EURO FOOD'S WATER

CLUSTERING AND WATER ACTIVITY IN CONCENTRATED SUCROSE SOLUTIONS

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UNIVERSITÉ DE REIMS CHAMPAGNE-ARDENNE

SURVEY

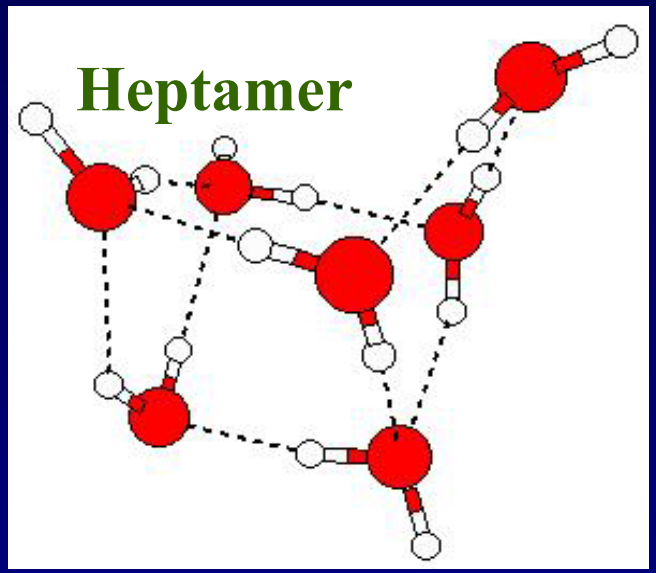
- **Introduction:**
  - **Molecular interactions in aqueous sucrose solutions (water-water ; water-sucrose; sucrose-sucrose)**
- **Water-Sucrose Interactions (Hydration):**
  - **H-bond characteristics and sucrose hydration**
  - **Hydration number and water activity**
- **Sucrose-Sucrose Interactions (Clustering):**
  - **evidence for sucrose cluster formation**
  - **Free energy, size of cluster and homogeneous nucleation**
- **Clusters and a molecular approach of crystallization**
  - **Current crystal growth theory: limitation of the role of diffusion**
  - **Role of clusters in crystal growth and heterogeneous nucleation**
- **From Clusters to Nanoparticles:**
  - **Sucrose nanoparticles identification by FTIR**
  - **Sucrose nanoparticles and Drug Release**
- **Conclusion**

INTRODUCTION

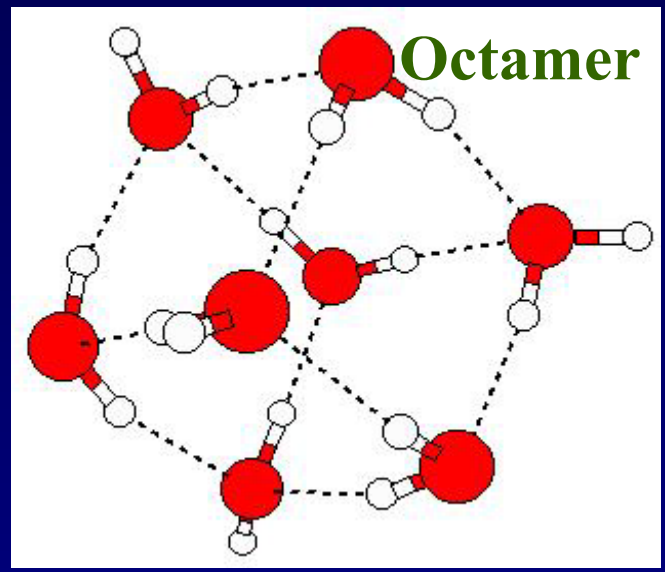
- **interactions in sucrose-water system:**
  - **Water – water interactions** (mixture of small clusters in a state of chemical equilibrium), M. Starzak, M. Mathlouthi, *Food Chem. 82(2003) 3-22.*
  - **Sucrose – water interactions** (relationships between hydration and density) A. Gharsallaoui, B. Rogé, J. Genotelle, M. Mathlouthi, *Food Chem. 106(2008)1443.*
  - **Sucrose – Sucrose interactions: Water activity in concentrated sucrose solutions,** M. Starzak, M. Mathlouthi, *Zuckerindustrie,127(2002) 175-185.*

    Clustering? *Lack of information*

INTRODUCTION



Small water clusters



Water clustering reaction scheme

$$(H_2O)_{i-1} + H_2O \overset{K_{A,i-1}}{\longleftrightarrow} (H_2O)_i \ , \quad i = 2, \ ....,n$$

From autocorrelation functions: H-bond of water-water comparable for pure water and bulk water in sugar solutions → same density

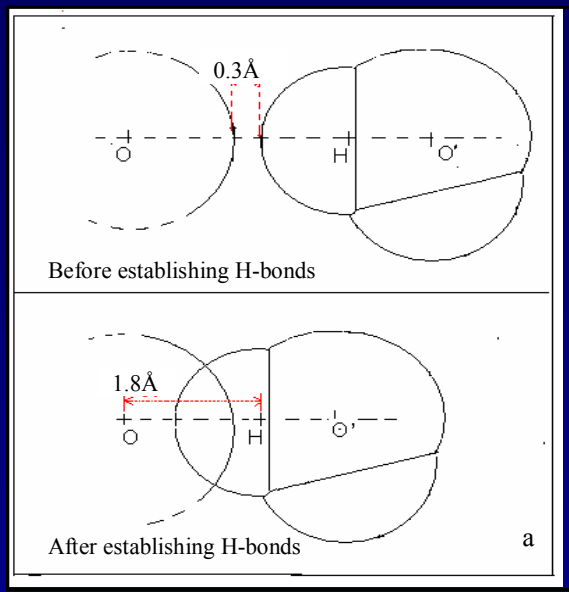
(Lee, Debenedetti, Errington, J. Chem Phys. 122(2005) 204511)

