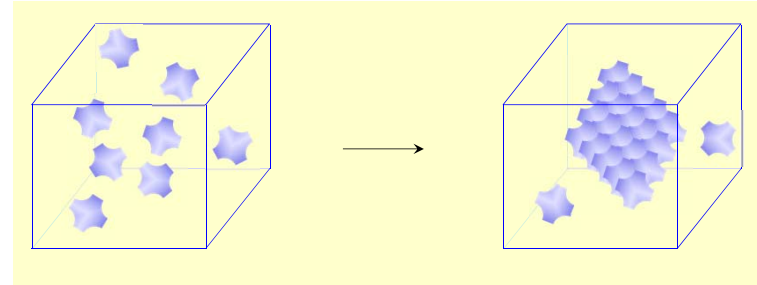


Classical and Non-classical Nucleation Mechanisms

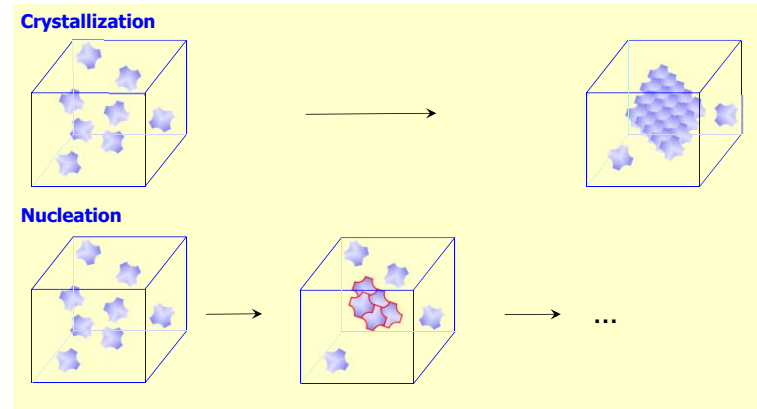
Peter Vekilov
University of Houston



Crystallization is a Miracle!



Crystallization and Nucleation



**Nucleation
Kinetics
Is Different**



Josiah Willard Gibbs
(1839 - 1903)

**Only God and Gibbs
never erred
... and this has been
strictly shown
for Gibbs only**

E.D. Shchukin

Free Surface Energy



Surface Free Energy

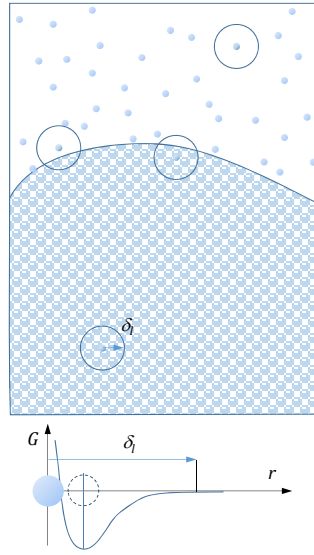
$$\gamma = \left(\frac{\partial A}{\partial \Sigma} \right)_{V, T, \mu_i}$$

$$\gamma = \left(\frac{\partial G}{\partial \Sigma} \right)_{p, T, \mu_i}$$

$$dG = Vdp - SdT + \gamma d\Sigma + \sum_1^N n_i d\mu_i$$

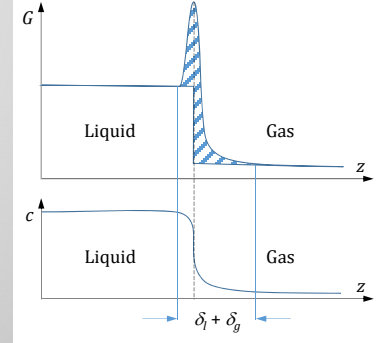
Molecular Origins of Surface Free Energy

Excess G at liquid side: enthalpic
 Excess G at vapor side: entropic



Molecular Origins of Surface Free Energy

γ – hatched area
 Position of interface:
 Zero concentration
 Equal energy



The contact angle of a droplet with a solid

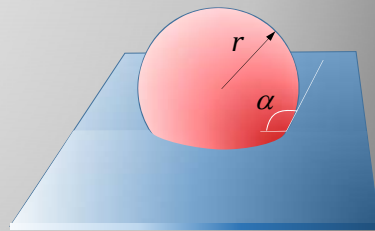
$$\Sigma = 2\pi r^2(1 - \cos \alpha)$$

$$\cos \alpha = \frac{\gamma_{sub} - \gamma_{int}}{\gamma} \quad \text{Young equation}$$

$$\Sigma_{int} = \pi r^2(1 - \cos^2 \alpha)$$

$$\Phi = \gamma \Sigma + (\gamma_{int} - \gamma_{sub}) \Sigma_{int} + \Phi_{sub}$$

$$V = \frac{1}{3} \pi r^3 (2 - 3 \cos \alpha + \cos^3 \alpha)$$



If the liquid and substrate are similar $\gamma \approx \gamma_{sub}, \gamma_{int} \ll \gamma_{sub}, \cos \alpha \approx 1$ and $\alpha \approx 0$

If the liquid is repelled by the substrate $\gamma_{int} > \gamma_{sub}, \cos \alpha < 0$ and $\alpha > \pi/2$.

The pressure within a small gas bubble

$$\Delta \Sigma = xy - (x + dx)(y + dy) \approx -(xdy + ydx)$$

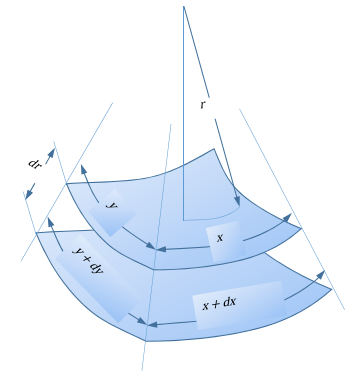
$$\Delta G = V \Delta p + \gamma \Delta \Sigma.$$

At equilibrium, $\Delta G = 0$ and

$$\gamma(xdy + ydx) = \Delta p xy dr.$$

$$dx = \frac{x}{r} dr \quad \text{and} \quad dy = \frac{y}{r} dr$$

$$\gamma \left(\frac{xy dr}{r} + \frac{xy dr}{r} \right) = \Delta p xy dr$$



$$\Delta p = \frac{2\gamma}{r} \quad \text{Young-Laplace relation} \quad \Delta \mu = \frac{2\gamma V_m}{r} \quad \text{Gibbs-Thomson relation}$$

$$\Delta \mu = \Delta p V_m$$

Surface Free Energy of Crystals

81 atoms
36 broken bonds

81 atoms
44 broken bonds

Surface Free Energy of Crystals

$W = nw$, $A = na$

$\gamma = \frac{W}{2A}$

$\gamma = \frac{w}{2a}$

The Turnbull Rule

$\gamma = \frac{w}{2a}$

$w = \frac{2\Delta H_{cryst}^0}{zN_A}$

$a = \Omega^{2/3}$

$\gamma = 0.3 \frac{\Delta H_{cryst}^0}{N_A \Omega^{2/3}}$

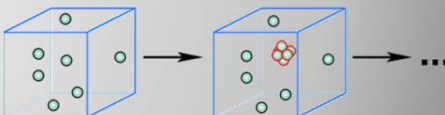
Classical Nucleation Theory: Thermodynamics

n molecules from solution into a crystalline cluster

Solution—supersaturated:
 $\mu_{soln} > \mu_{crystal}$
 $\Delta\mu = \mu_{soln} - \mu_{crystal} > 0$

