FUNDAMENTOS DE CRISTALIZACIÓN

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Insubria International Summer School
Crystallography for Health and Biosciences

La cristalización es un fenómeno que consiste en dos procesos diferentes. El primero de ellos se llama nucleación, y consiste en la formación de clusters nanoscópicos de la nueva fase sólida que pueden crecer hasta formar cristales macroscópicos de forma irreversible. El segundo es el proceso de crecimiento del cristal.

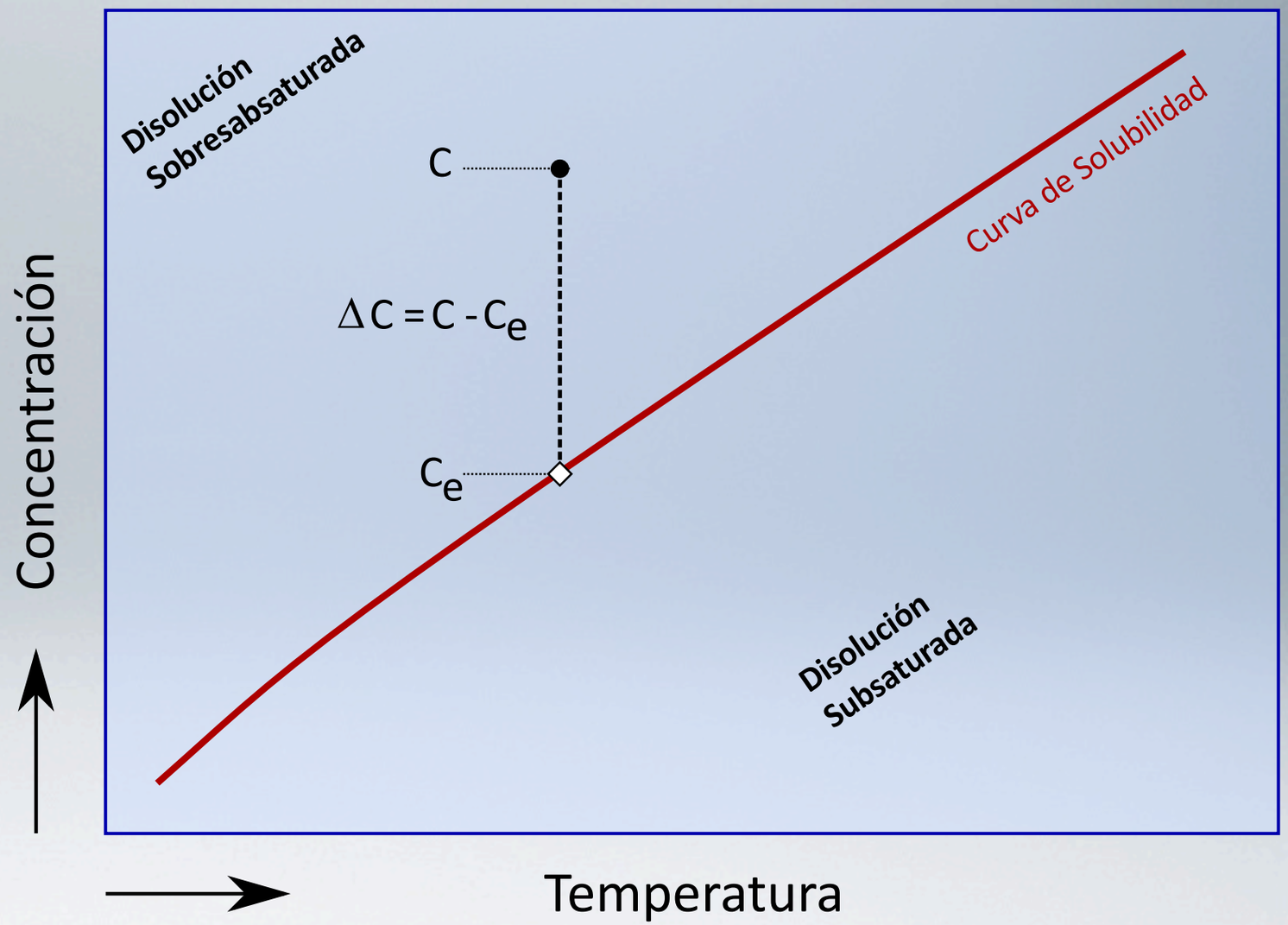
Recordando conceptos sencillos pero importantes

Las disoluciones subsaturadas son termodinámicamente estables

Las disoluciones saturadas están en equilibrio

Las disoluciones sobresaturadas son termodinámicamente inestable

Una solución sobresaturada debería crear una fase sólida. Sin embargo, esto sólo es cierto cuando la sobresaturación alcanza un valor crítico.



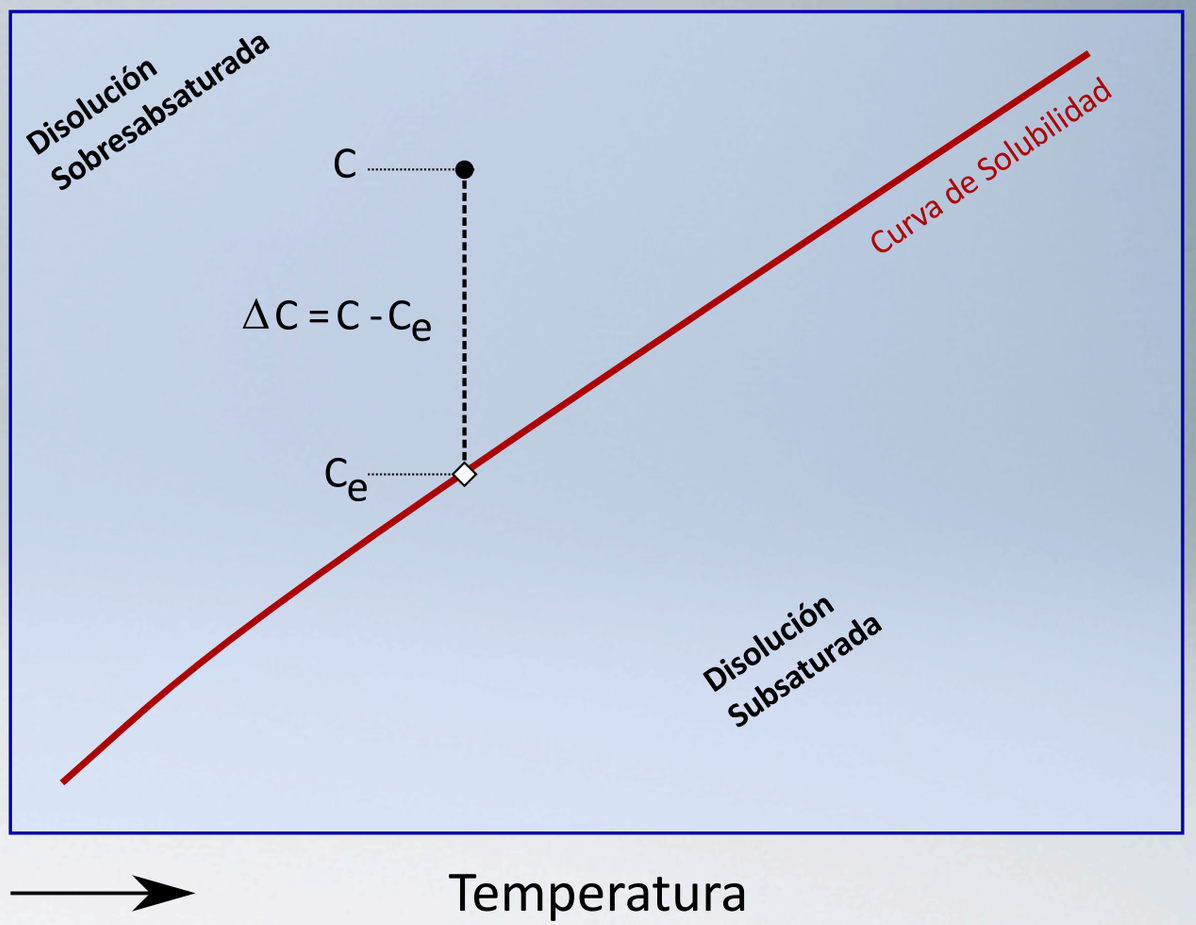
Juan Ma. Garcia-Ruiz

Recordando conceptos sencillos pero importantes

Disolución: fase homogénea que contiene moléculas de soluto y las moléculas de disolvente

Concentración de equilibrio o solubilidad (C_e):
La concentración de soluto en un disolvente en equilibrio con soluto no disuelto, a una temperatura y presión dadas.

Disolución saturada: $C = C_e$
Disolución sobresaturada: $C > C_e$
Disolución subsaturada: $C < C_e$

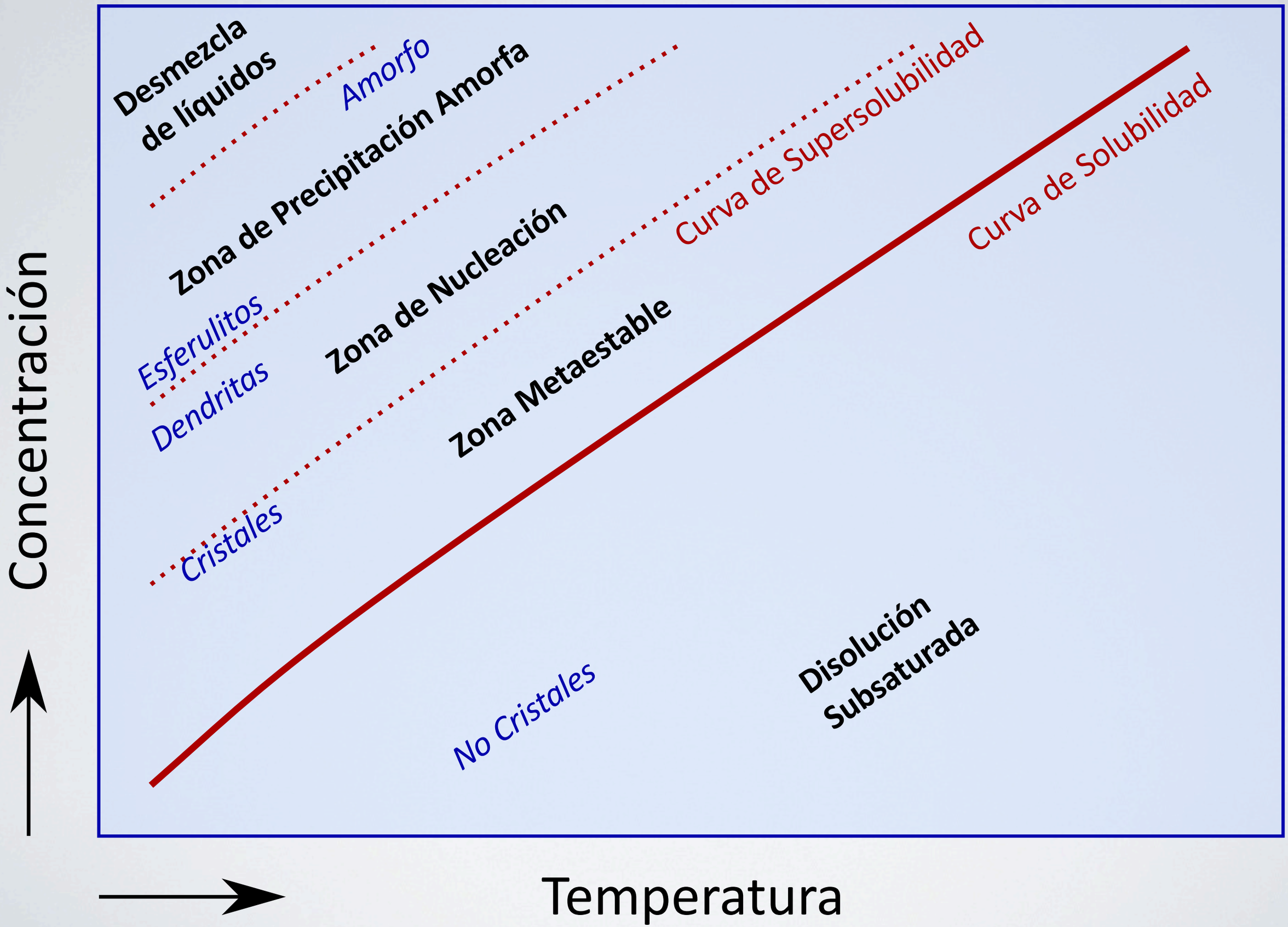


Expresiones de la sobresaturación

Sobresaturation : $c - c_e$

Razón de sobresaturación: $\frac{c}{c_e}$

Sobresaturaciónn relativa: $\frac{c - c_e}{c_e}$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Disolución Subsaturada

¿Por qué hay una **zona metaestable** donde los cristales pueden crecer pero no pueden nuclear, es decir, no pueden formarse