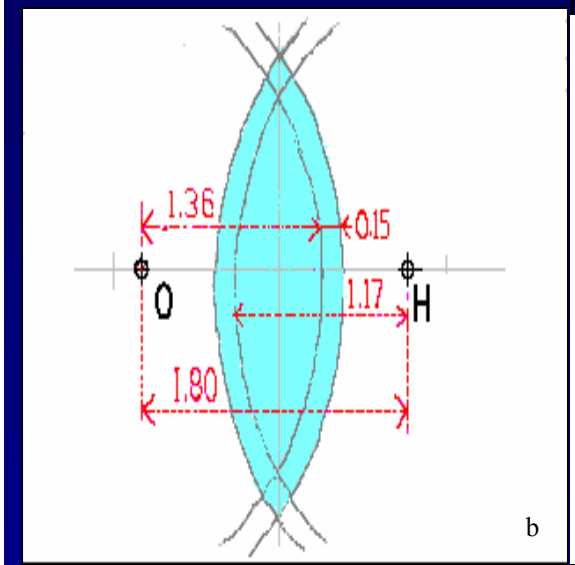
INTRODUCTION

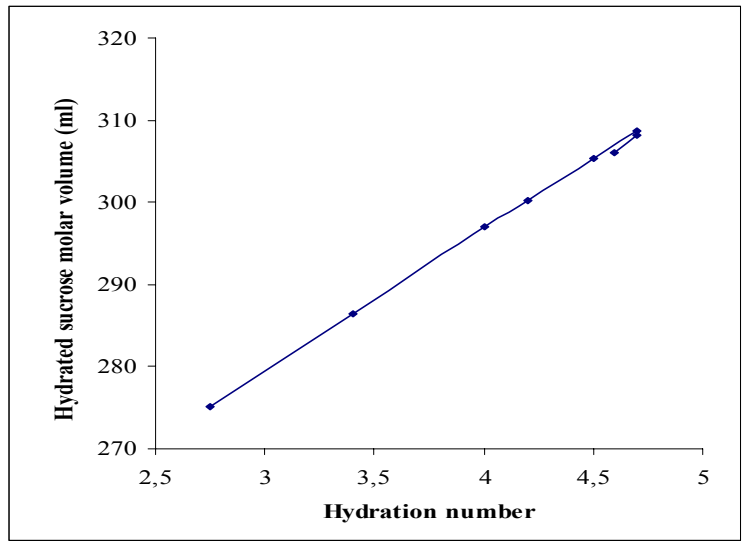
Sucrose-water interactions

volume $V_{hS,20}$ occupied by a hydrated sucrose molecule :

$V_{hS,20} = 221 + 16.4\ n_h$







From overlapping of vdW spheres upon water-sucrose intercation: 9% contraction

16.4 mL increase of volume per mole of hydration water 9.2% contraction

A. Gharsallaoui, B. Rogé, J. Genotelle, M. Mathlouthi, *Food Chem. 106(2008)1443*

INTRODUCTION

Sucrose-sucrose interactions

$$S_i + S \xleftrightarrow{K_{Ci}} S_{i+1}\,, \qquad i = 1,\ 2,\ \ldots,\ m-1$$

$$K_{Ci} = q_i\, K_C$$

$$K_C = K_C^{\circ} \exp\left[\frac{\Delta H_C}{R}\left(\frac{1}{T_{\circ}} - \frac{1}{T}\right)\right]$$

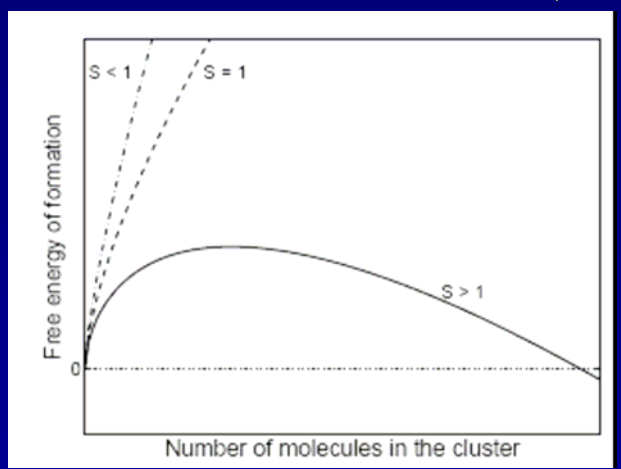
where K_C° is the value of K_C at $T_{\circ} = 25°C$.

$$K_{Ci} = \frac{[S_{i+1}]}{[S_i][S]} = \frac{x_{i+1,\,0}}{x_{i,\,0}\, x_S}\,, \qquad i = 1,\ 2\ \ldots,\ m-1$$

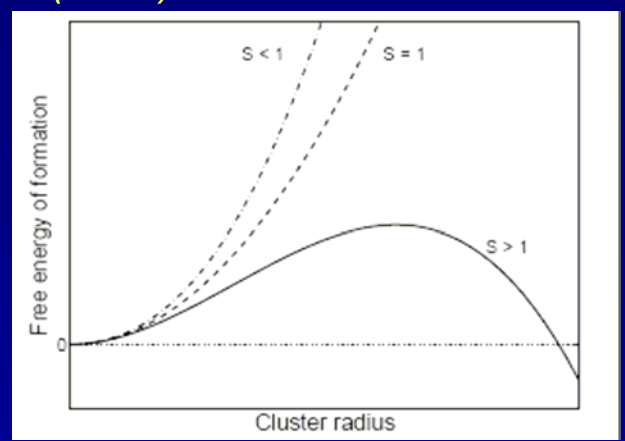
q_i: *clustering frequency independent from T*

K_{ci}: *Clustering equilibrium constant*

M. Starzak, M. Mathlouthi, *Zuckerindustrie,127(2002) 175-185.*



Schematic picture of free energy of cluster formation in function of number molecules (left) and cluster radius (right)
S: saturation ratio

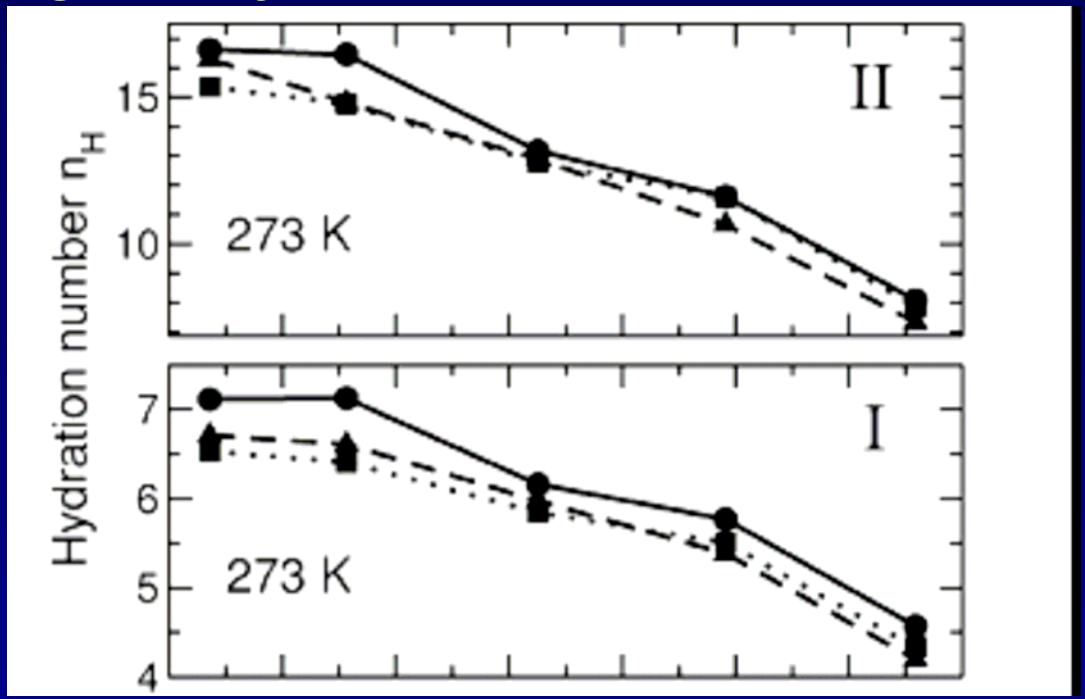


Antti Lauri, M. Sc. Thesis, Helsinki, 2006

SUCROSE HYDRATION

Criteria for H-bonding in highly associated liquids:

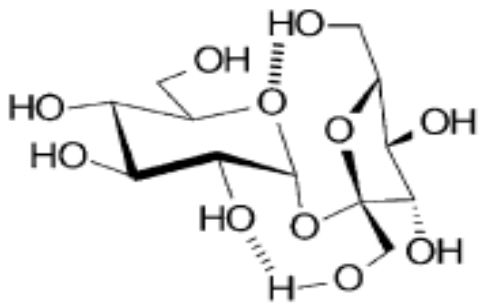
- **energy threshold E_{ij} < 8 kJ/mol (Temperature dependent)**
- **geometry condition OHO > 150°**



I: d_{OO} < 34 nm – OHO > 160°
II: d_{OO} > 34 nm – OHO < 160°

Lerbret et al., *J. Phys. Chem. B, 109(2005) 11046*

SUCROSE HYDRATION



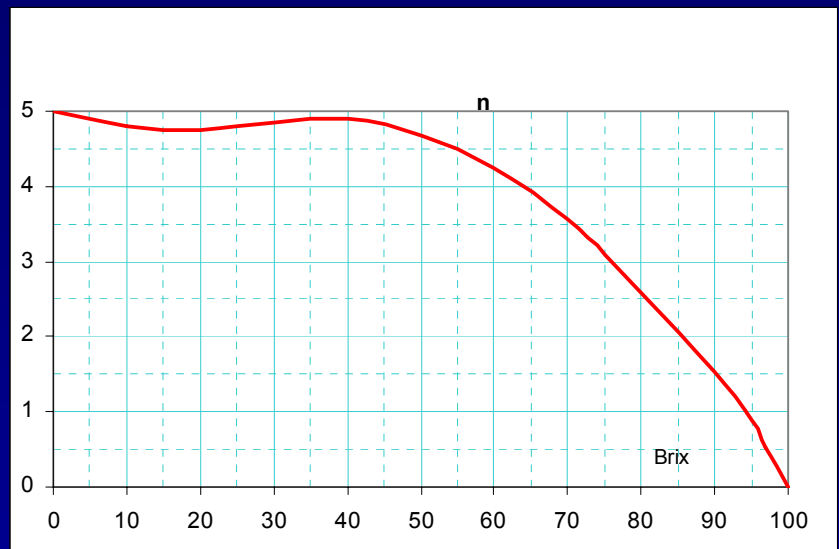
Sucrose molecule:

- **8 OHs**
- **2 intra-molecular H bonds (C>40%)**
- **6 equatorial OHs**
- **OH on C_4 not fitting H-bond criteria**

$$Aw = \frac{55.51 - w}{55.51 - w + m}$$

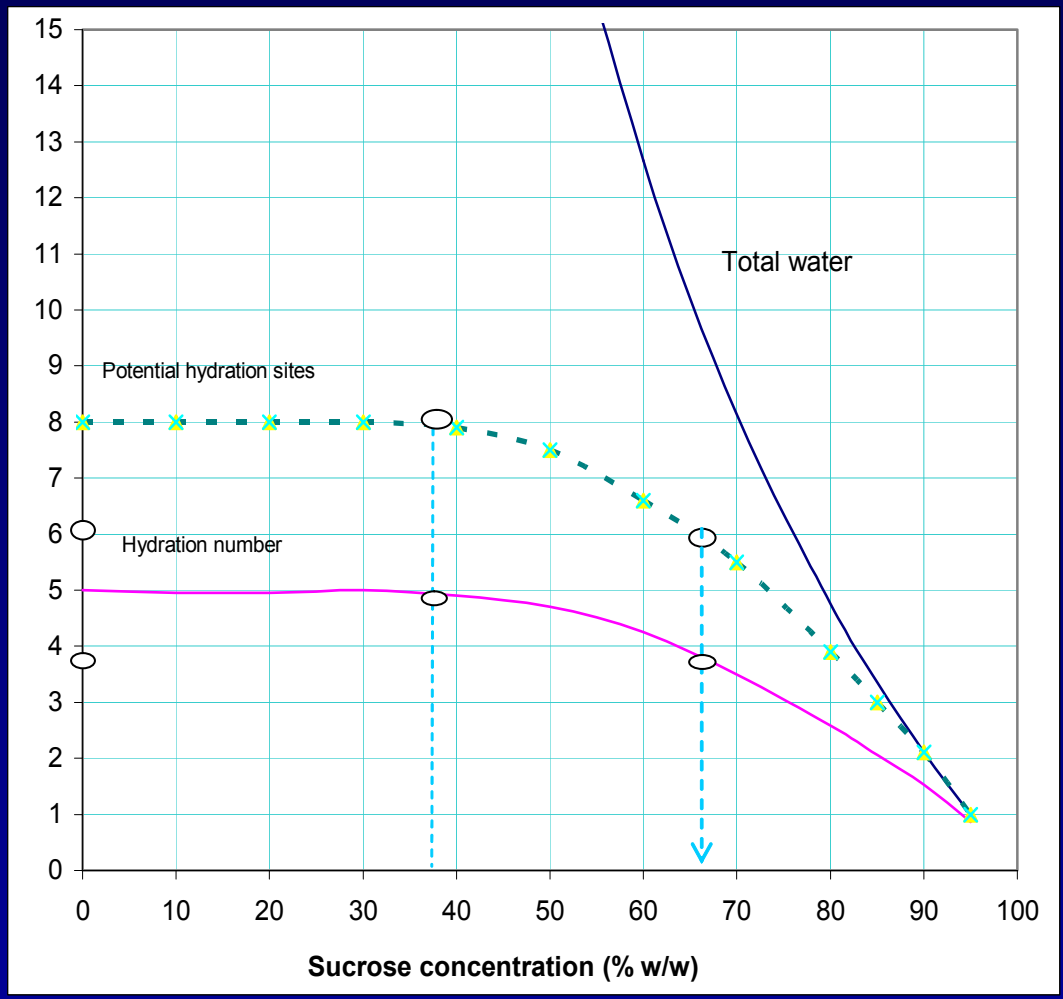
$$w = nm$$

n_h = 5 for C< 40%



n = w/m average hydration number
w = hydration water; m:molality
n = f(Brix) from a_w values (Norrish;
Bressan C., Mathlouthi, M., *Zuckerindustrie, 119(1994)652-658*