Gibbs JW
 On the equilibrium of heterogeneous substances
Trans. Connect. Acad. Sci. (1876) **3**, 108;
 (1978) **16**, 343

Classical Nucleation Theory: Thermodynamics



Free energy gain = $-n\Delta\mu$

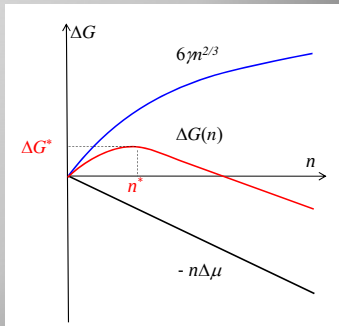
Free energy loss = $6\gamma n^{2/3}$
creation of new surface

$\Delta G(n) = -n\Delta\mu + 6\gamma(n\Omega)^{2/3}$

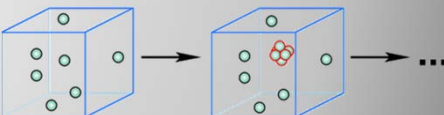
$\frac{dG(n)}{dn} = -\Delta\mu + \frac{4\gamma}{n^{1/3}}$

$n^* = \frac{64\gamma^3\Omega^2}{\Delta\mu^3}$

$\Delta G^* = \frac{32\gamma^3\Omega^3}{\Delta\mu^2}$

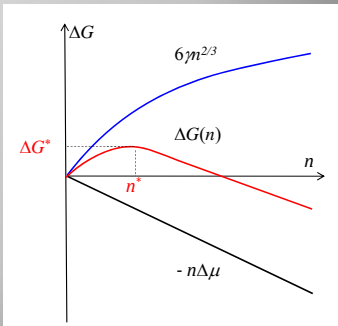


Classical Nucleation Theory: Thermodynamics

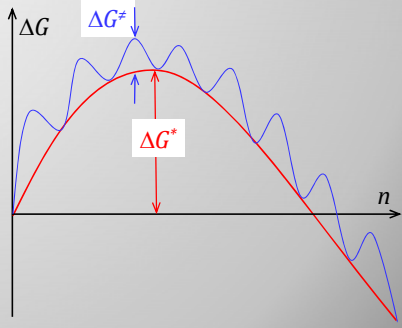


$n^* = \frac{64\gamma^3\Omega^2}{\Delta\mu^3}$

$\Delta G^* = \frac{32\gamma^3\Omega^3}{\Delta\mu^2} = \frac{1}{2}n^*\Delta\mu$




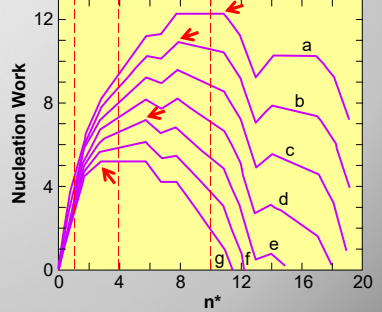
Creation of Chemical bonds in the Crystal



The Structure of the Crystal Nucleus

Suggested nuclei shapes

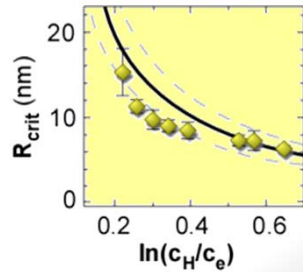
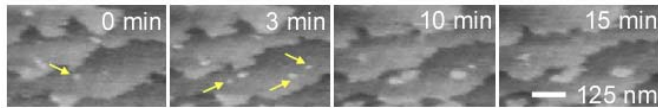




Milchev, *Contemp. Phys.* **32** (1991) 321

Experimental Tests

- Radius of 2D nucleus

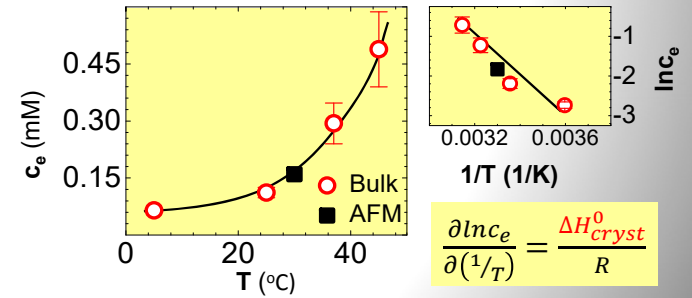


Critical Radius $R_c = \frac{\Omega\alpha}{\Delta\mu}$

Supersaturation $\Delta\mu = kT \ln\left(\frac{c}{c_e}\right)$

21

Thermodynamics of Hematin Crystallization



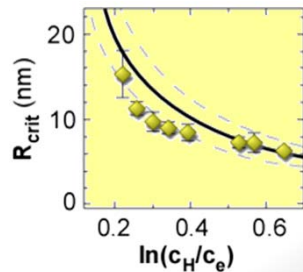
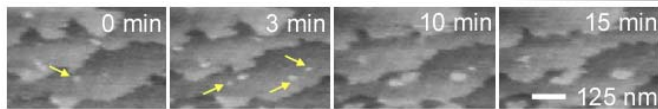
The crystallization enthalpy $\Delta H_{cryst}^0 = -37 \pm 8 \text{ kJ mol}^{-1}$

$$\frac{\partial \ln c_e}{\partial (1/T)} = \frac{\Delta H_{cryst}^0}{R}$$

22

Experimental Tests

- Radius of 2D nucleus



Critical Radius $R_c = \frac{\Omega\alpha}{\Delta\mu}$

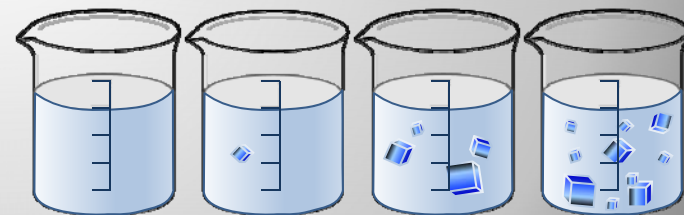
$\Delta H_{cryst}^0 = -37 \pm 8 \text{ kJ mol}^{-1}$

Turnbull's Rule $\alpha = 0.3 \frac{\Delta H_{cryst}^0}{N_A \Omega^{2/3}}$

$\alpha = 27 \pm 4 \text{ mJ m}^{-2}$

23

Kinetics of Crystal Nucleation



Nucleation rate J ,
nuclei per unit volume per unit time



Classical Nucleation Theory: Kinetics

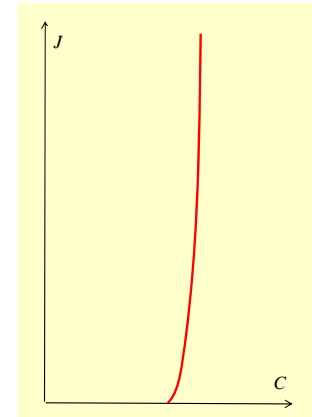
$$J = J_0 \exp\left(-\frac{\Delta G^*}{k_B T}\right)$$