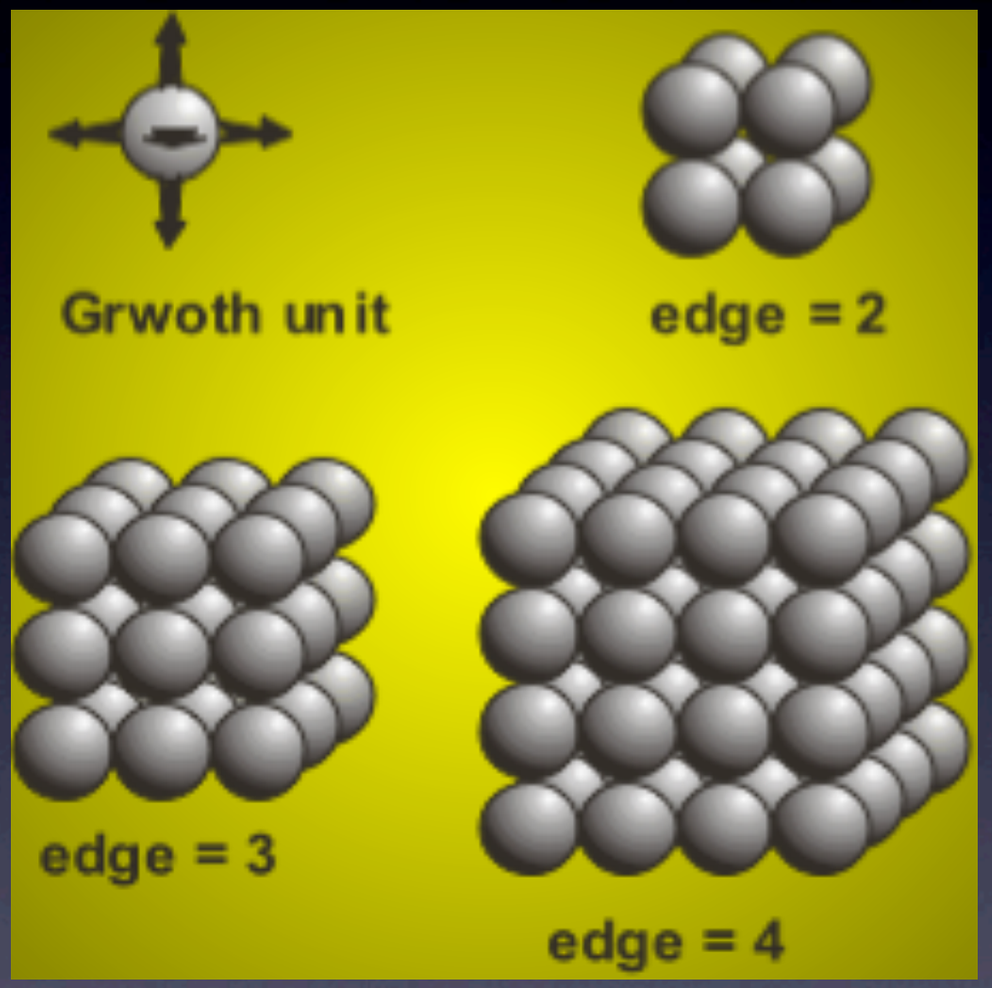
Una visión intuitiva del proceso de nucleación

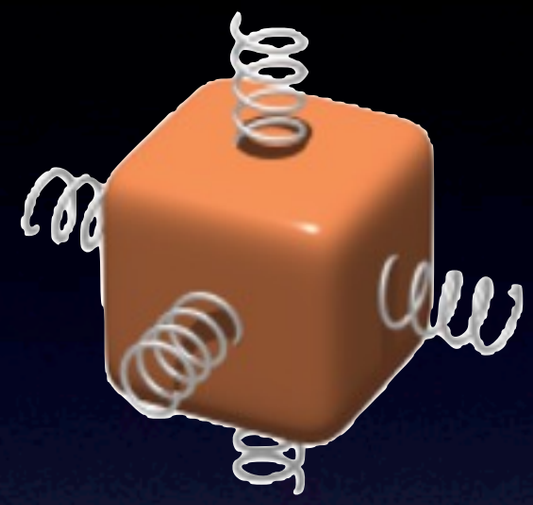
Nucleaciónn

Simulación de nucleación

When a cluster form, a surface is created that separates two volumes (the cluster and the mother solution) quite different from a structural viewpoint

El cristal Kossel. La unidad virtual de crecimiento tiene seis enlaces insaturados situados perpendicular a cada cara del cubo





La cohesión del cluster es proporcional al número de enlaces saturados internos versus el número de enlaces en dirección hacia la solución madre

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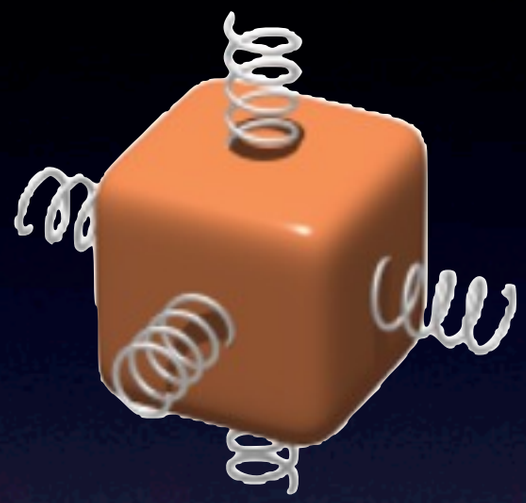
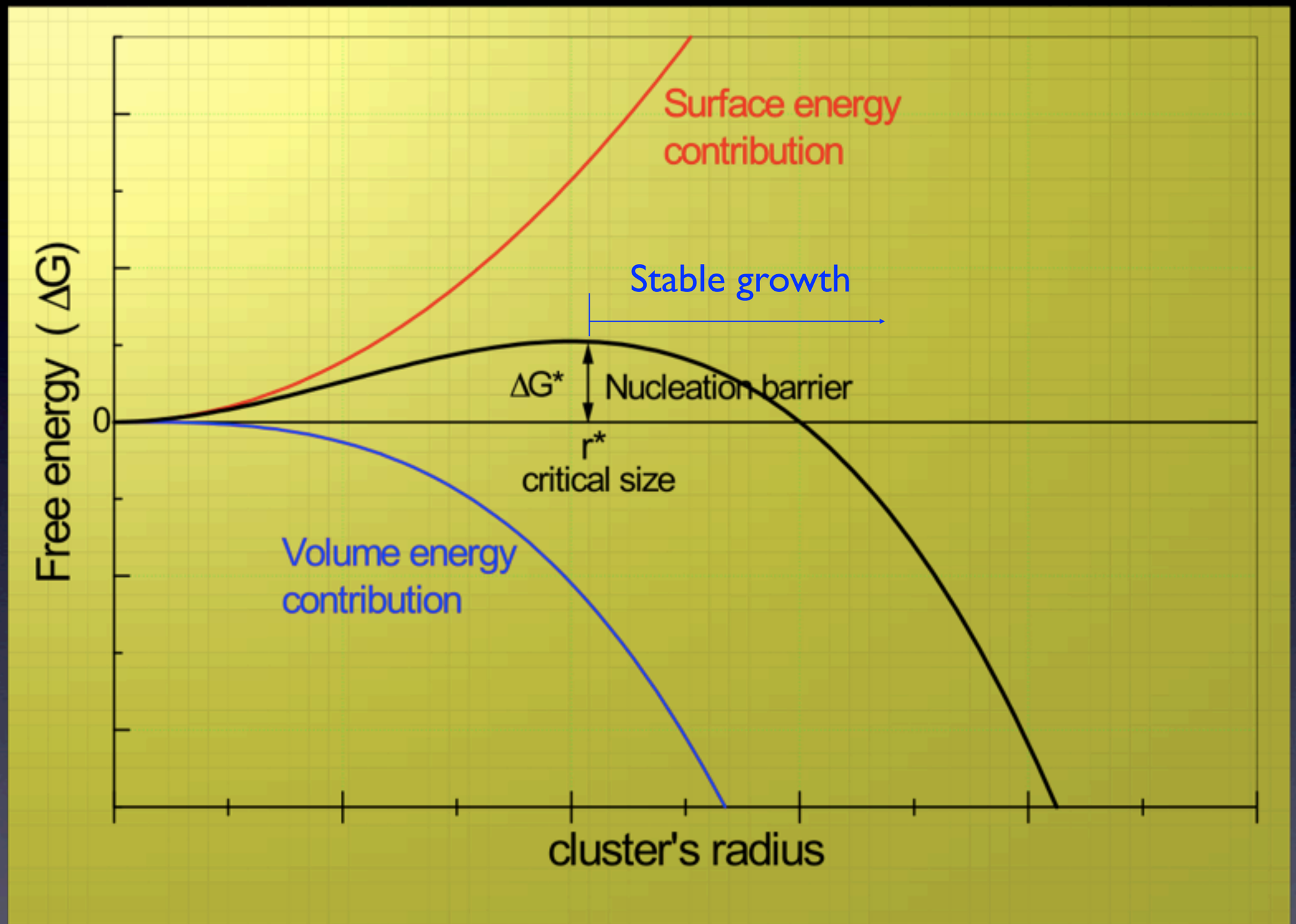
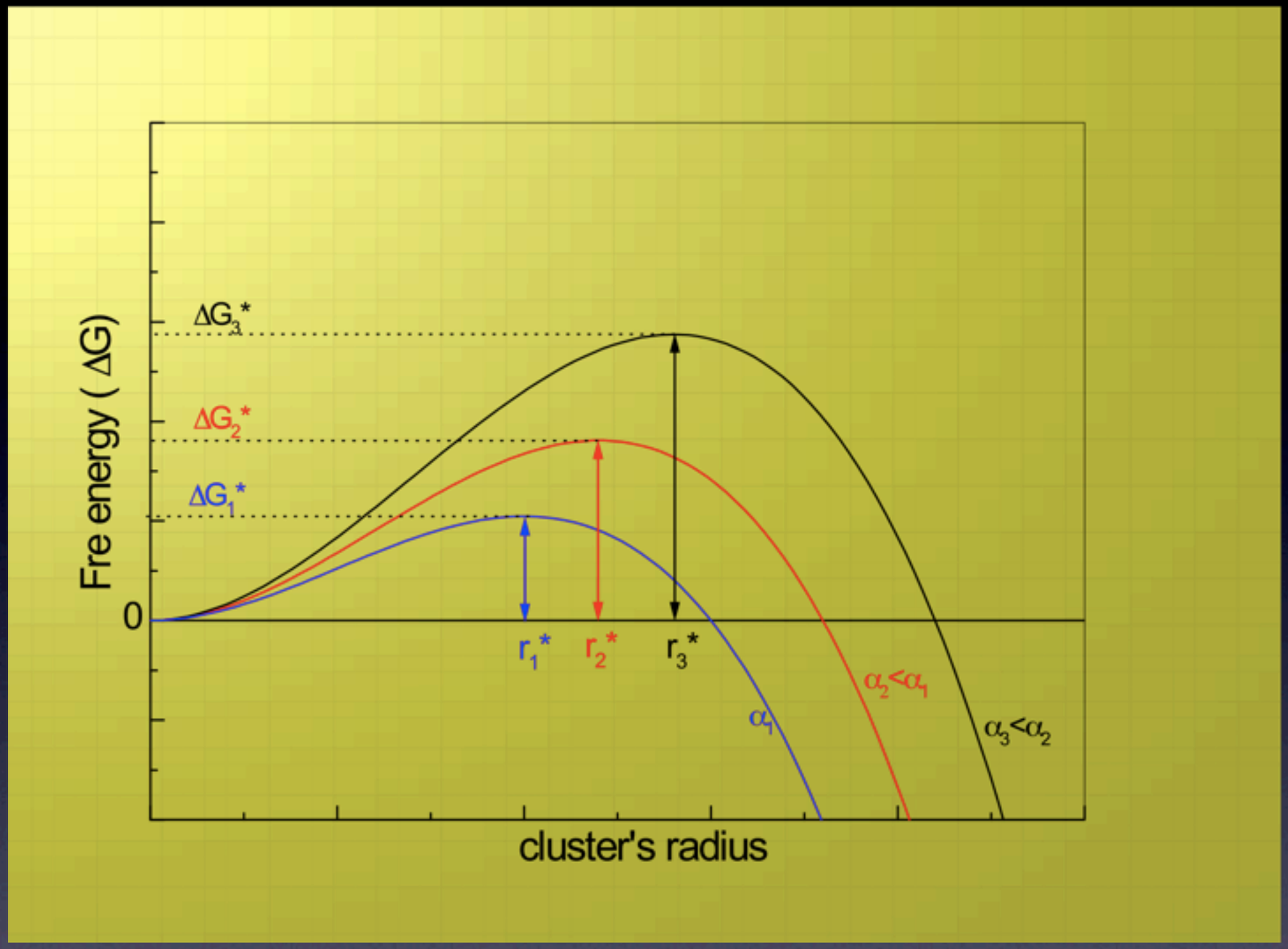
Cohesion energy is proportional to the cluster's volume
The probability to disagregate is proportional to the cluster's surface

a	$F_S=6*a^2$	$F_A= a^3$
1	6×1^2	$a\ (1)^3$
2	6×2^2	$a\ (2)^3$
3	6×3^2	$a\ (3)^3$
4	6×4^2	$a\ (4)^3$
5	6×5^2	$a\ (5)^3$
6	6×6^2	$a\ (6)^3$
7	6×7^2	$a\ (7)^3$
8	6×8^2	$a\ (8)^3$
9	6×9^2	$a\ (9)^3$