SUCROSE HYDRATION



n_h/OH sites = 5/8 = 0.63 for C<38% sucrose at 20°C consistent with the ratio of 70% of stable H-bonds at 0°C and 30% at 100°C

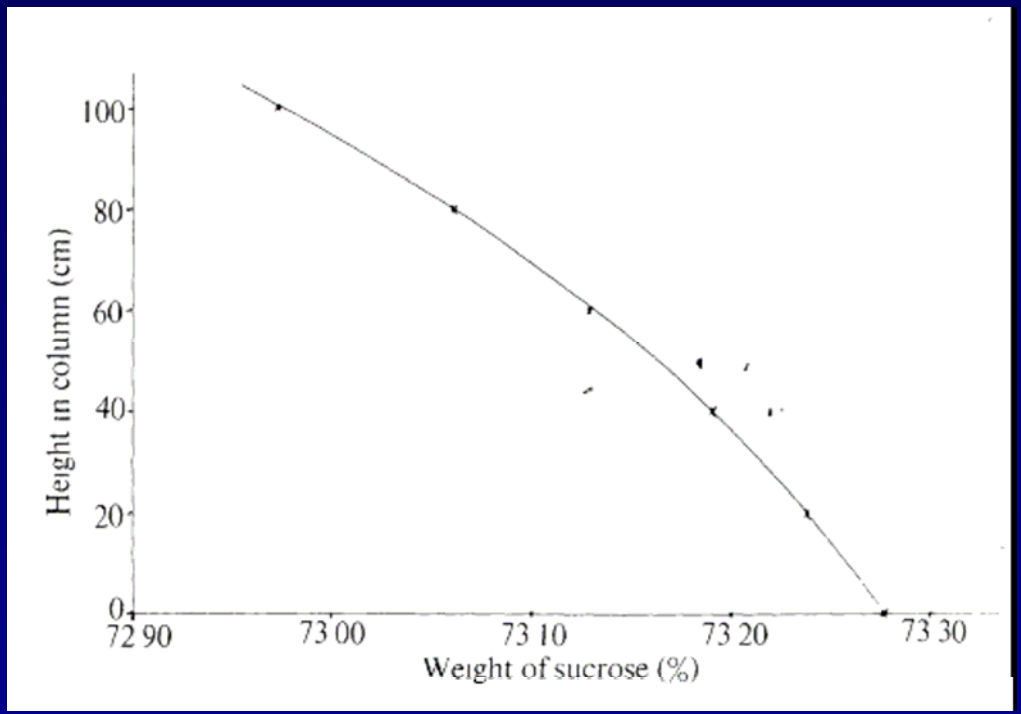
by J.Texeira *(Courrier CNRS, 2005)*

For C>38%,reduction of number of OH sites: folding of sucrose molecule between ~40 and 66%

At C = 66% (saturation at 20°C) : n_h/OH sites = 3.8/6 = 0.63
C>66% : Clustering

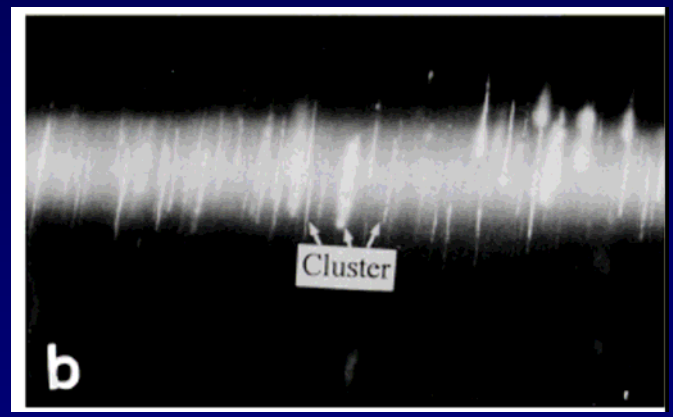
Evidence for sucrose clusters

Sedimentation in supersaturated solutions



Sucrose concentration vs depth of solution
Allen et al., *Nature Phys Sci.235(1972) 36*