Volmer M (1939)
Kinetik der Phasenbildung (Steinkopff, Dresden)

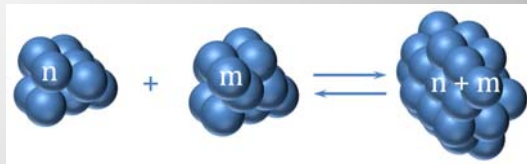
Assumes that crystal nuclei form directly in solution

Predicts steep $J(C, \Delta\mu(C))$

$J_0 = \text{?????}$

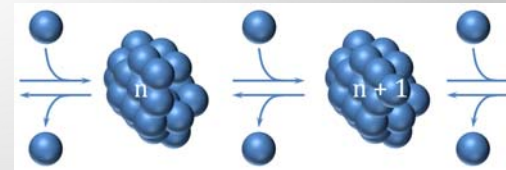


The General Aggregation Scheme



$$\frac{d}{dt} C(n, t) = \sum_{m=1}^N [f_{mn}(t)C(m, t) - f_{nm}(t)C(n, t)] ,$$

The Szilard Assumption

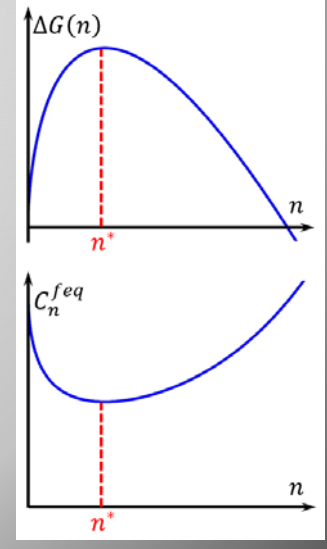


$$J(n, t) = f_{nn+1}(t)C(n, t) - f_{n+1n}(t)C(n+1, t)$$

$$\begin{cases} \frac{\partial C(n, t)}{\partial t} = f_{n+1}^-(t)C(n+1, t) + f_{n-1}^+(t)C(n-1, t) - (f_n^-(t) + f_n^+(t))C(n, t) \\ \frac{\partial C(1, t)}{\partial t} = -f_1^+(t)C(1, t) + f_2^-(t)C(2, t) + \sum_{n=2}^{\infty} f_n^+(t)C(n, t) - \sum_{n=3}^{\infty} f_n^-(t)C(n, t) \end{cases}$$

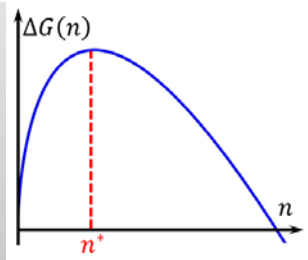
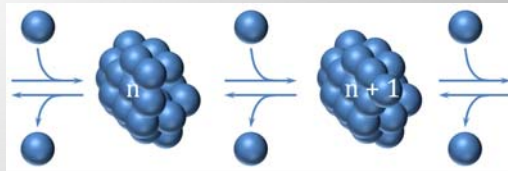


The "Equilibrium" Concentration of Nuclei



Y. B. Zel'dovich,
Acta Physicochimica URSS 18, 1 (1943).

Diffusion in the Space of n over a Barrier

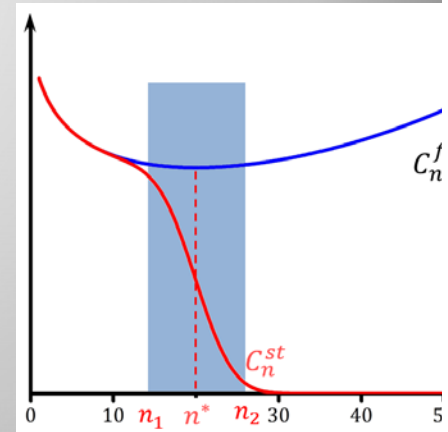


The Zeldovich Factor

$$J^{st} = f_n^+ C_n^{feq} z$$

$$z = \frac{1}{n^*} \left(\frac{\Delta G^*}{3\pi k_B T} \right)^{1/2}$$

$$z \approx 0.1 - 0.01$$



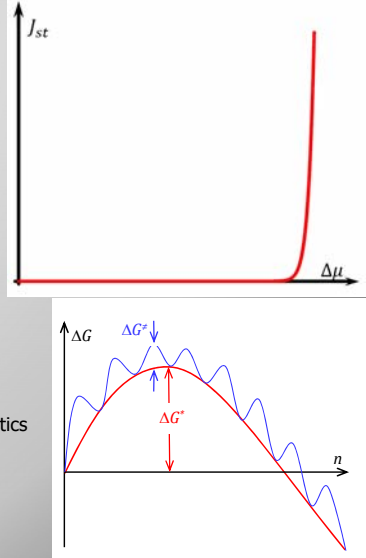
The Nucleation Rate Law

$$J^{st} = f_n^+ C_n^{feq} z$$

$$J^{st} = f_n^+ C_o z \exp(-\Delta G^*/k_B T)$$

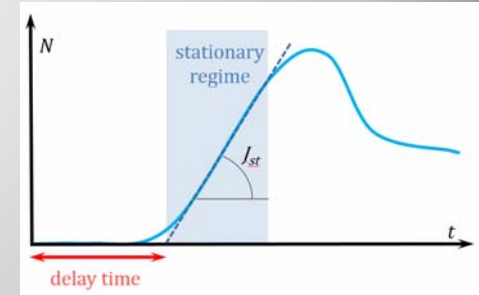
f_n^+ NOT limited by diffusion

- Experimentally measured
- Evaluated based on reaction kinetics



Time Evolution of Nucleation

$$\tau_D = \frac{2}{3\pi z^2 f^+}$$



$$\tau_{exp} = \tau_D + \tau_{st} + \tau_G = \tau_D + 1/J_{st}V + d/R$$

Non-classical Behaviors

- Solution-to-crystal spinodal: $n^* \leq 1$
- Two-step nucleation of crystals
- Non-equilibrium crystal shape

Mysteries of Nucleation Kinetics

- Sharp leveling of $J(\Delta\mu)$
- Large data scatter
- Nucleation rate lower by $10^9 \times$ then prediction of CNT

$$J = J_0 \exp\left(-\frac{\Delta G^*}{k_B T}\right)$$

$$J_{\lambda}(\text{experiment}) \sim 10^{10} \text{ cm}^{-3} \text{ s}^{-1}$$

$$J_{\lambda}(\text{CNT}) \sim 10^{19} \text{ cm}^{-3} \text{ s}^{-1}$$

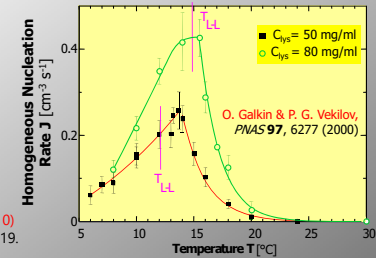
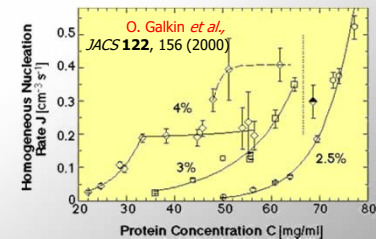
$$J_{\lambda}(\text{CNT}) = f^+ z C$$

$$f^+ \approx 300 \text{ s}^{-1}$$

$$z \approx 0.1$$

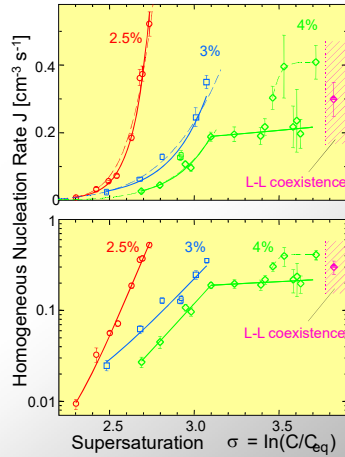
$$C \approx 10^{18} \text{ cm}^{-3}$$

- Non-monotonic behavior of $J(T)$



Vekilov PG (2010)
Nucleation. *Crystal Growth & Design* 10(12):5007-5019.