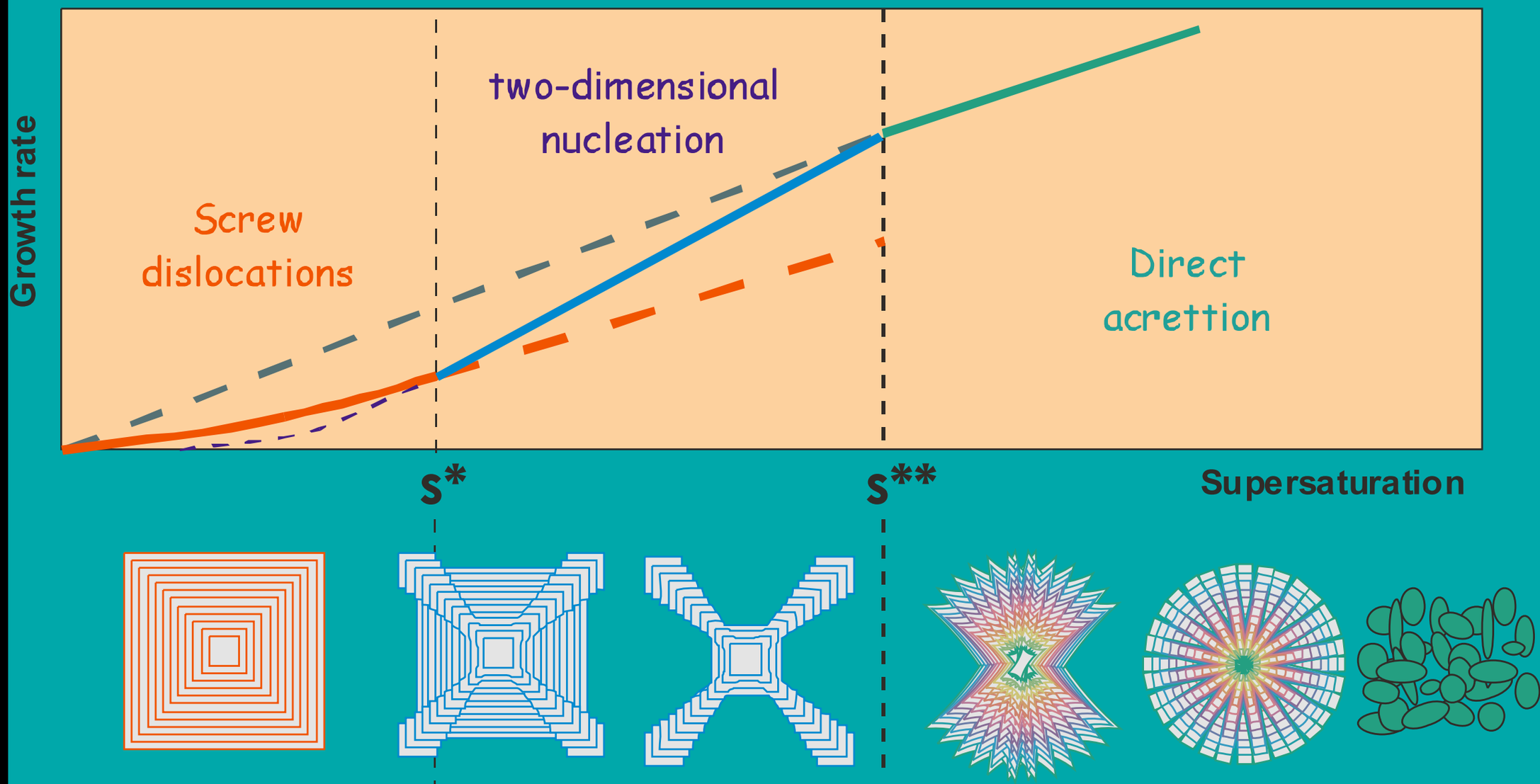

Surface energy
contribution
Stable growth
ΔG*
Nucleation barrier
r*
critical size
Volume energy
contribution
0
Free energy (ΔG)
cluster's radius



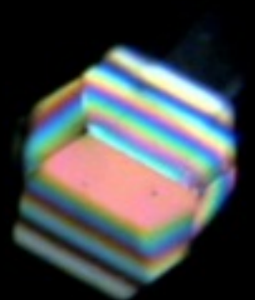
$$r^* = \frac{2\nu\gamma}{kT\ln S}$$

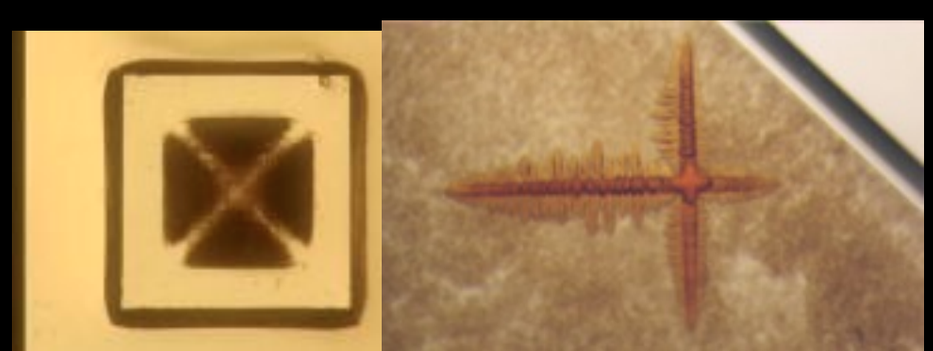
$$\Delta G^* = \frac{16\pi\nu^2\gamma^3}{3\left[kT\ln S\right]^2}$$

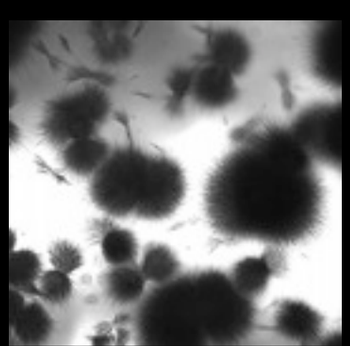
Growth mechanisms



Morphological output







According to the Boltzman's law, the probability of a fluctuation of magnitude W is given by : $e^{-\frac{W}{kT}}$. Thus, the probability of a nucleus of size i+1 growth units being created from a cluster of size i is: $e^{\frac{-\Delta G_i}{kT}}$, where ΔG_i is the change of free energy associated to the addition of one growth unit to a cluster of size i. As $n\Delta G_i = \Delta G$, then,

$$\frac{N_n}{N_1} = \exp\left(\frac{-\Delta G}{kT}\right)$$

The nucleation frequency J, i.e. The number of nuclei per unit of volume and unit of time that achieve the critical size can be expressed as:

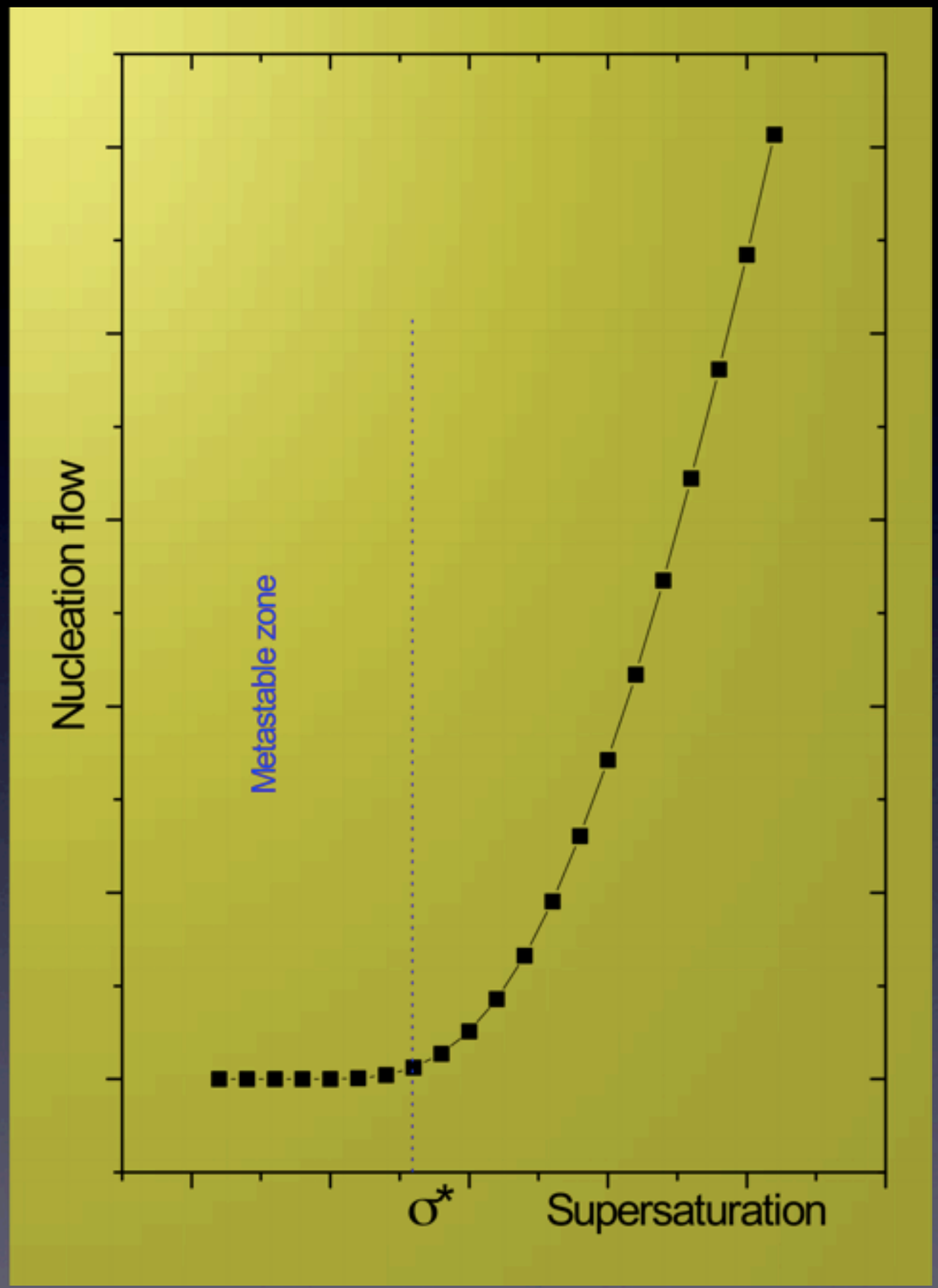
$$J = \kappa_0 \exp\left(\frac{-\Delta G^*}{kT}\right)$$

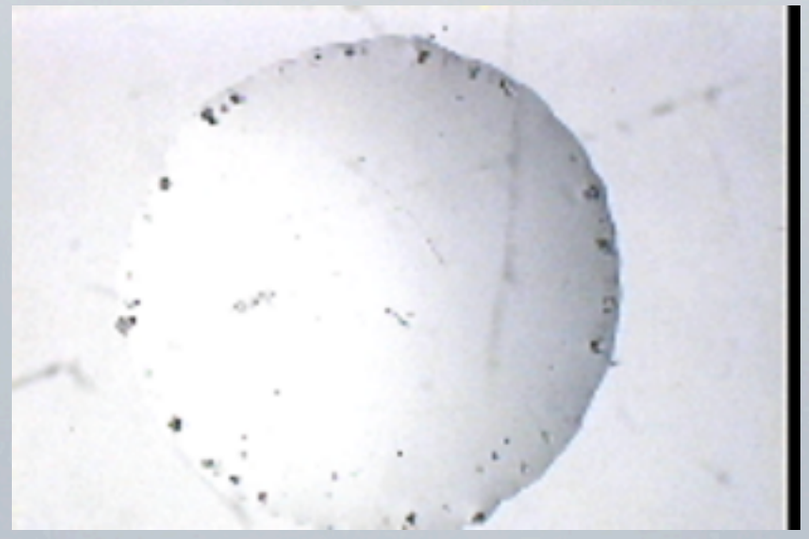
Substituying the value of ΔG^* in the last equation we got:

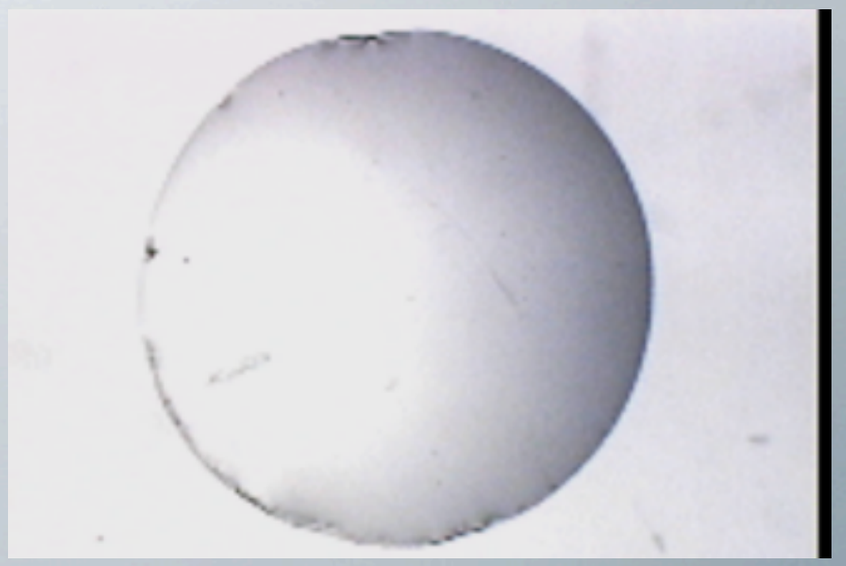
$$J = \kappa_0 \exp\left(-\frac{16\pi \upsilon^2 \gamma^3}{3(kT)^3 [\ln S]^2}\right)$$

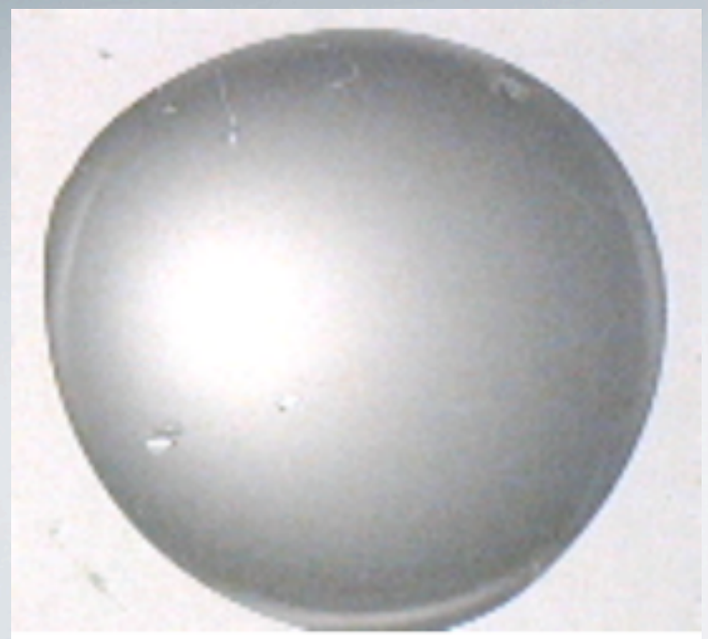
Nucleation frequency J is defined as the number of stable nuclei forming per unit of time and unit of volumen. It is given by:

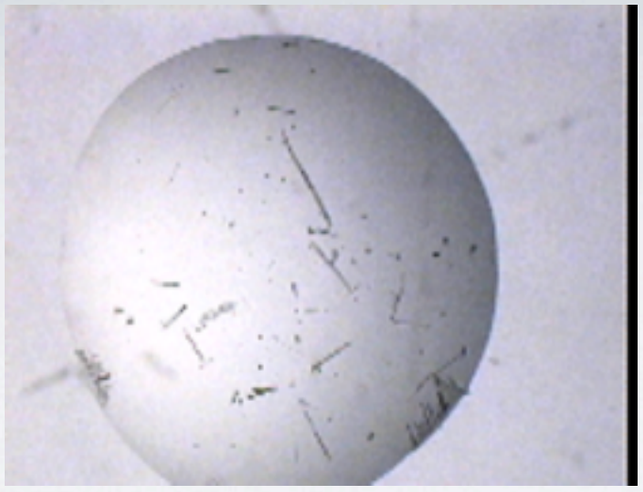
$$J = \kappa_0 \exp\left(-\frac{16\pi \upsilon^2 \gamma^3}{3(kT)^3 [\ln S]^2} \right)$$