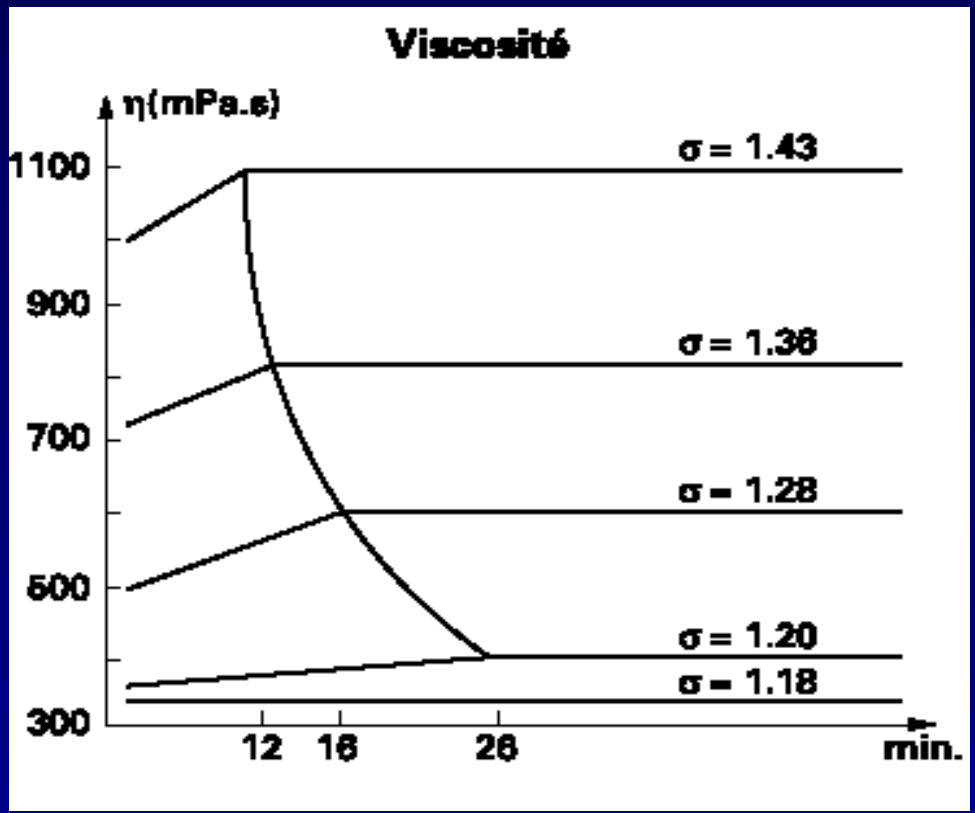
Sucrose solution



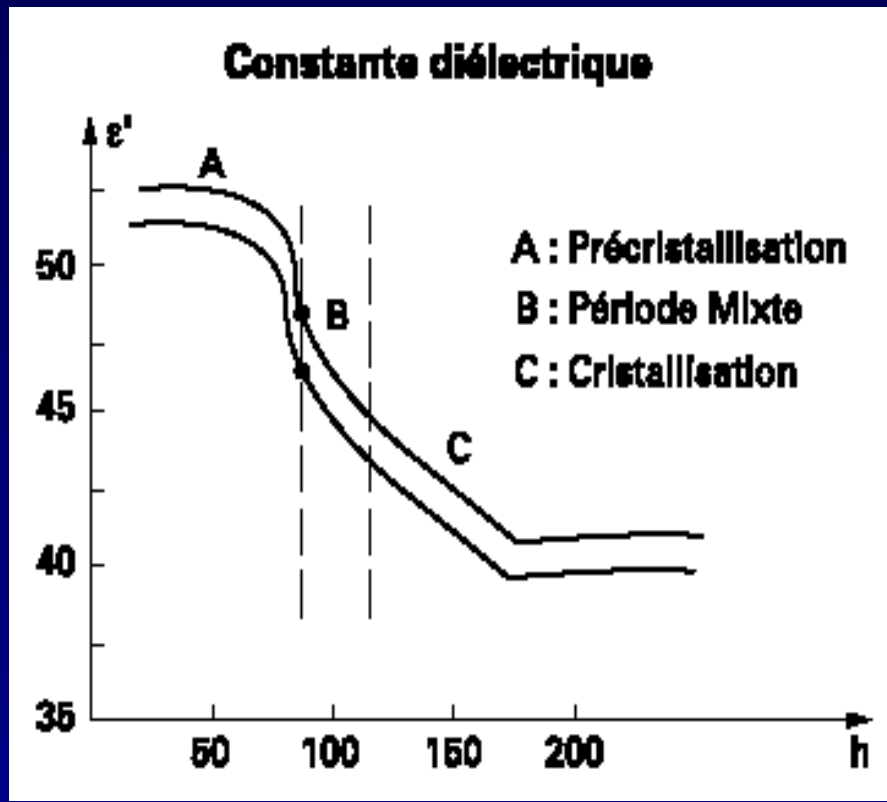
Pure water

Light scattering images
Li & Ogawa, *J. Crystal Growth,211(2000*

Evidence for sucrose clusters



Change in viscosity vs time of storage due to clustering for $\sigma > 1.2$
Tiknomiroff, *Indus. Agri. Alim. 82(1965)755*



Variation of dielectric constant of supersaturated sucrose solution
Tiknomiroff, *Indus. Agri. Alim. 82(1965)755*

Evidence for sucrose clusters

- Massive instantaneous nucleation in quiescent supersaturated solution upon onset of agitation
- Agitation makes clusters meet other clusters, coalesce to reach critical size of nucleus r_c

Gibbs free Energy of Embryo (cluster having radius r, σ surface tension and ΔG_v Free energy change associated with phase change)