Determination of Nucleus Size



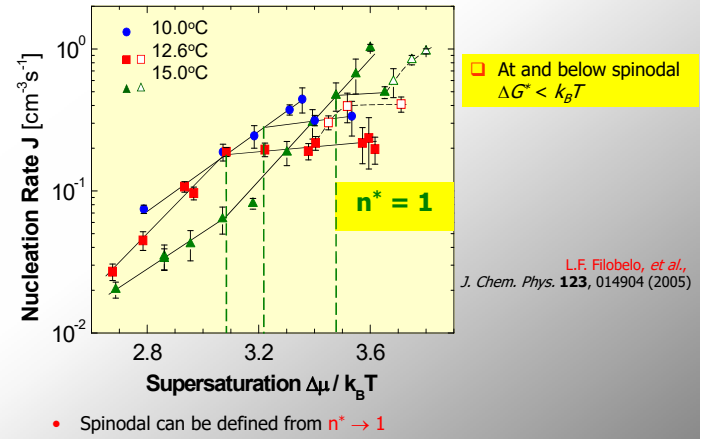
• Nucleation theorem
 D. Kashchiev, D. Oxtoby *JCP* 100 (1994) 7665

$$n^* = \frac{d(\ln J)}{d(\Delta\mu / k_B T)} + O(1)$$

allows determination of nuclei sizes
 (10 → 4 → 1)

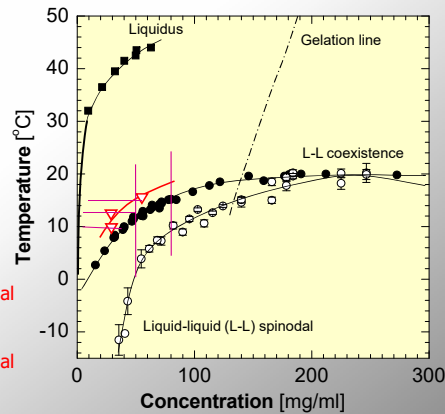
O. Galkin, P.G. Vekilov, *JACS* 122 (2000) 156

Solution-to-crystal Spinodal



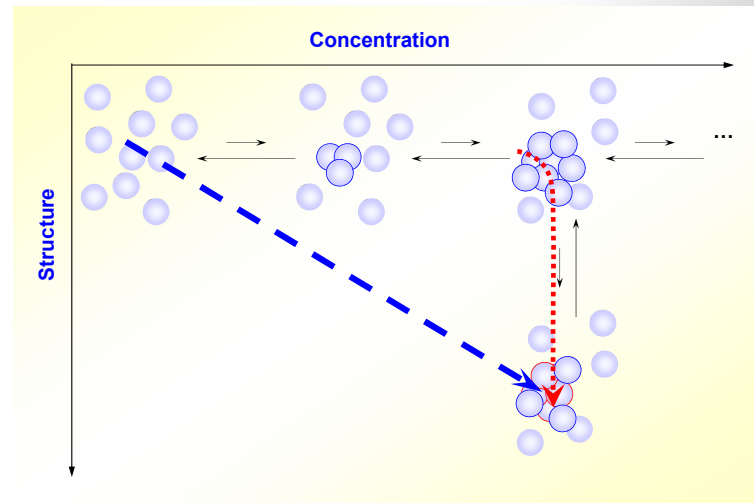
• Spinodal can be defined from $n^* \rightarrow 1$

Why is the maximum in J(T) sharp?

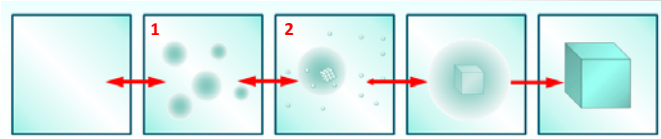


- J(T) reaches sharp max at solution-crystal spinodal
- J(σ) levels off at solution-crystal spinodal

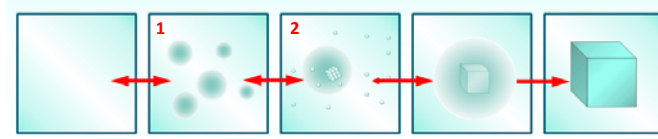
Direct and Two-step Nucleation



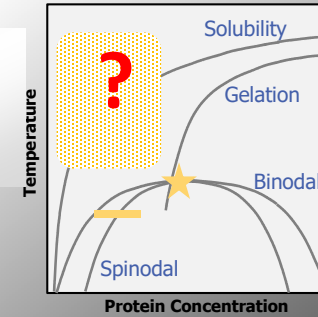
The Two-step Nucleation Mechanism



The Two-step Nucleation Mechanism

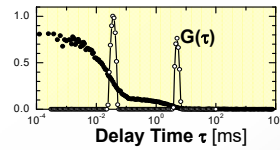


What are the **structures** that serve as precursors above the L-L coexistence line and persist in the **homogeneous** region?



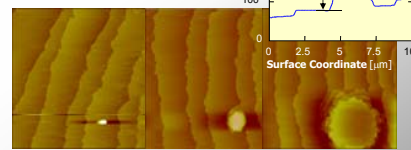
Protein-Rich Clusters

Dynamic light scattering, lysozyme



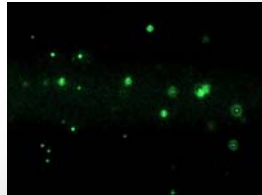
W. Pan, *et al.*, *Biophys. J.* **92**, 267 (2007)

Atomic force microscopy, lumazine synthase

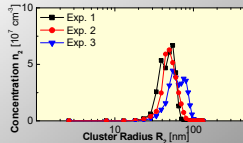


O. Gilko, *et al.*, *JACS* **127**, 3433 (2005)

Brownian microscopy



Y. Li, *et al.*, *Rev. Sci. Instr.* **82**, 053106 (2011)

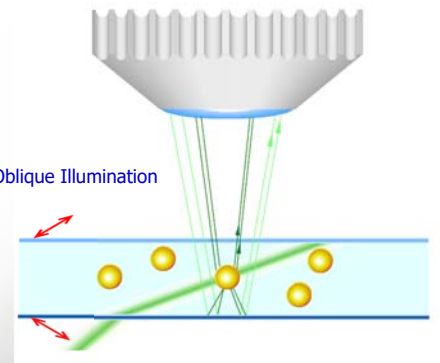


Reproduces results on R_2 and n_2 from dynamic light scattering

Do Crystals Nucleate in the Clusters?