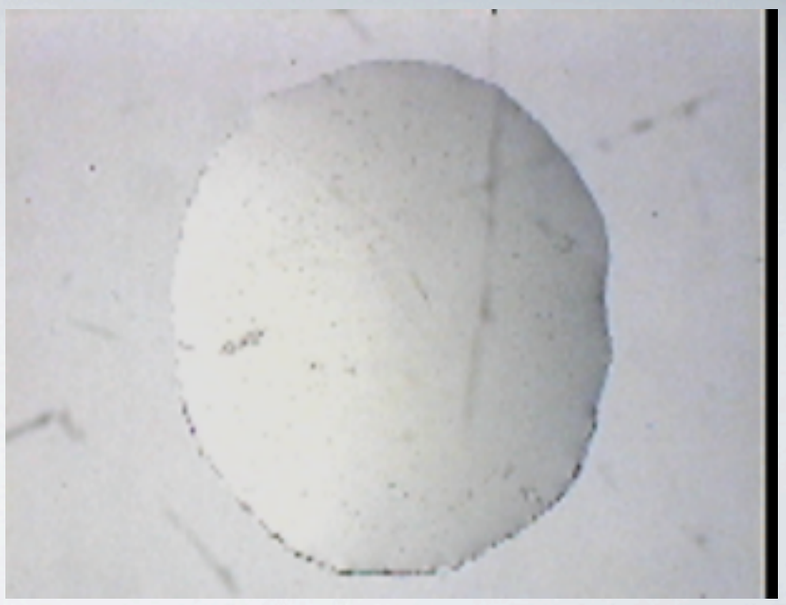


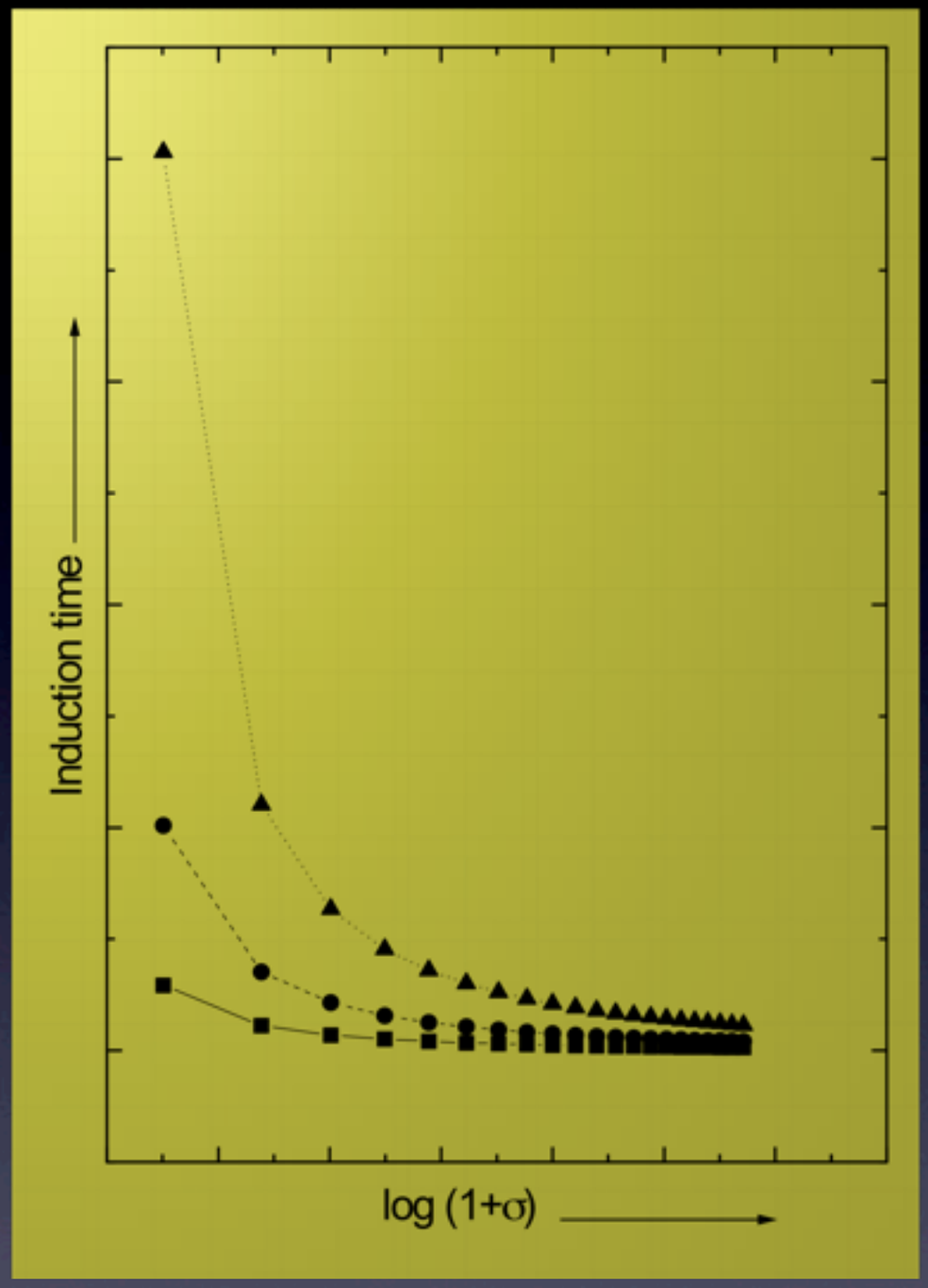












$$t_N = \frac{\kappa^{te}}{J_N} = \kappa_1 \exp\left(\frac{\kappa_2}{T^3 \ln(1+\sigma)^2}\right)$$

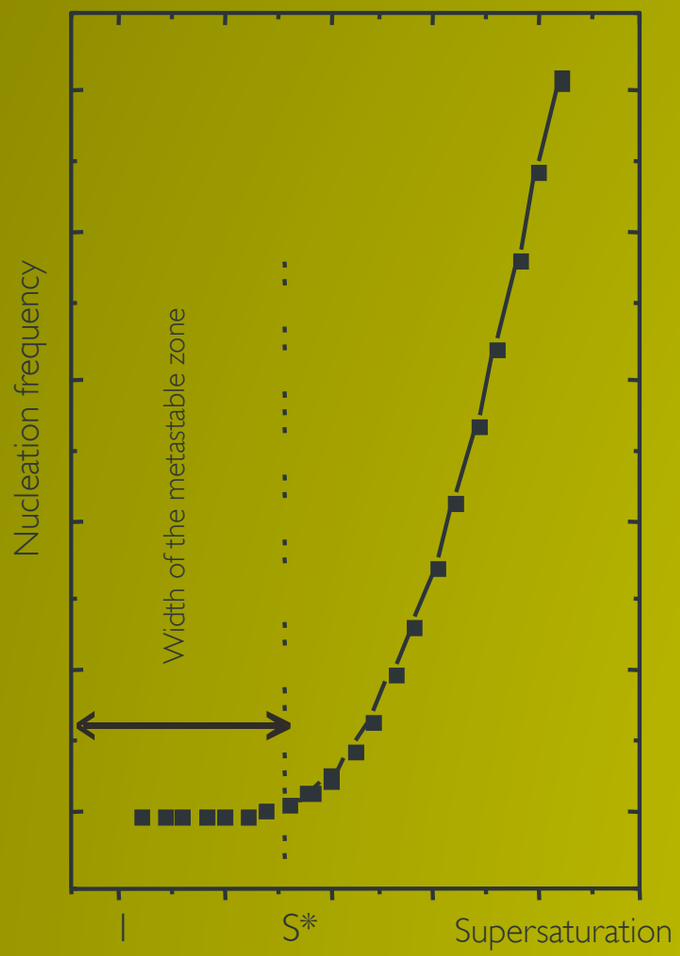
The induction time is the reverse of the nucleation flow and is the summation of three factors:

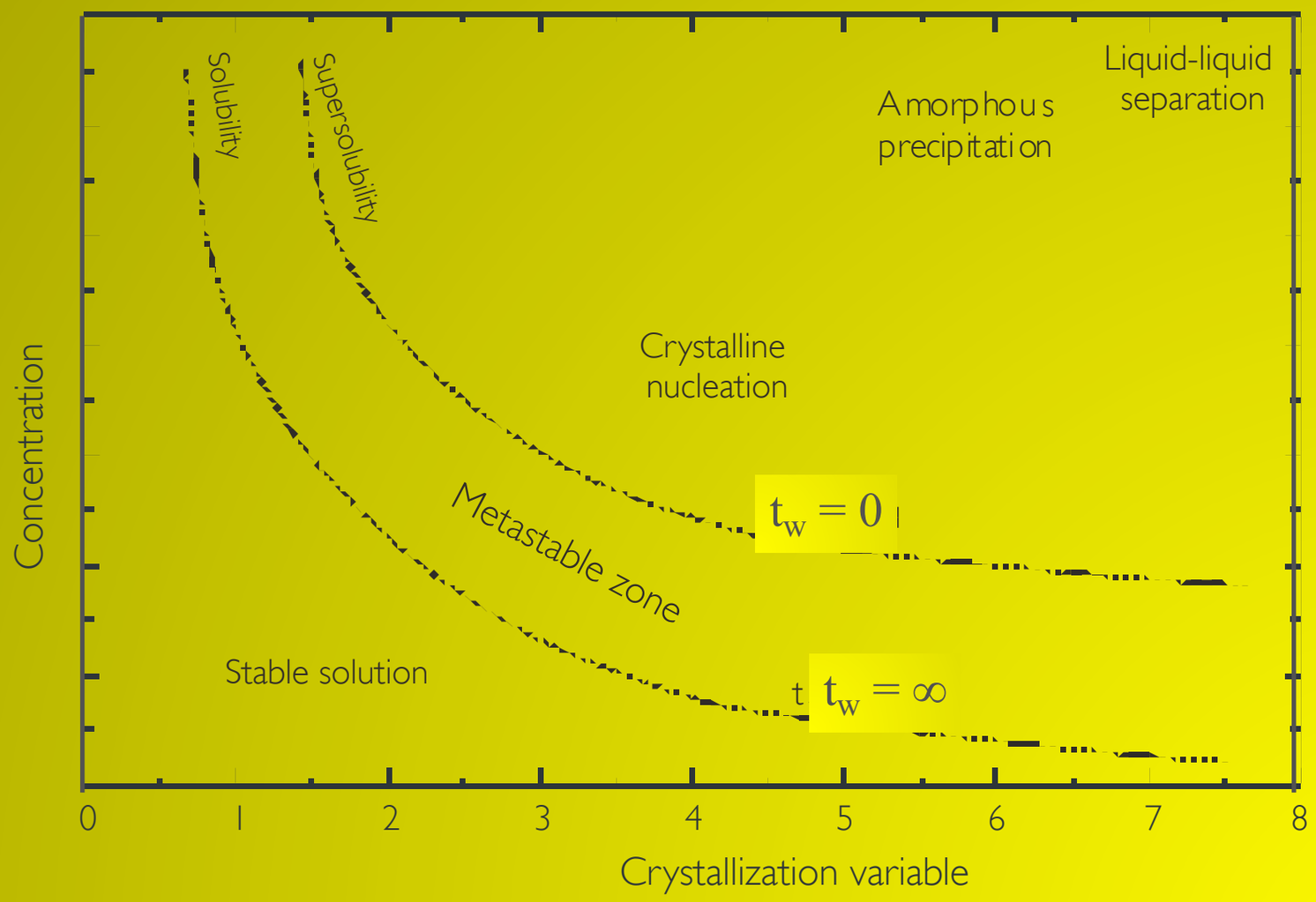
$$t_n = t_d + t_{n*} + t_g$$

The first is the time required to get a stationary distribution of size of precritical size, the second, the waiting time to obtain clusters of a critical size and the third one, is the waiting time for a stable cluster to reach the size to be detectable. This last parameter depends strongly of the experimental technique used to detect nucleation.