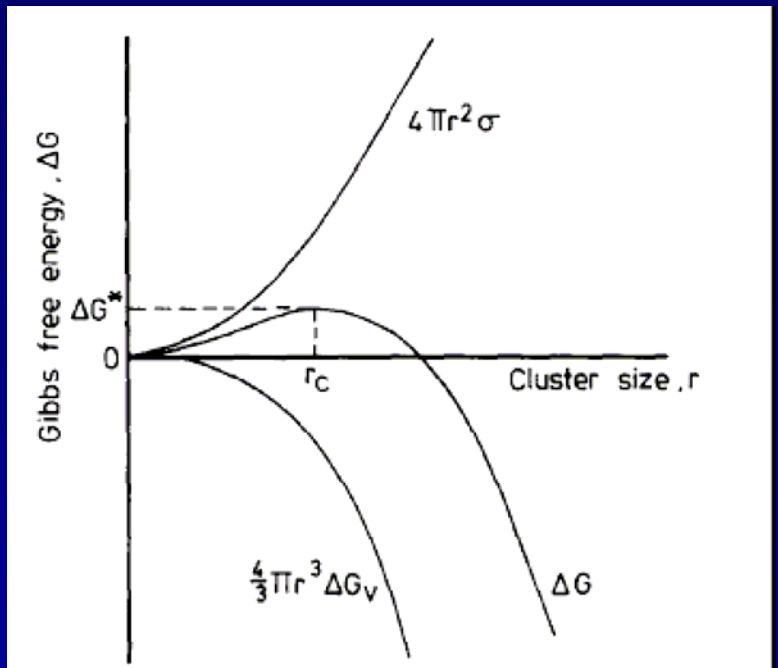


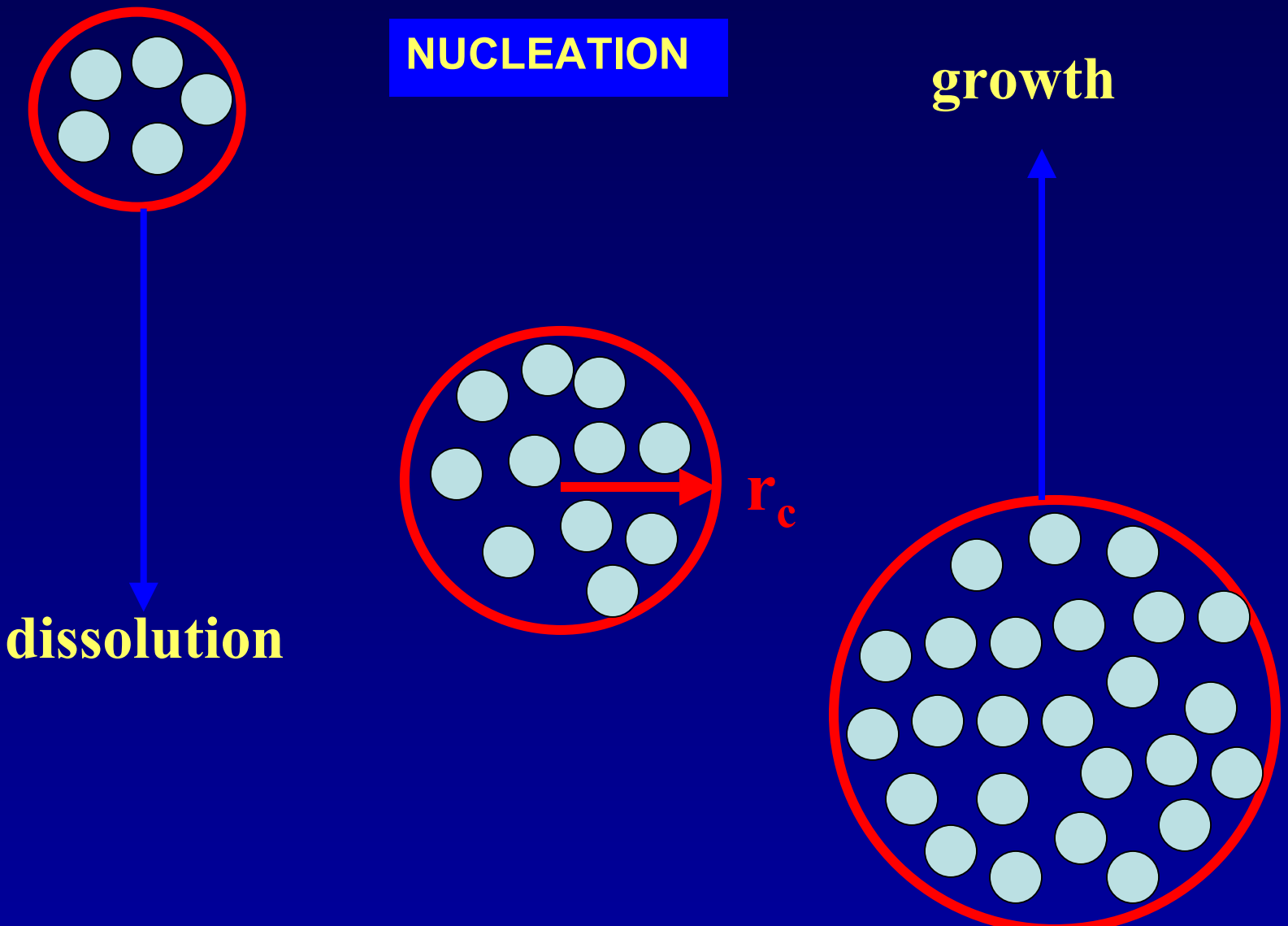
Fig. 1. Free energy change for cluster formation; size independent surface tension.

$$\Delta G = 4\pi r^2\sigma + \tfrac{4}{3}\pi r^3 \Delta G_v .$$

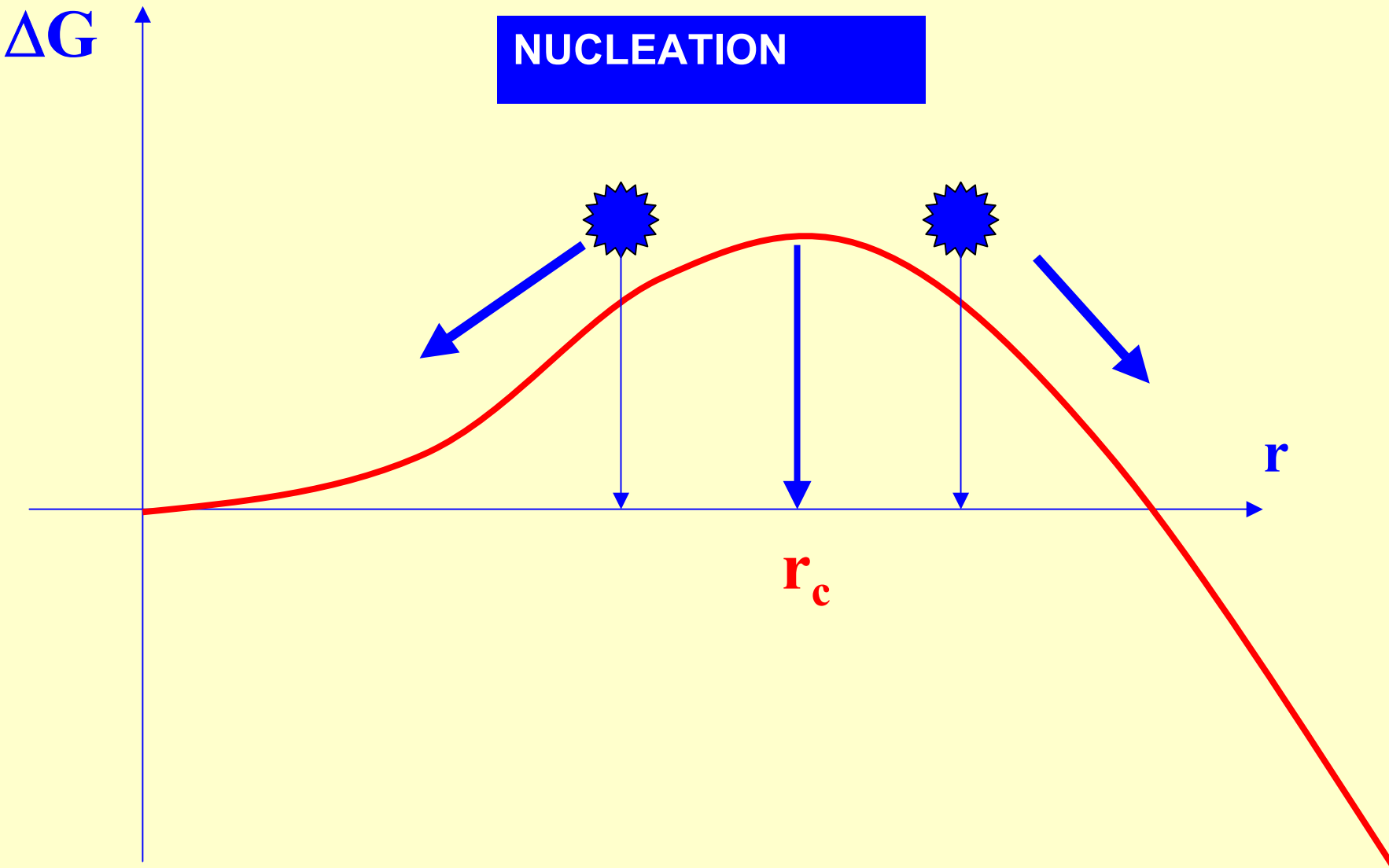
Maximum free energy at cluster critical size r_c