You can observe a lot by watching. [Yogi Berra](#)

Depolarized Oblique Illumination Microscopy



Do Crystals Nucleate in the Clusters?

Depolarized Oblique Illumination Microscopy



Phenomenological Theory of Two-step Nucleation

$$0 \rightleftharpoons 1 \rightarrow 2 \quad \tau = \frac{1}{u_0(T)} + \frac{u_1(T)}{u_0(T)u_2(T)} + \frac{1}{u_2(T)}$$

τ - mean first-passage time

$J = \tau^{-1}$, 2 - rate-limiting

$$J = \frac{k_2 C_1 T \exp\left(-\frac{\Delta G_2^*}{k_B T}\right)}{\eta(C_1, T) \left[1 + \frac{U_1}{U_0} \exp\left(\frac{\Delta G_{inhd}^0}{k_B T}\right) \right]}$$

Viscosity inside dense liquid

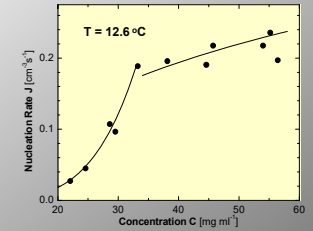
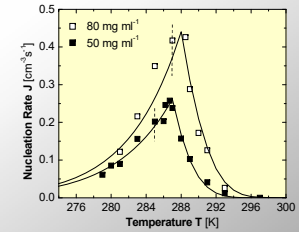
$$\eta = \eta_0 \{1 + [\eta] C_1 \exp(k_\eta [\eta] C_1)\} \exp(-E_\eta / k_B T)$$

Nucleation barrier on approach to spinodal

$$\Delta G_2^*(T) = \frac{E^*}{(T_c - T)^2} \left[1 - \frac{(T_c - T)^2}{(T_c - T_{sp})^2} \right]$$

- Single adjustable k_2 reproduces 3 complex kinetic curves

W. Pan, et al., J. Chem. Phys. 122, 174905 (2005)



The Pre-exponential Factor in the Nucleation Rate Law

$$J = J_0 \exp\left(-\frac{\Delta G^*}{k_B T}\right)$$

- From experiments: $J_0 \sim 10^{10} \text{ cm}^{-3} \text{ s}^{-1}$

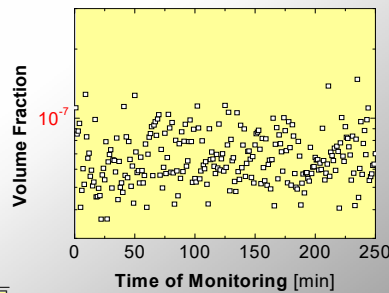
- From classical theory: $J_0 \sim 10^{18} \text{ cm}^{-3} \text{ s}^{-1}$

- From phenomenological theory:

$$J = \frac{k_2 C_1 T \exp\left(-\frac{E_2}{k_B T}\right)}{\eta(C_1, T) \left[1 + \frac{U_1}{U_0} \exp\left(\frac{\Delta G}{k_B T}\right) \right]}$$

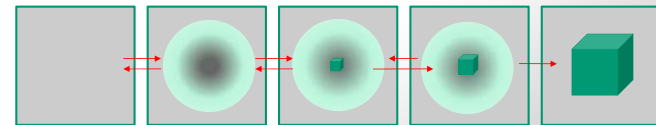
$$\frac{U_1}{U_0} \exp\left(\frac{\Delta G}{k_B T}\right) = \frac{1}{\phi}, \quad \phi - \text{cluster volume fraction}$$

- Low J_0 - due to nucleation within clusters

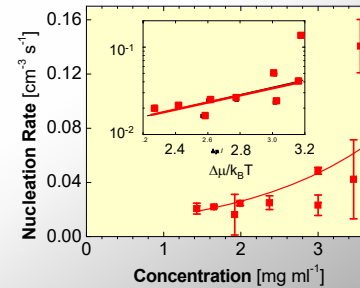


- η inside clusters $\approx 10 \text{ cP}$
- $\eta \times \phi^{-1} \approx 10^8$
- Explains low J_0

Why is the Two-step Mechanism Faster?



Nucleation rate data for insulin



$$J = J_0 \exp\left(-\frac{\Delta G^*}{k_B T}\right)$$

$$\Delta G^* \approx 10^{-20} \text{ J}$$

$$\Delta G^* = \frac{32 \gamma^3 \Omega^2}{\Delta \mu^2}$$

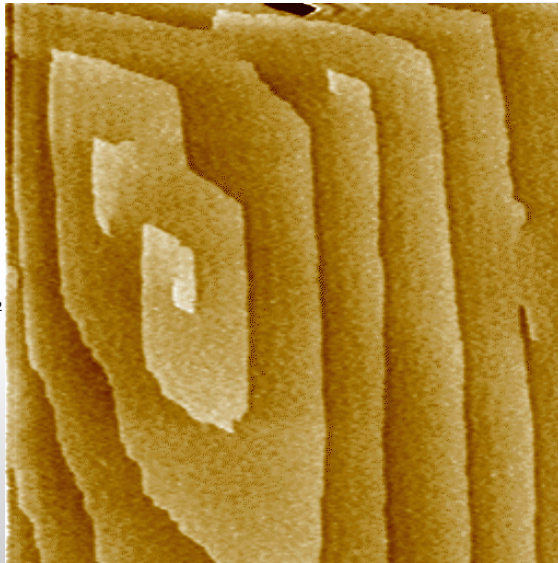
$$\gamma \approx 0.2 \text{ mJ/m}^2$$

Vekilov, P. G. Crystal Growth & Design 2010, 10, 5007

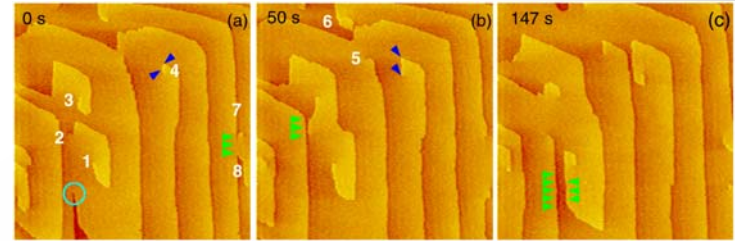
Growth of Insulin Crystals

94 frames
 Size: 9.5 x 9.5 μm^2
 50 s per frame
 Real time: 95 min

I. Reviakine, *et al.*,
J. Am. Chem. Soc. **125**, 11684 (2003)
 O. Gilko, *et al.*,
Phys. Rev. Lett. **90**, 225503 (2003)



Estimate of Crystal Solution Surface Free Energy



$L_c \approx 320 \text{ nm}$

$$L_c = \frac{\gamma\Omega}{\Delta\mu}$$

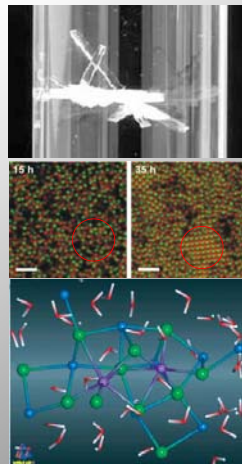
$\gamma \approx 28 \text{ mJ/m}^2$

Reviakine, I., *et al.*,
J. Am. Chem. Soc. **125**, 11684-11693, (2003)