$t = 1/J$

Nucleation is a probablistic phenomenon





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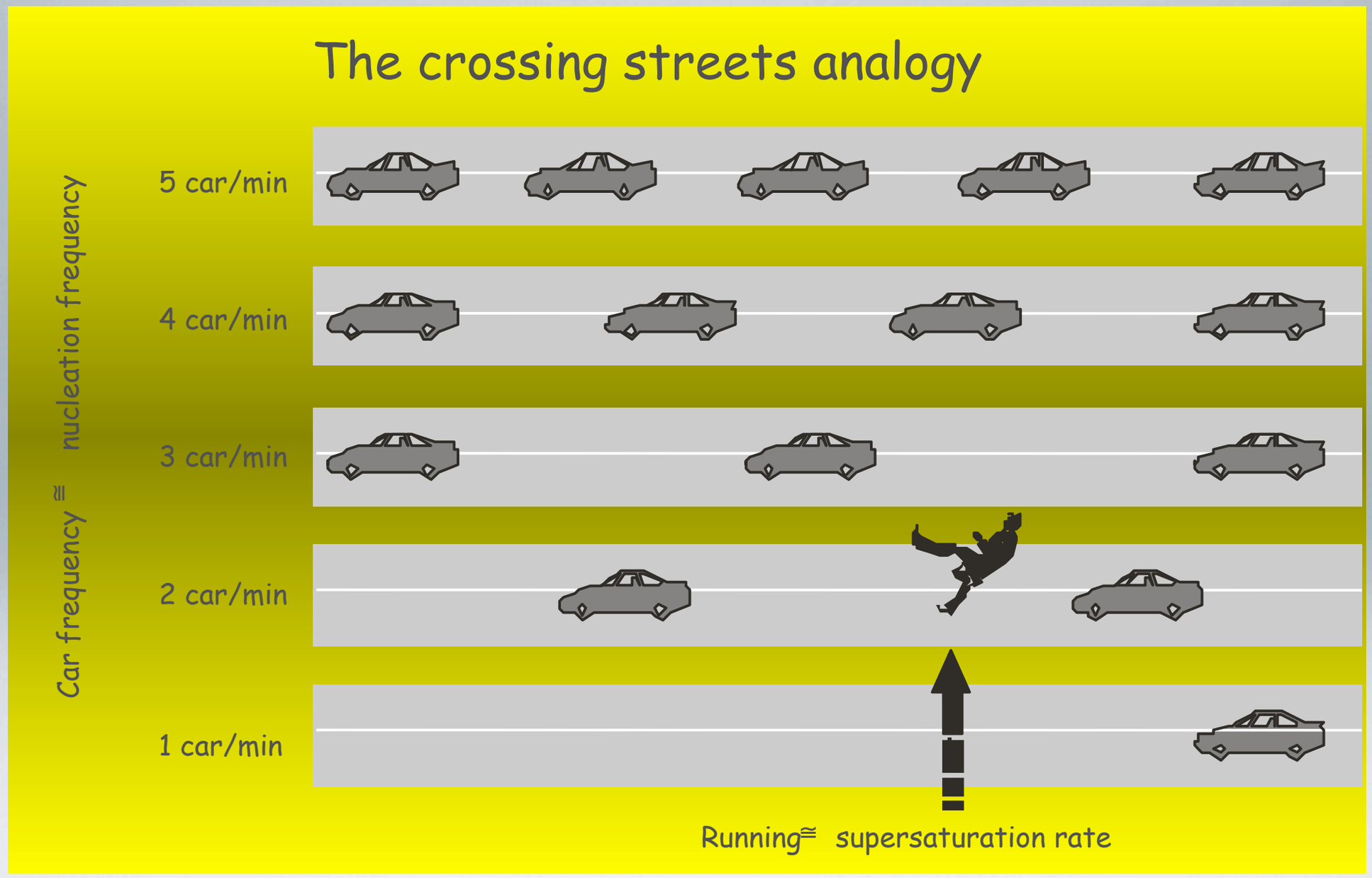

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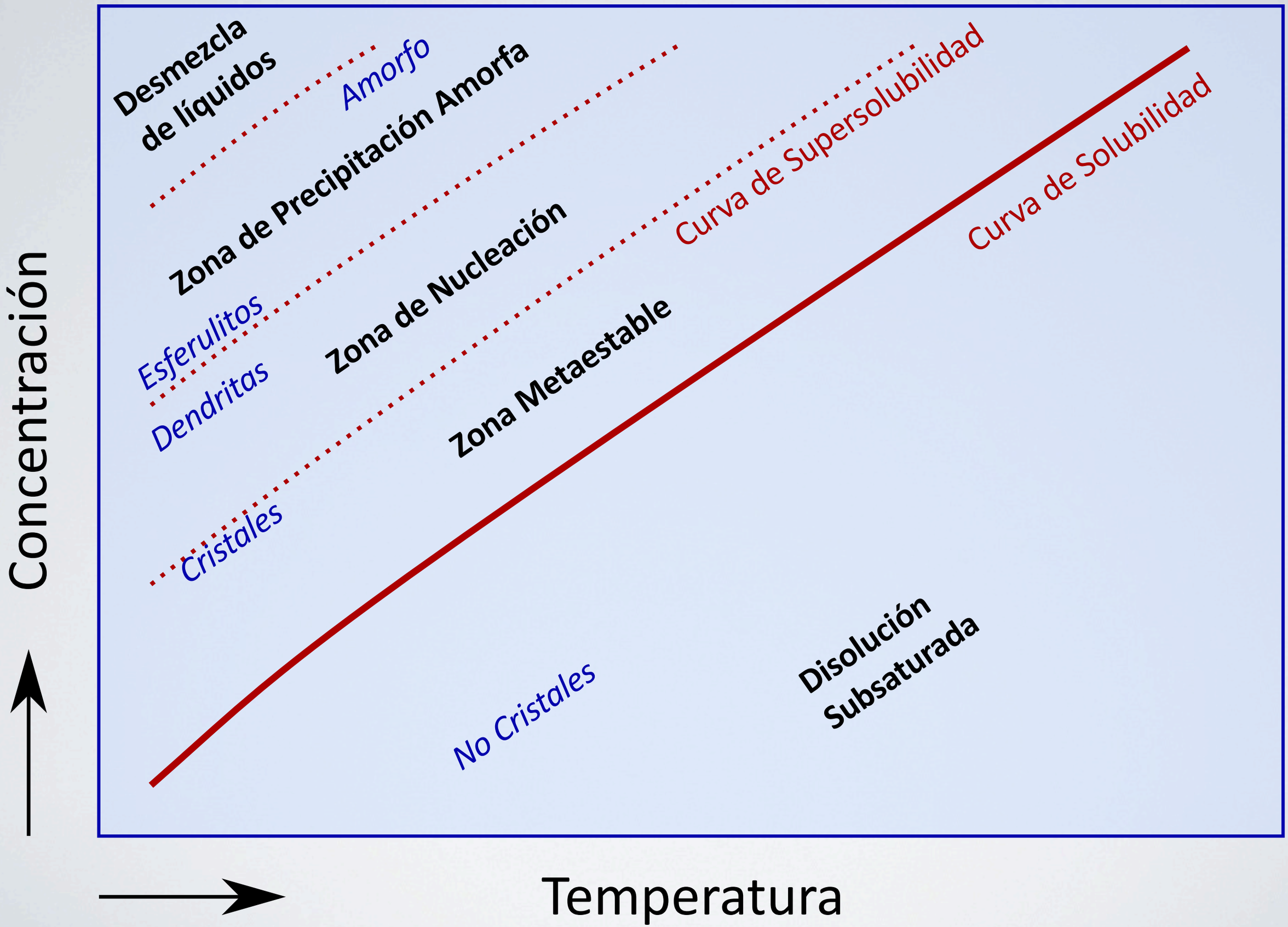
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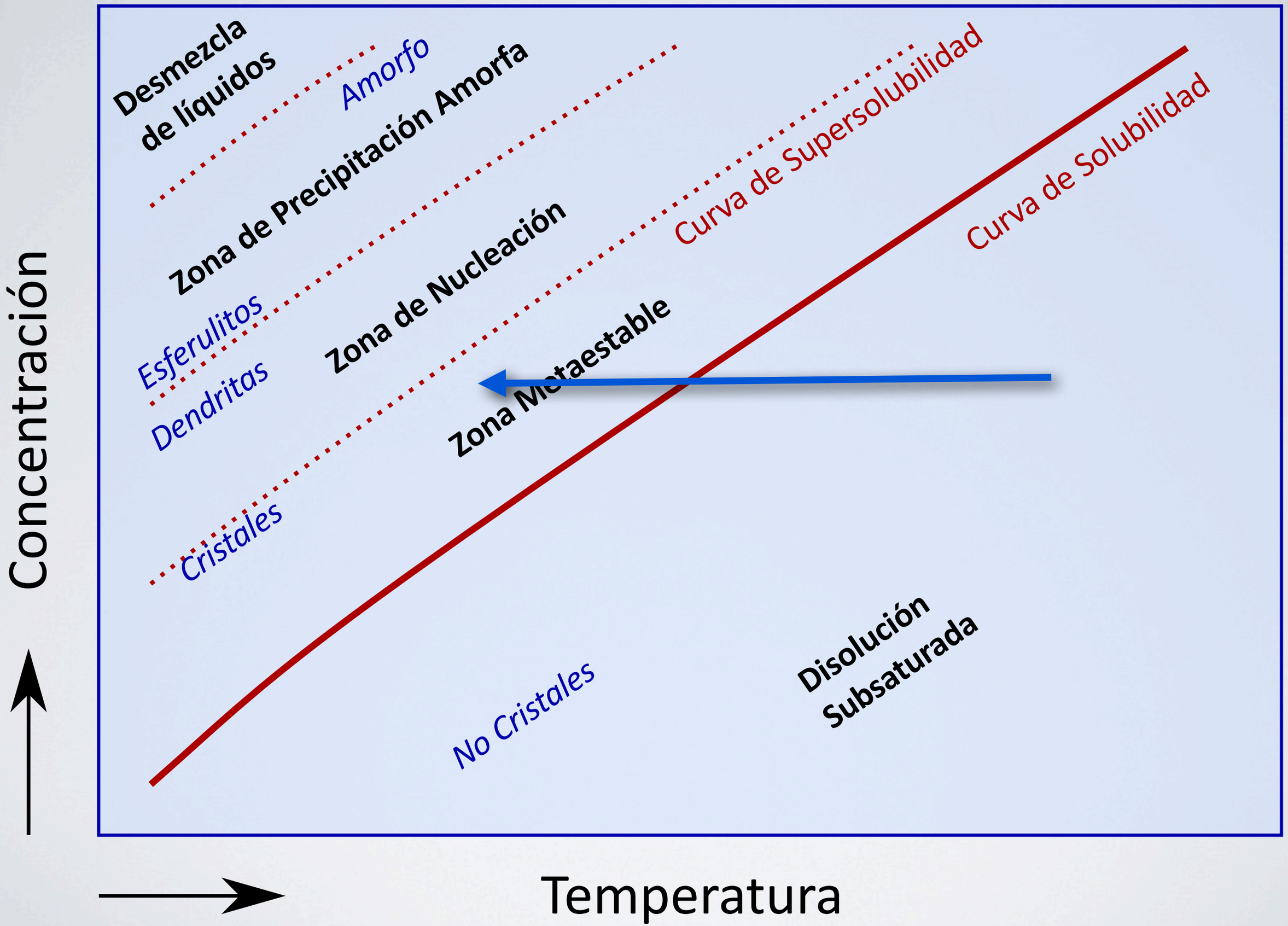
Disolución Subsaturada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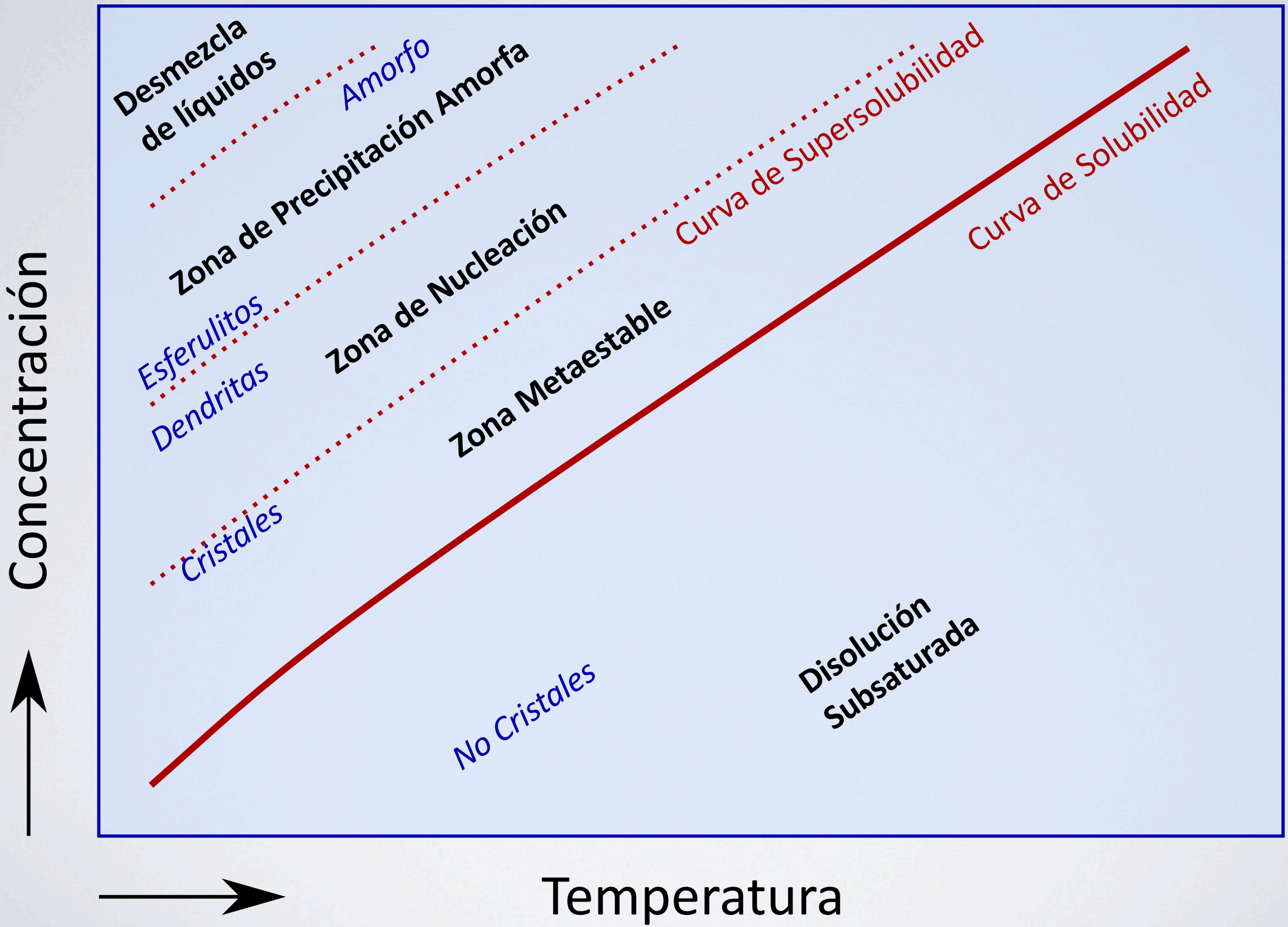
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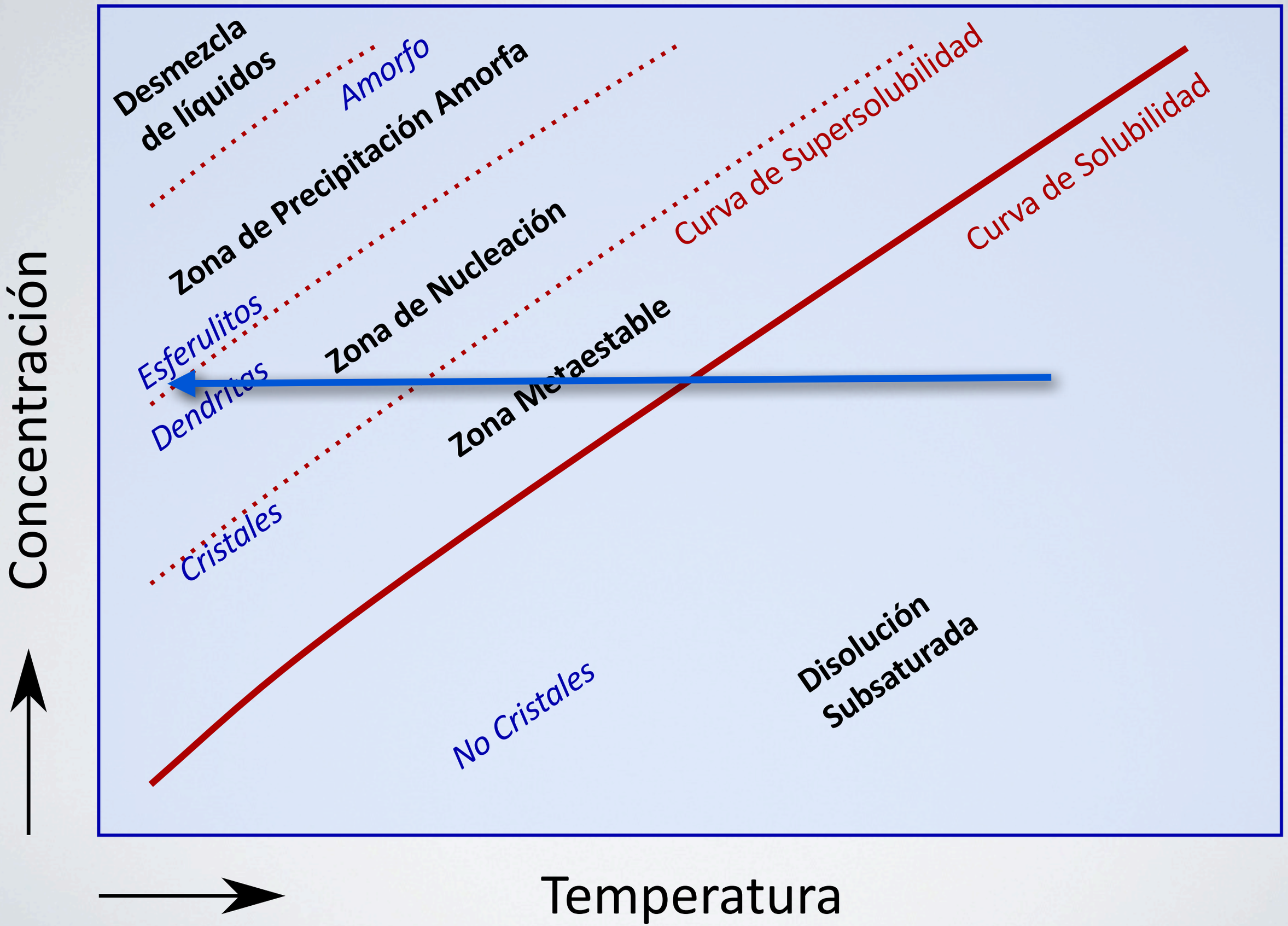
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Nucleation