Larson & Garside, *J. Crystal Growth, 76(1986)88*

SUCROSE CLUSTERS AND CRISTALLISATION

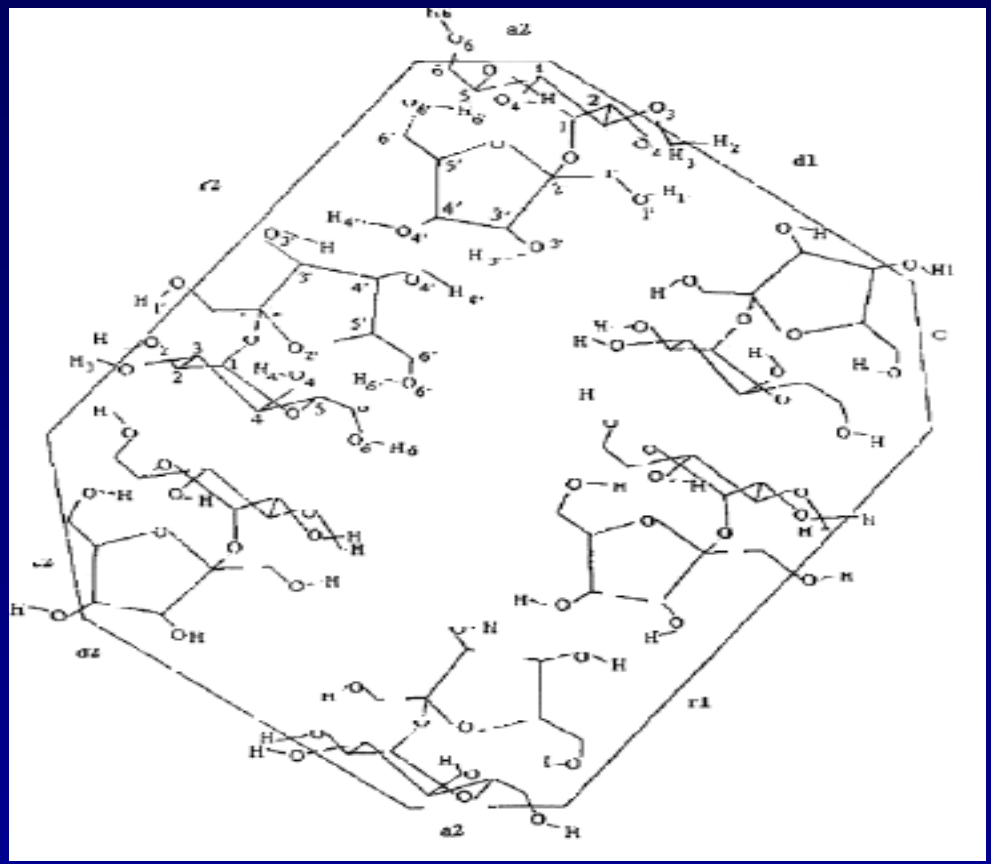


SUCROSE CLUSTERS AND CRISTALLISATION



SUCROSE CLUSTERS AND CRISTALLISATION

FROM EMBRYO TO NUCLEATION



Minimal size of embryo is the hexamer (Kelly & Mak, 1975)

Staking of sucrose molecules around the hexamer leads to the clustering of ~ 80-100 molecules with r_c = 20 A°

The rate for passing from embryo to nucleus lower than that of embryo (cluster) formation

CLUSTER SIZE ESTIMATION

-Initial assumptions (for smplification):

- all sucrose molecules are clustered in supersaturated solution
- Spherical shape of sucrose (D = 8.9A°); spherical cluster
- OH sites available for H-bonding at the surface of cluster
- Sphere (cluster) volume = N/0.74 (Nmolecules; 0.74 to account for vacuum

N mol/cluster	10	20	40	80	160	600
Cluster Volume(A^3)(1)	4959,5	9918,9	19837,8	39675,7	79351,4	297567,6
Diam equiv. sphere	21,1	26,6	33,5	42,2	53,1	82,5
Surface of sphere	1397,6	2217,5	3518,5	5582,7	8857,8	21361,5
Nb of S mol at surface	17,8	28,2	44,8	71,1	112,7	271,9
Nb OH sites in cluster	53,4	84,7	134,4	213,2	338,2	815,7
Average Nb per mol S	5,3	4,2	3,4	2,7	2,1	1,4
nh H_2O/S (2)	3,3	2,6	2,1	1,7	1,3	0,85
Volume of 1 mole S (A^3	367		(1)_ = vol molecule S / 0.74			
Diam sphère équival.	8,9		(2) _ = nb sites x 0.63			

CLUSTER SIZE ESTIMATION

Brix.solution	70	80	85	90
n_h (20°C)	3.41	2.53	2.1	1.53
Cluster size N	10	20	45	100

This estimation is in good agreement (2 to 100 molecules) with R.M. Ginde & A.S Meyerson *J. Crystal Growth, 116(1992)41-47*