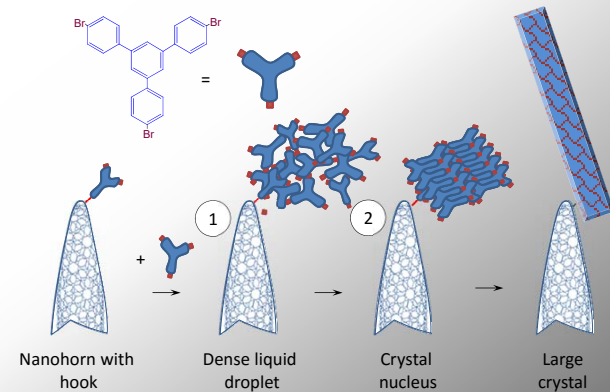
- Nucleation in dense liquid clusters lowers
 - γ by $\sim 140\times$ and
 - ΔG^* by 10^6
 - Increases J by 14 orders of magnitude

The Two-step Mechanism for Solution Crystallization

- Protein Crystallization
 - O. Galkin & P. G. Vekilov, *PNAS* **97**, 6277 (2000)
 - P. G. Vekilov, *Cryst. Growth & Design* **4**, 671 (2004)
 - M. Sleutel, A. van Driesche, *PNAS* (2013)
- Glycine, urea
 - B. Garetz, *et al.*, *Phys. Rev. Lett.* **89**, 175501 (2002)
 - J.E. Aber, *et al.*, *Phys. Rev. Lett.* **94**, 145503 (2005)
 - D.W. Oxtoby, *Nature* **420**, 277 (2002)
- Colloid crystals
 - M. E. Leunissen, *et al.*, *Nature* **437**, 235 (2005)
 - J. R. Savage and A. D. Dinsmore, *PRL* **102**, 198302 (2009)
 - T. H. Zhang and X. Y. Liu, *JPCB* **111**, 14001 (2007)
- NaClO_3
 - R.Y. Qian, G.D. Botsaris, *Chem. Eng. Sci.* **59**, 2841 (2004)
- Calcite nucleation in bulk solutions
 - L. Gower, *Chem. Rev.* **108**, 4551 (2008)
 - H. Coelfen, *et al.*, *Science* **322**, 1819 (2008)
 - E. M. Pouget, *et al.*, *Science* **323**, 1455 (2009)
 - A.F. Wallace, *et al.*, *Science* **341**, 885 (2013)



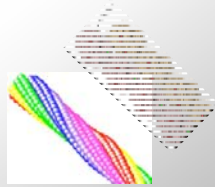
The Case of Y-Br



Harano, K. *et al.*,
Nature Mater. **11**, 877-881 (2012).

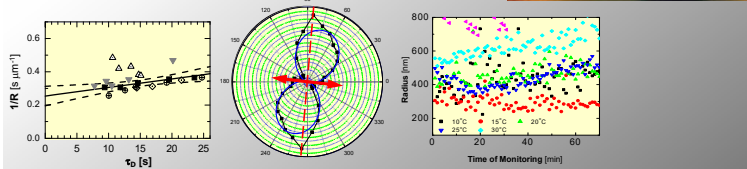
HbS Polymer Nucleation

- $\tau_D(\tau)$ much stronger than $R(\tau)$ contradicts 1-step nucleation and agrees with 2-step
- Polymers are **perpendicular to plane of polarization** of polarized light
- Dependencies of V_f of mesoscopic metastable clusters on C and T follow those of nucleated polymers

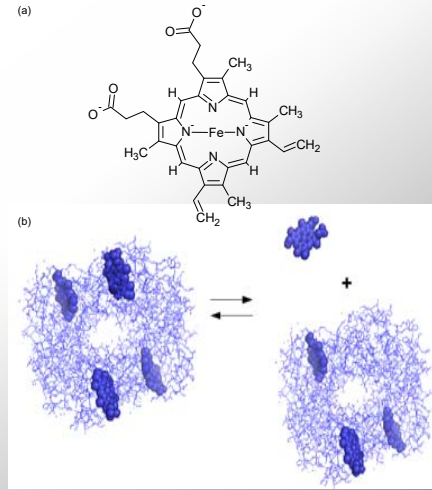


⇒ Clusters are **precursors** for polymer nuclei

- O. Galkin, P.G. Vekilov, *J. Mol. Biol.* **336**, 43 (2004)
- O. Galkin, et al., *J. Mol. Biol.* **365** 425 (2007)
- O. Galkin, et al., *Biophys. J.* **92**, 902 (2007)
- P.G. Vekilov, *Brit. J. Haematol.* **139**, 173 (2007)



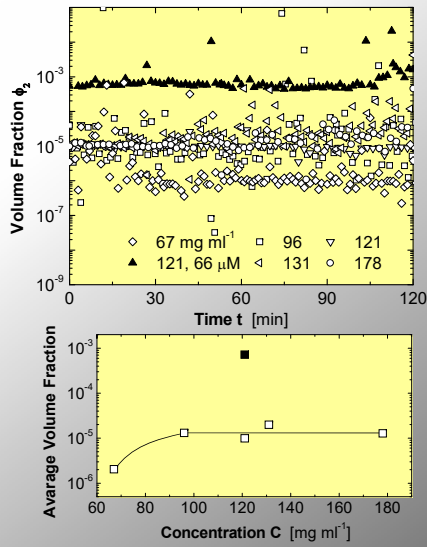
So What: the Heme and Sickle Cell Polymerization



Dependence of Cluster Volume Fraction on HbS Concentration

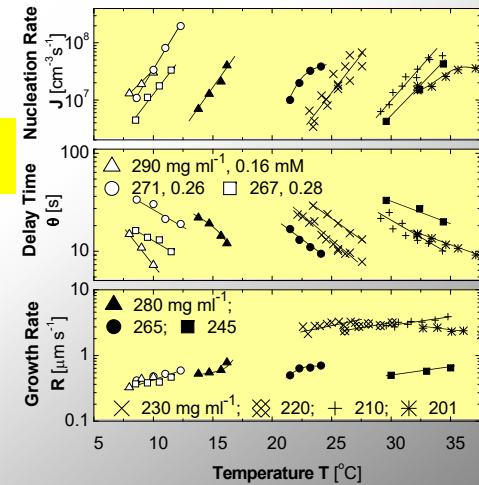
- ϕ_2 for hemoglobin S
- Increases with C from 67 to 96 mg ml⁻¹
- Similar at 96, 121, 131, and 178 mg ml⁻¹
- as per theory
- Heme addition: ϕ_2 higher by **80x**

The nucleation rate ??



The Nucleation Rate

- In the presence of heme, J is ~ 100x faster



How Can We Image the Critical Clusters?