Primary Nucleation

Homogeneous Nucleation

Spontaneously in the bulk of pure solution

Heterogeneous Nucleation

Induced by surfaces other that the forming crystals

Secondary Nucleation

Induced by the forming crystals

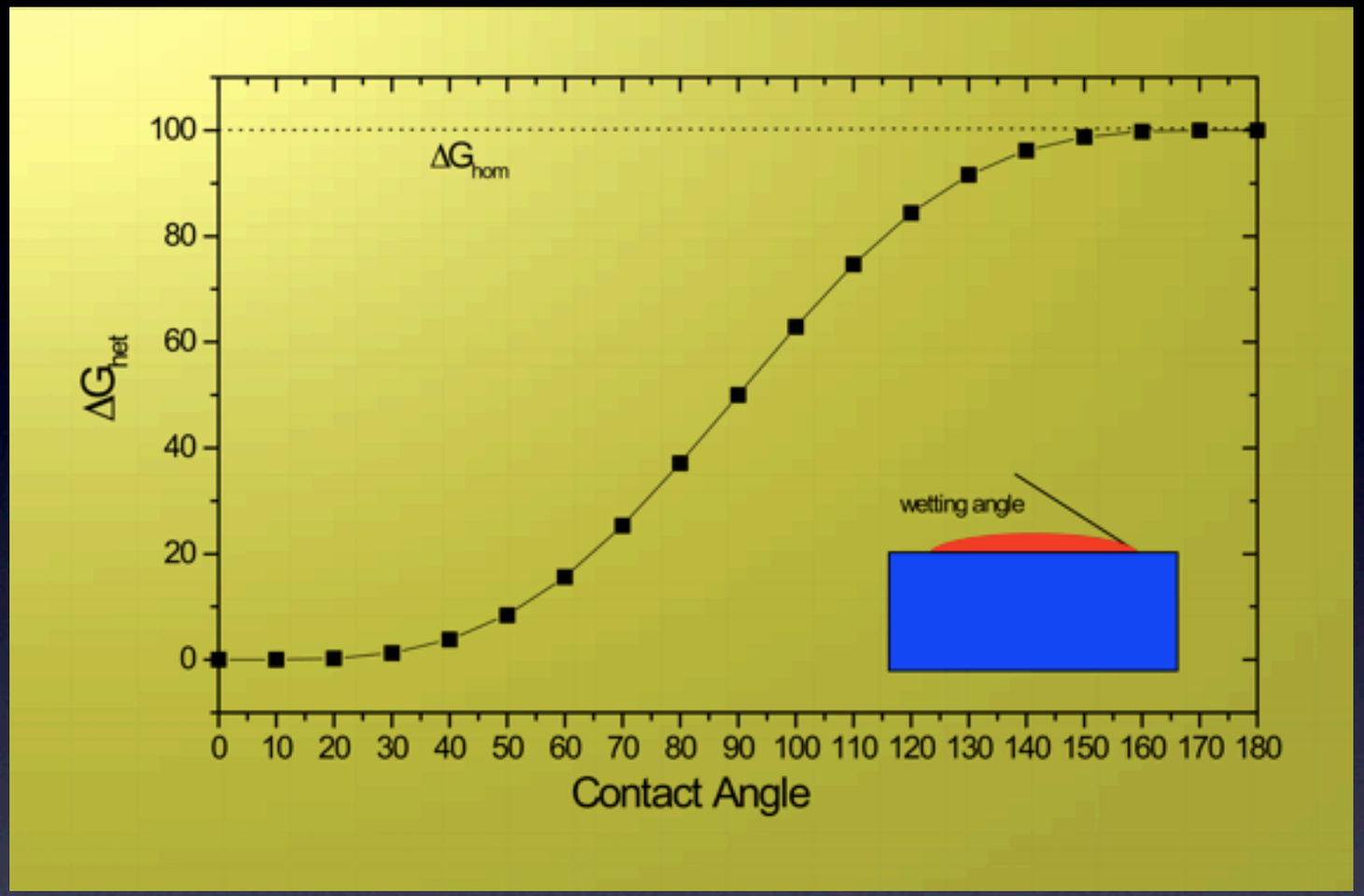
In most real systems, nucleation is hetereogeneous

Hetereogeneous nucleation

$$\Delta G_{het} = \Delta G_{hom}\left(\frac{1}{2} - \frac{3}{4}\cos\alpha + \frac{1}{4}\cos^3\alpha\right)$$

Seeding:

The crystal is used as substrate



If we plot the above expression for a given value of ΔG_{hom} we found that if the nucleus wet the substrate (α = 180) , then $\Delta G_{het} = \Delta G_{hom}$; if α = 90, ΔG_{het} = ½ ΔG_{hom}. Smaller the value of α, smaller the value of the activation energy for nucleation and it tends to zero for α = 0.

In general, any form of nucleation takes place by action of a solid surface composition different from that of the compound that crystallize is called hetereogeneous nucleation.

http://www.dailymotion.com/video/xacduc_homogeneous-nucleation_school

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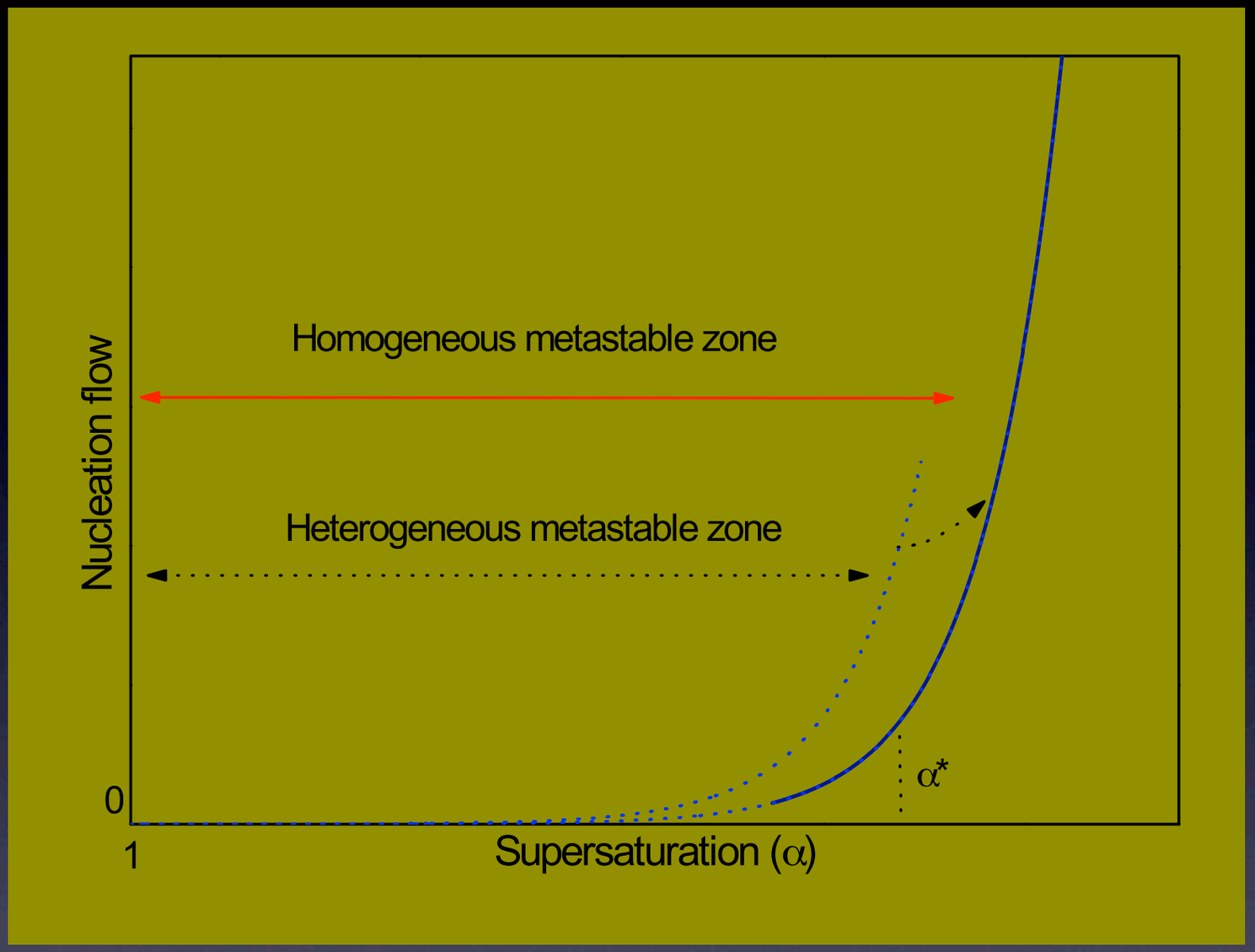

