)

JFL, "A dynamical theory of nucleation for colloids and macromolecules", J. of Chemical Physics, 136, 34509 (2012)