- 1) They exist for a very **short time**
- 2) They are **freely floating** in the solution

- Protein crystallization is **very slow**
At $\Delta\mu = 1.2 k_B T$
Solution/crystal net exchange frequency
 $f = 0.065 \text{ s}^{-1} = 1 \text{ molecule}/50 \text{ s}/\text{active site}$

At $d\Delta G/dn = 0$ – even slower
Comparable to **AFM imaging time**

- Clusters are **Brownian particles**

$$D_{\text{cluster}} = \frac{D_1}{n_{\text{edge}}} = \frac{3 \times 10^{-7} \text{ cm}^2/\text{s}}{5} = 6 \times 10^{-8} \text{ cm}^2/\text{s}$$

From $\langle x^2 \rangle = 2D\tau$

$$\tau = (100 \mu\text{m})^2 / 2D_{\text{cluster}} = 850 \text{ s} \approx 15 \text{ min}$$

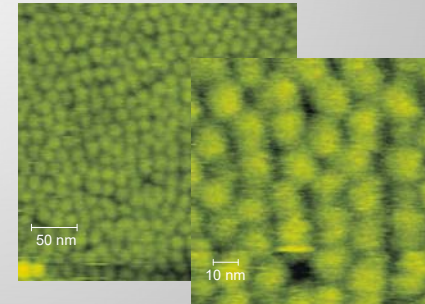


- A cluster needs **15 min** to reach surface after nucleation 100 μm above substrate
- Ferritin molecules **readily adsorb** on glass

⇒ Near-critical and sub-critical clusters **could be viewed by AFM**

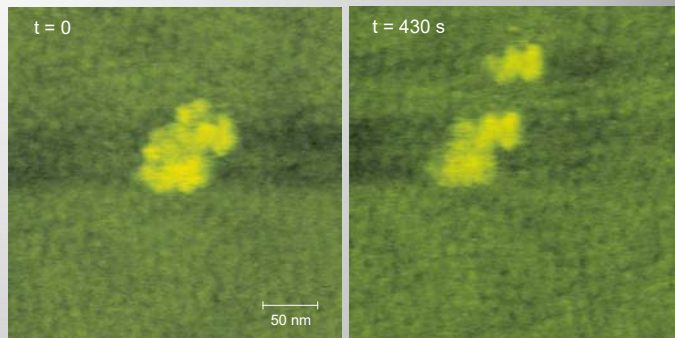
Adsorption of Ferritin Molecules on the Substrate

Full coverage with a disordered monomolecular layer of ferritin – **2D ferritin glass**



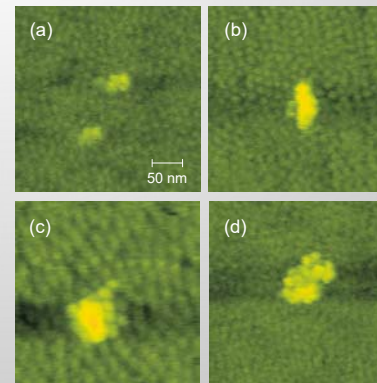
- Strong adsorption, **no surface mobility** of the molecules
No crystallization occurs in the adsorbed layer
- All crystalline aggregates seen on the surface come from the **solution bulk** and lie on top of adsorbed layer

Clusters Are Formed in the Bulk and Land on the Surface



- For ~ 7 min the monitored cluster loses 2 molecules
- Another cluster lands next to it from the solution
- Observed for many clusters, supported by indirect evidence

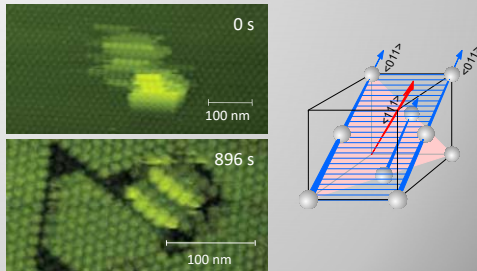
Structures of Aggregates Adsorbed on Substrate



- Aggregates containing **2, 4, 6, ~16 and ~20** molecules
- Molecules in the 6-membered aggregate in (b) are arranged in **2 rods** with 4 and 2 molecules
- Molecules in larger aggregates (c) and (d) form a **single layer** consisting of a few **rods of 4-5 molecules**
- Disordered aggregates also seen
- Ordered aggregates are in dynamic exchange with solution, disordered aggregates are "dead"

Structures of Aggregates Adsorbed on a Crystal

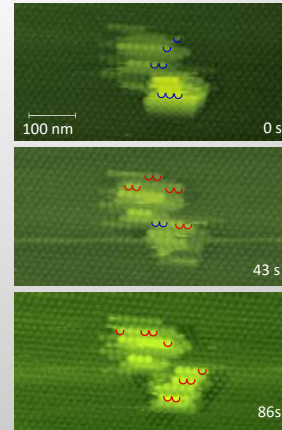
Better visibility of cluster structure, likely due to stronger adsorption on structured surface of crystal



- Arrangement of molecules – same as in the bulk of a large crystal, intermolecular distance = 13 nm
- Shape: (110) rods forming 1 or 2 (110) layers
- Structure compatible with clusters seen on the substrate

S.-T. Yau, P.G. Vekilov, *Nature* 406 (2000) 494.

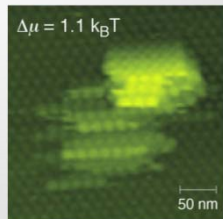
Dynamics of Exchange with Solution



Blue molecules: detach from cluster after frame recorded
 Red molecules: attach to cluster after previous frame recorded

- Clusters are in dynamic exchange with solution: these are not dead-end aggregates
- Net attachment frequency: 4 molecules / 43 s \approx 0.1 attachment event / second
 20 possible sites
 $f = 0.005 \text{ s}^{-1}$ per site
 $\ll 0.065 \text{ s}^{-1} = f$ on a large crystal
 S.-T. Yau, B.R. Thomas, P.G. Vekilov, *Phys. Rev. Lett* 85 (2000) 353.
- Cluster is close to labile equilibrium with a supersaturated solution due to small size

Dependence of Cluster Size on Supersaturation



- In all experiments larger clusters are seen, statistically, at higher supersaturation
- At $\Delta\mu = 1.1 \text{ k}_B T$, the cluster has $n^* \sim 6$ molecules on an edge
- At $\Delta\mu = 1.6 \text{ k}_B T$, the cluster has $n^* = 4$ molecules on an edge
- Size scales approximately with $1/\Delta\mu$, as per Gibbs-Thomson relation

$$n^* = \frac{2\phi}{\Delta\mu}$$

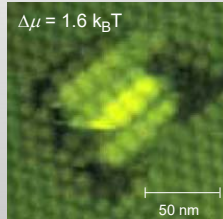
R. Kaischew and I. Stranski, *Z. Phys. Chem.* B35 (1937) 427