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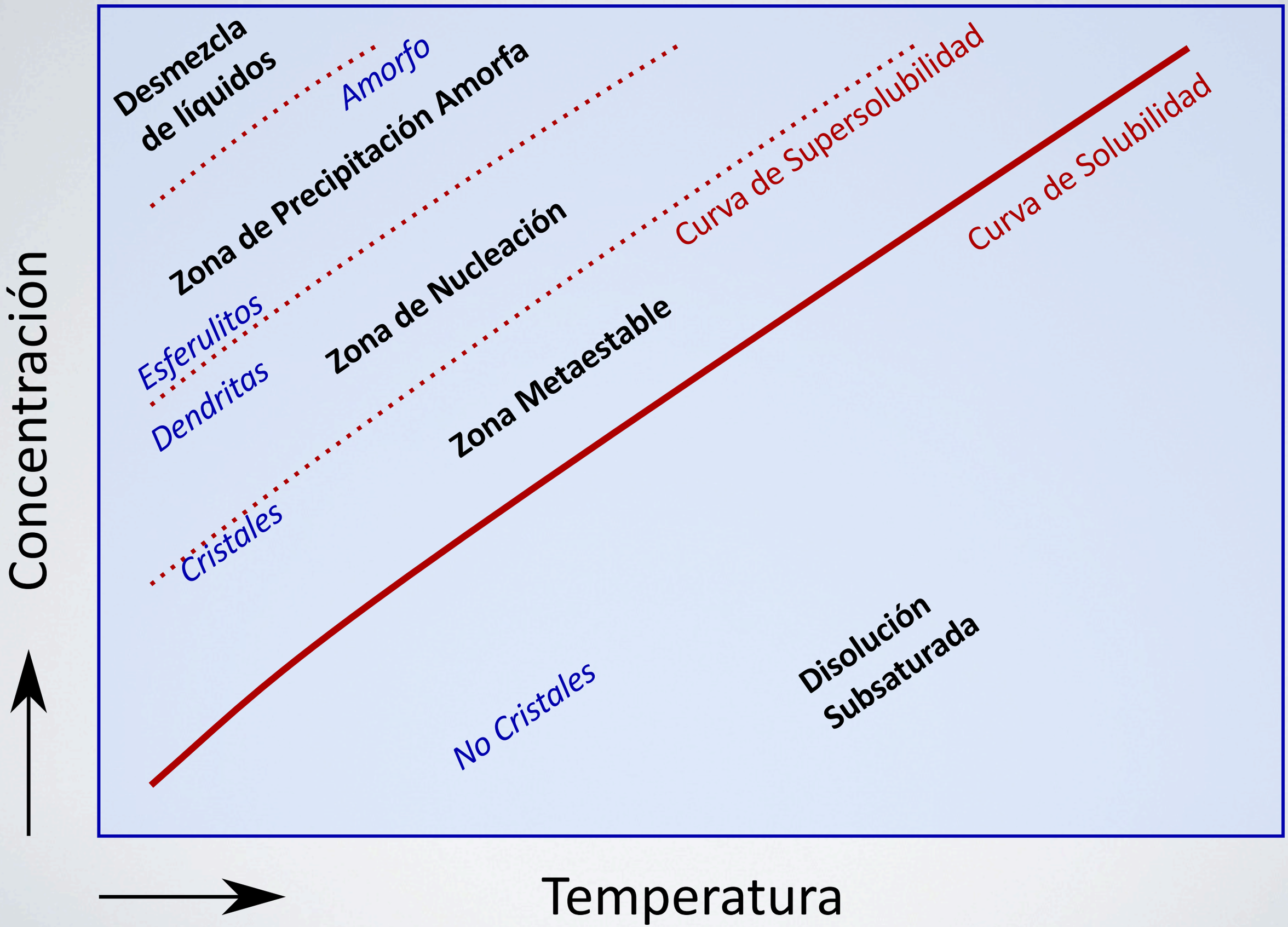
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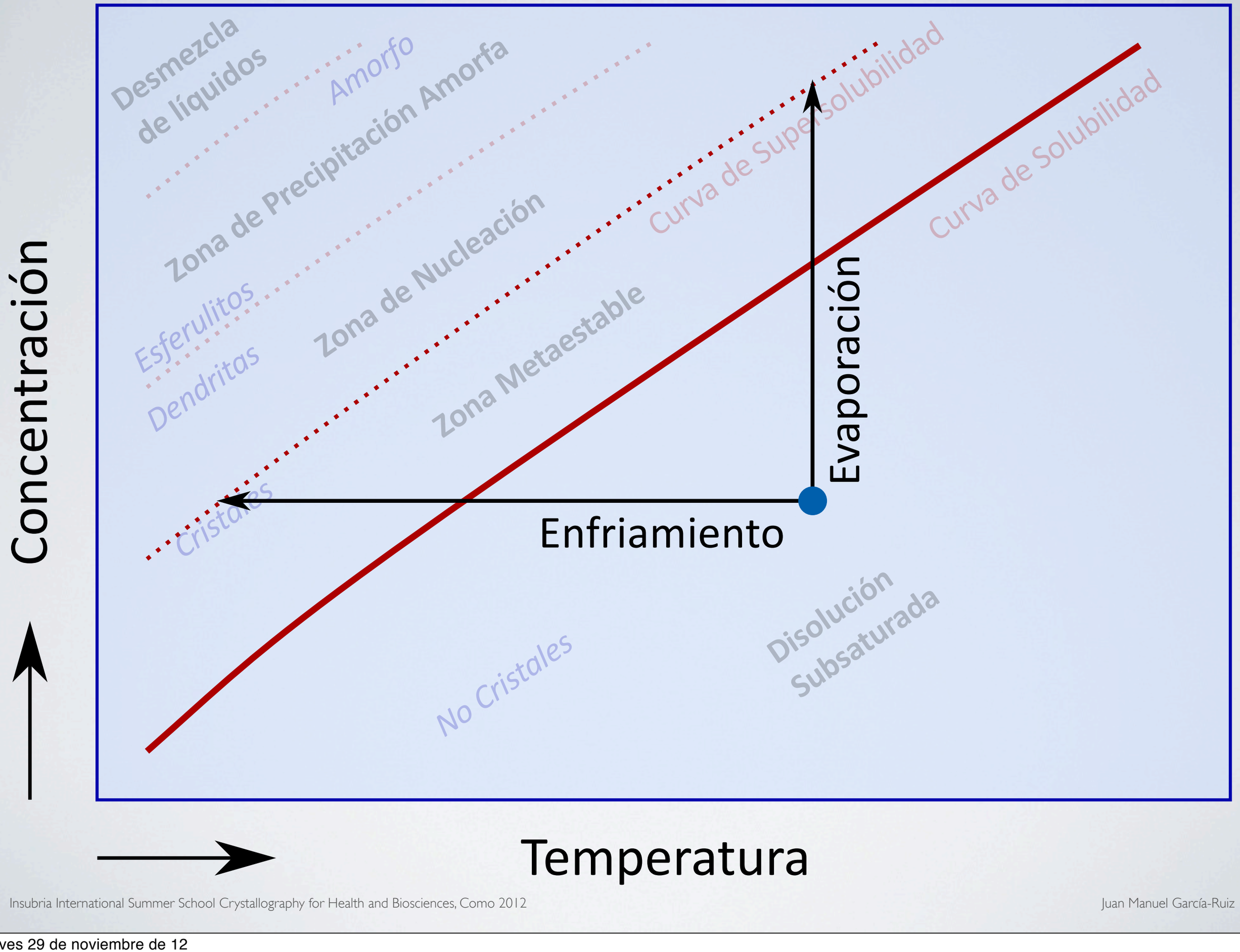
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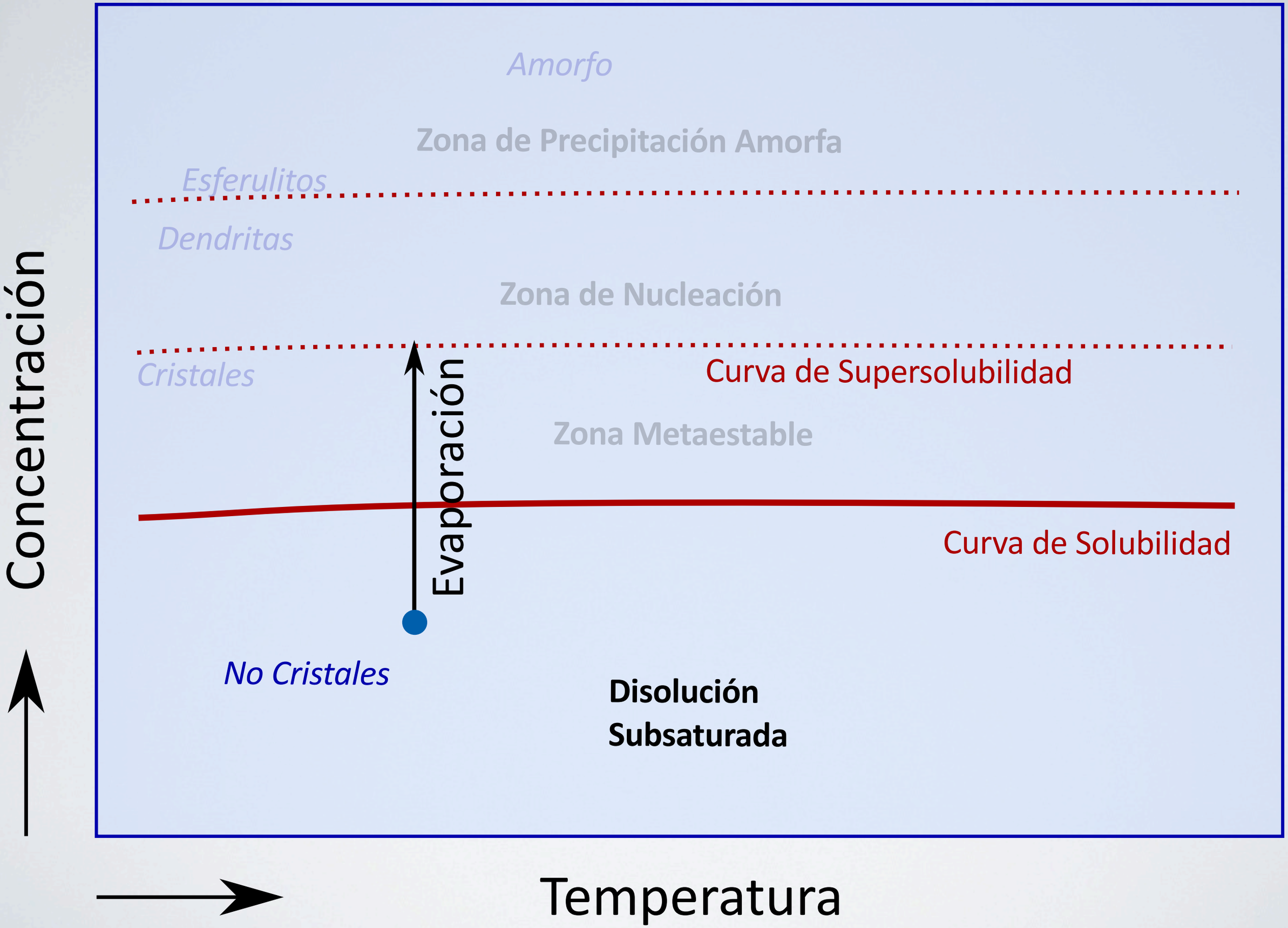
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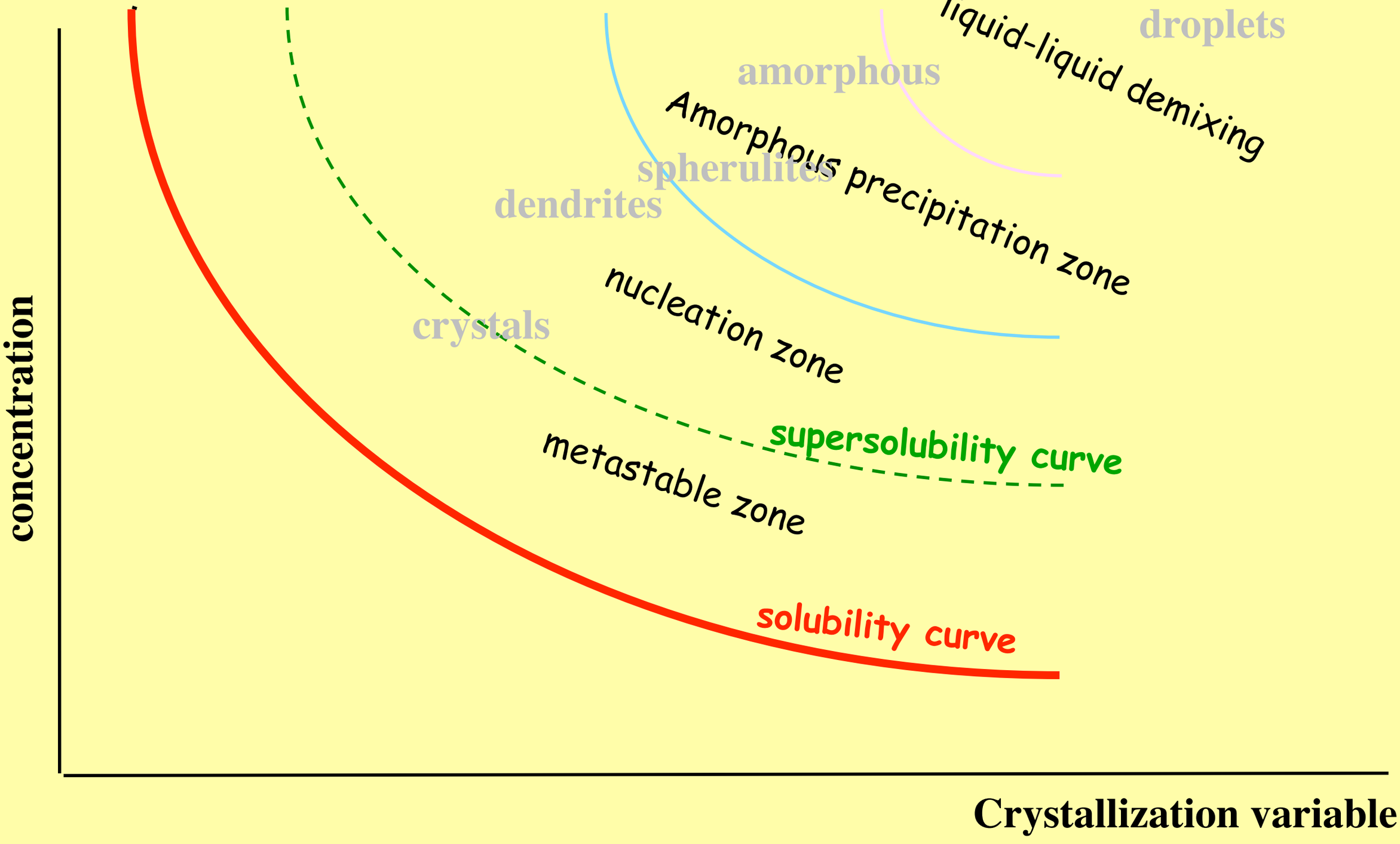

For the same path in the solubility diagram (i.e., for the same chemistry), the result of a crystallization experiment may vary drastically as a function of the rate of development of supersaturation

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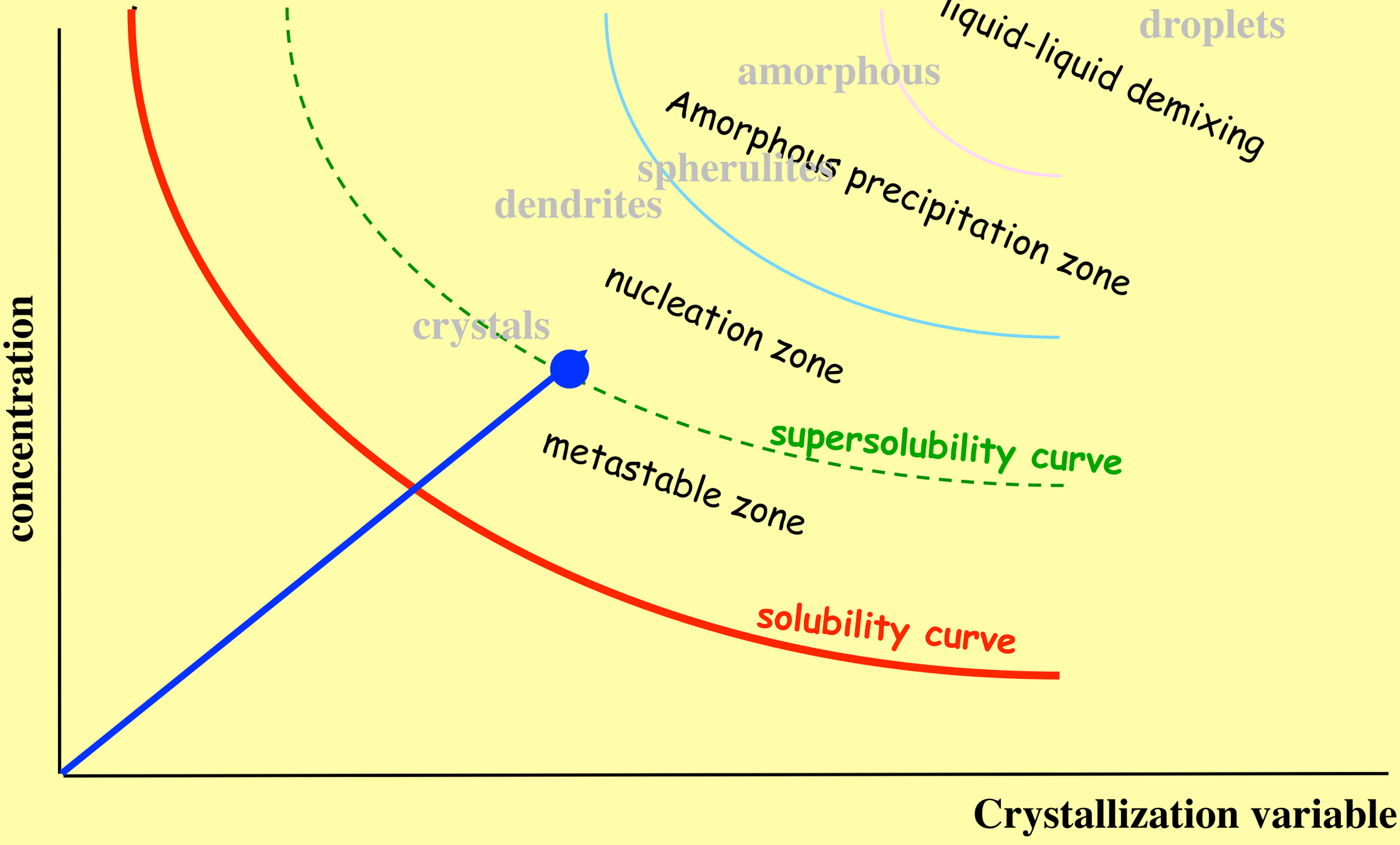

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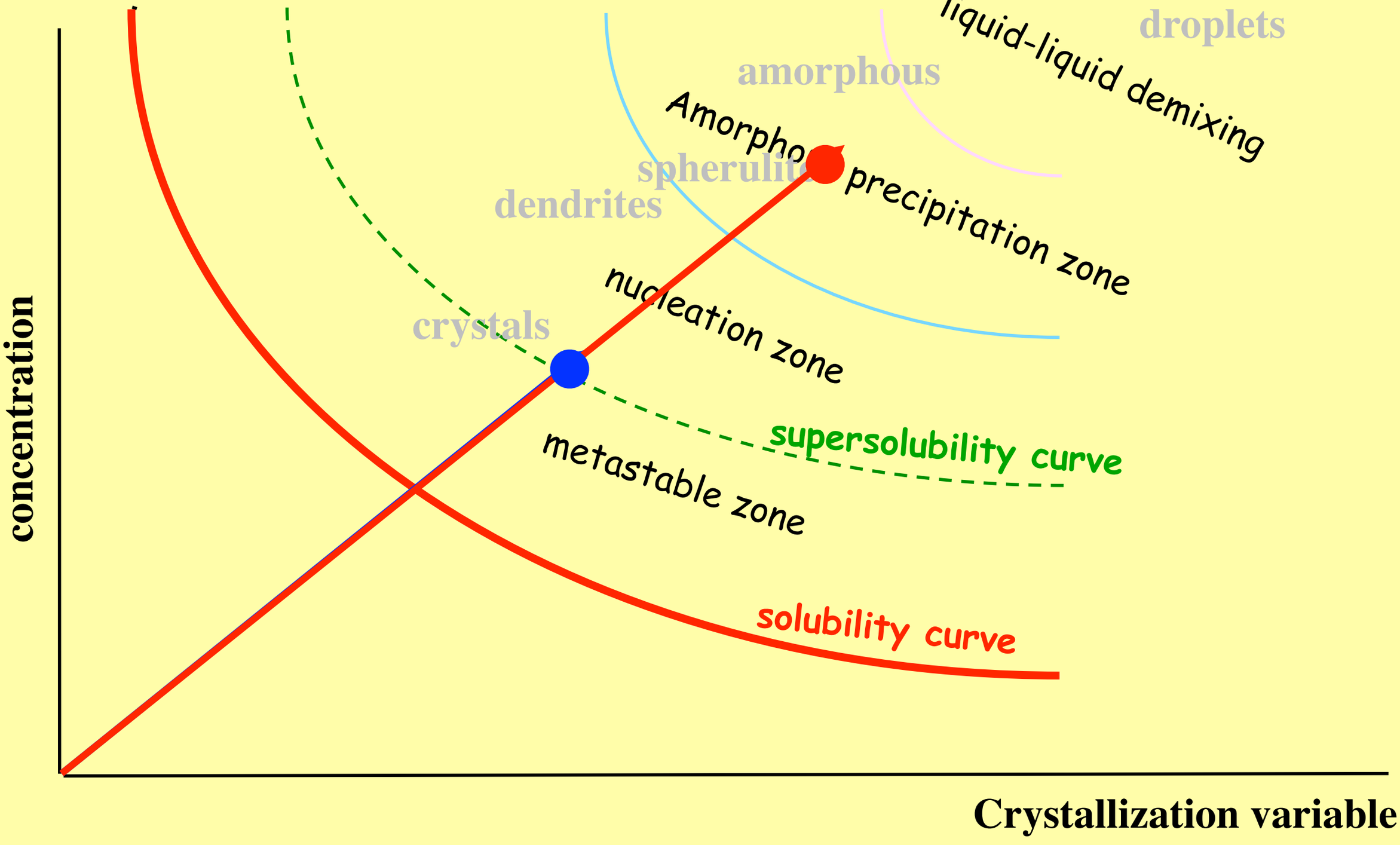

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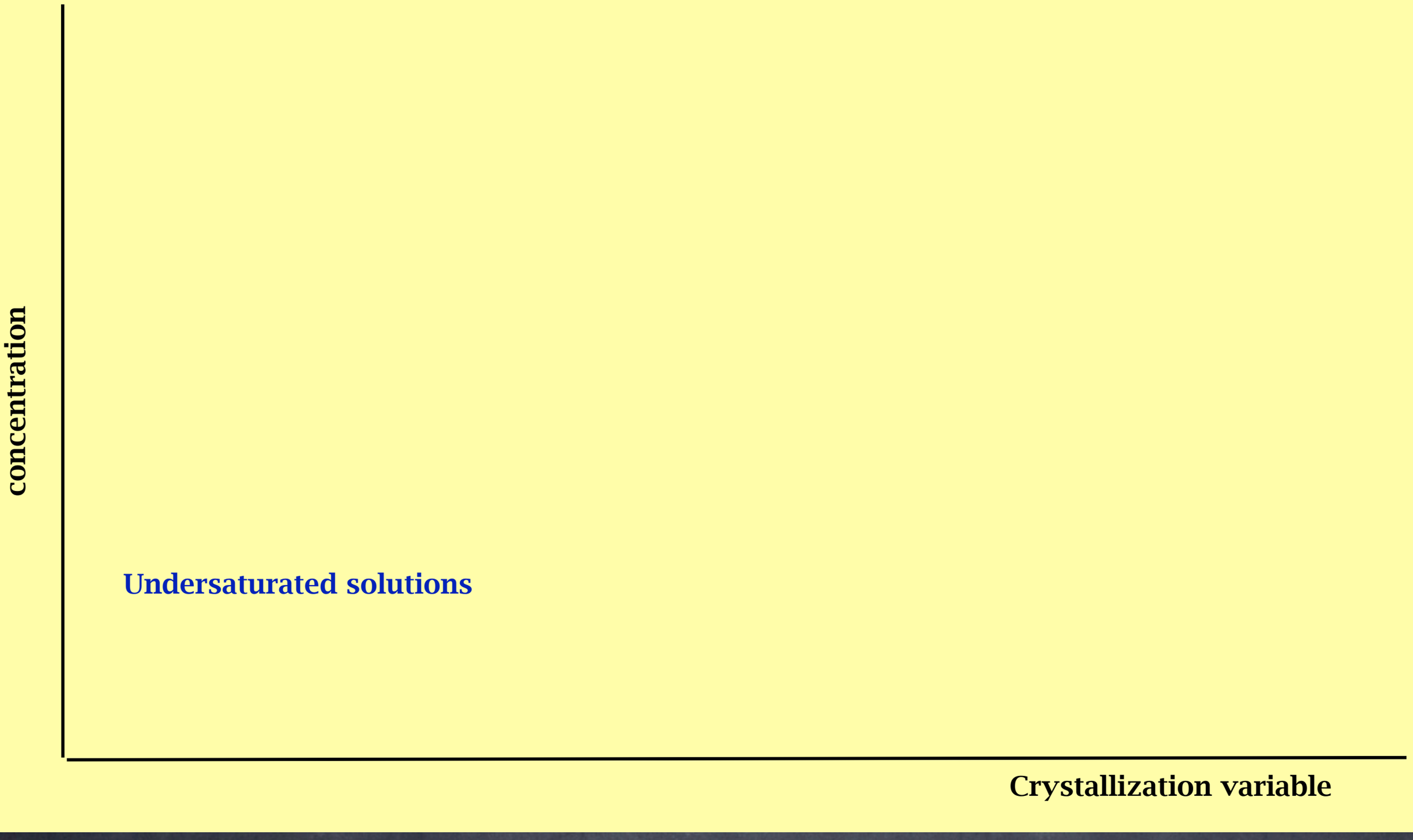
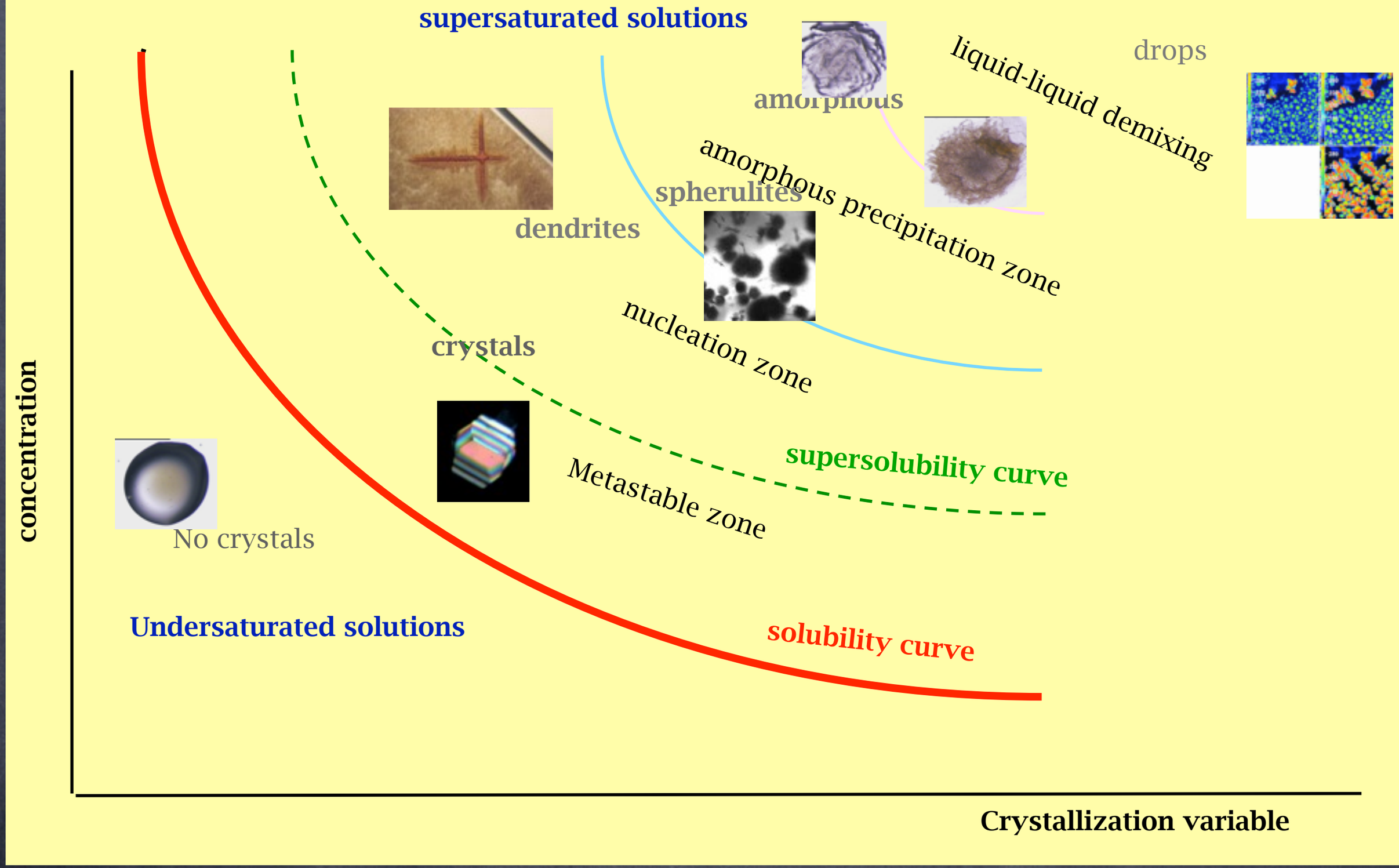
J. M. García-Ruiz, Nucleation of protein crystals, *Journal of Structural Biology*, 142 (2003) 22-31.



This diagram represents the zones for the different states of the solute (dissolved, solid or liquid) for a range of solute concentration as a function of a crystallisation variable (for example, concentration of solubility reductor, pH, temperature, etc) all other variables being kept constant.



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