ϕ — intermolecular bond energy

$\phi = 3.2 \text{ k}_B T$ Yau et al., *PRL* 85 (2000) 353

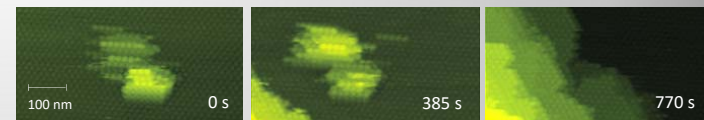
at $\Delta\mu = 1.1 \text{ k}_B T$ $n^* = 6$

at $\Delta\mu = 1.6 \text{ k}_B T$ $n^* = 4$



Long-term Evolution

Growth and rejection by incoming layer

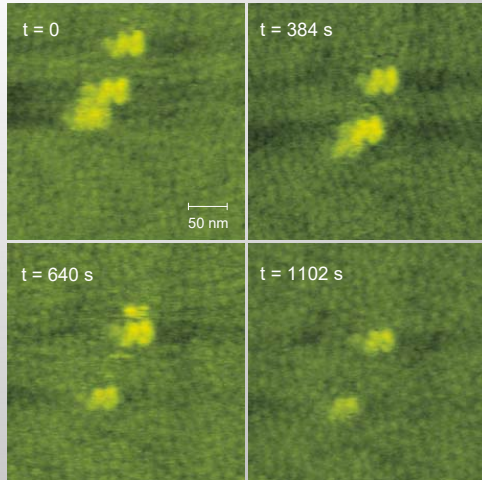


Dissolution and incorporation with misfit into underlying crystal



- Equilibrium with supersaturated solution is only labile
- At a certain $\Delta\mu$, statistically, larger clusters grow, smaller clusters dissolve
- Agrees with Gibbs-Thomson relation and Oswald ripening rules

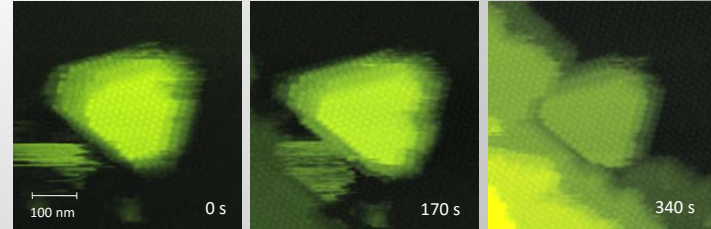
Random Selection of Cluster Behavior



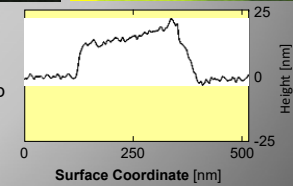
- Larger cluster **dissolves** over long times, **smaller** cluster adds and loses 1 molecule
- Seeming **violation of Oswald ripening** rules?
- Oswald ripening describes evolution of **large populations of crystallites**

Are These Precrystalline Clusters?

Do they evolve into crystals?



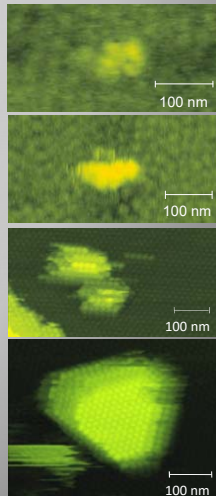
- (111)-faceted microcrystal consisting of 3 layers **formed in solution**:
 - inclined with respect to underlying face
 - misfit upon incorporation by oncoming step
- Contains ~ 140 molecules: slightly **larger** than the near critical clusters
- Slowly **grows**
- It has evolved from **near-critical clusters** similar to those above



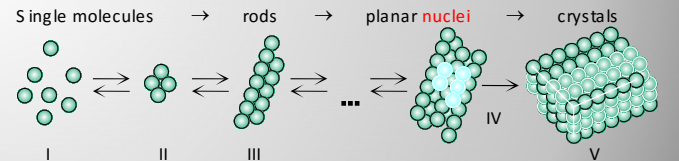
Do These Clusters Belong to the Crystal Nucleation Pathway?

We have shown that the clusters:

- Form in the solution **bulk**
 - Have **arrangement** of molecules same as in crystal
 - Are in **dynamic exchange** with the medium
 - The net exchange frequency is very **low**, indicative of near equilibrium
 - **Grow or dissolve** over longer time periods
 - **Size** is inversely proportional to supersaturation
 - **Evolve** into crystals
- These are **subcritical and near critical clusters** in the nucleation pathway of ferritin crystals
 - Their structure is representative of the **structure of the crystal nuclei**



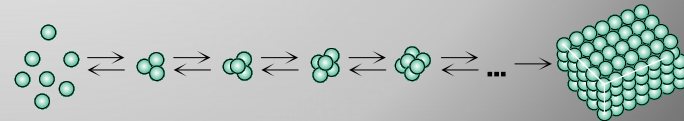
Suggested Nucleation Pathway



All 5 steps are evidenced by the images above

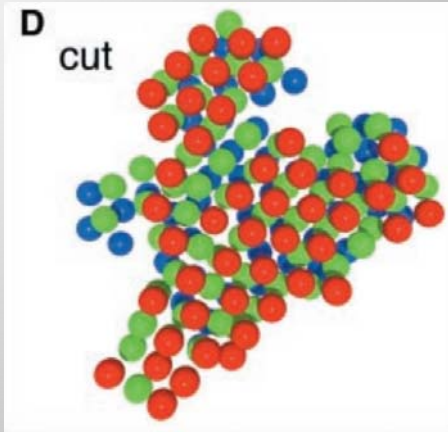
(110) layers stack to form a crystal faceted by (111) planes

Rather than Compact structure of all subcritical clusters



S.-T. Yau, P.G. Vekilov, Nature 406 (2000) 494

Shape of Colloid Crystal Nuclei

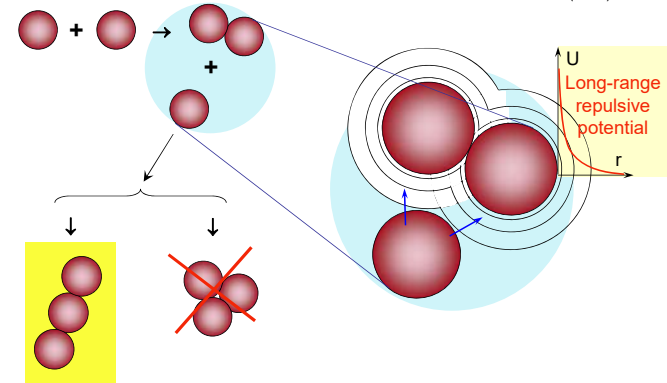


U. Gasser, E. Weeks, A. Schofield, P. Pusey, and D. Weitz, *Science* **292**, 258 (2001).

Why Would Spherical Molecules Form Linear and Planar Clusters?

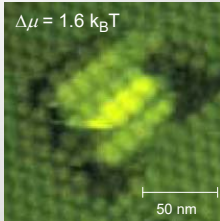
- If long-range repulsion acts, after a dimer is formed, the axis sites are preferred loci for attachment of third molecule, etc.

A.J. Hurd, D.W. Shaefer *PRL* **54** (1985) 1043



Do All Crystals Follow the Two-step Mechanism?

- Ferritin: nucleus size fully explained by classical theory



$\Delta\mu = 1.6 k_B T$

$n^* = 4$ molecules
 n^* scales ~ with $1/\Delta\mu$,
 as per Gibbs-Thomson relation

$$n^* = \frac{2\phi}{\Delta\mu}$$

R. Kaischew and I. Stranski,
Z. Phys. Chem. B35 (1937) 427

ϕ — intermolecular bond energy

$\phi = 3.2 k_B T$

S.-T. Yau *et al.*, *PRL* **85** (2000) 353

at $\Delta\mu = 1.6 k_B T$ $n^* = 4$



S.-T. Yau, P.G. Vekilov, *Nature* **406** (2000) 494