Summary of hydration and clustering

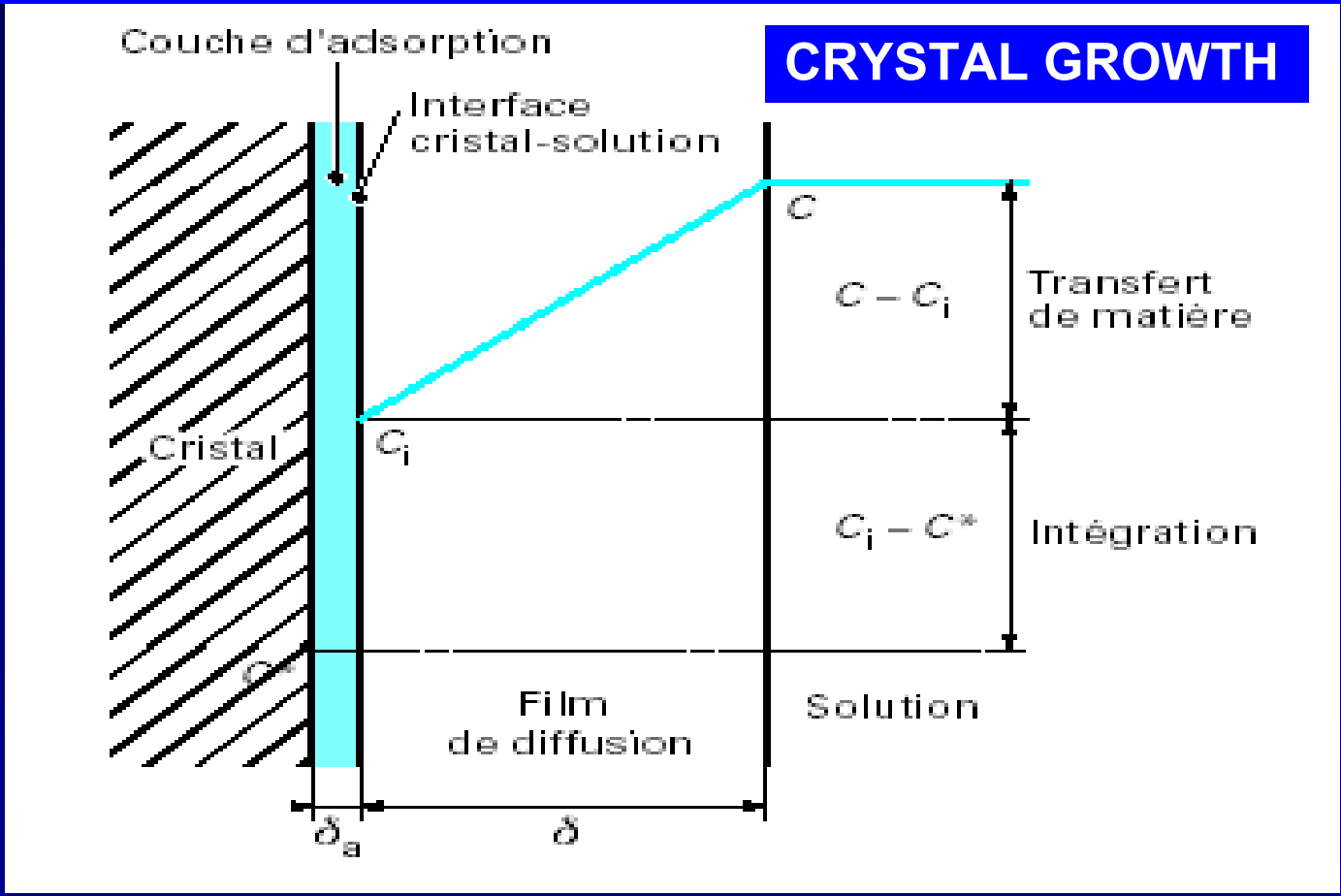
-Sucrose-water interactions depend on concentration, sucrose molecule conformation (folding) and H-bond lifetime: n_h, the sucrose hydration number is nearly constant = 5 below C = 38%, and 20°C, then it decreases with increase of concentration.

- Existence of sucrose clusters is given by different and independent experimental evidences

-As sucrose molecular associates (clusters) reach a critical size, there is appearance of a nucleus which grows to give an observable (X-Ray, …) crystal

-Assuming a spherical sucrose molecule and a certain hydration number, it is possible to estimate the size of cluster in sucrose solution at different concentrations

SUCROSE CLUSTERS AND CRISTALLISATION
A MOLECULAR APPROACH



Classical theory: a diffusional step followed by a reaction (incorpration) step

SUCROSE CLUSTERS AND CRISTALLISATION
A MOLECULAR APPROACH

DIFFUSIVITY of solute tends towards 0 for Cluster size reaching 80 after 80 hours

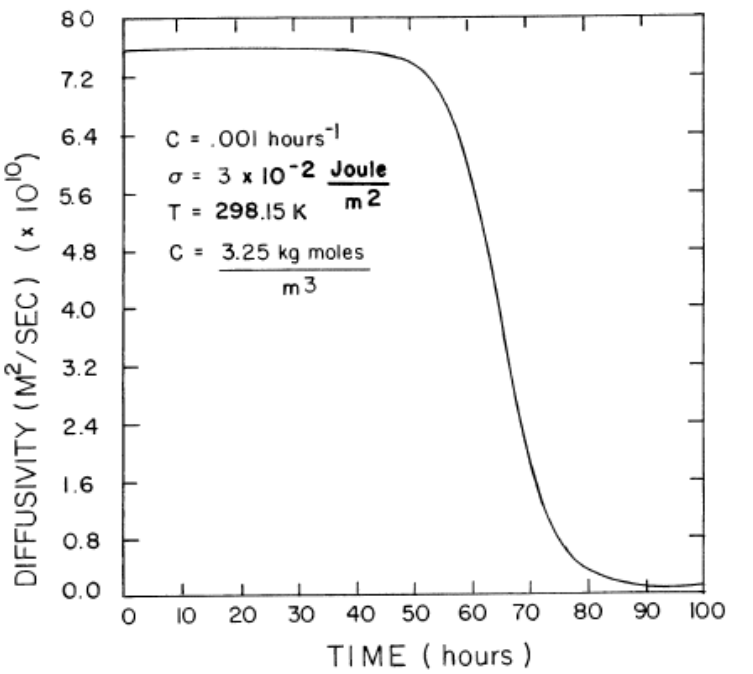


Figure 2. Predicted diffusion coefficient in a supersaturated solution as a function of time.

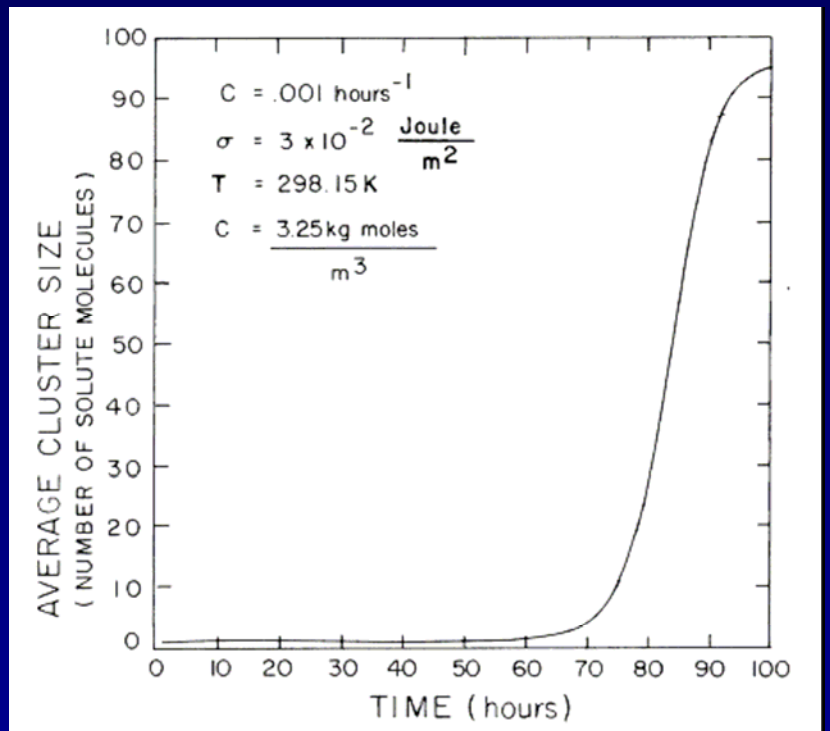
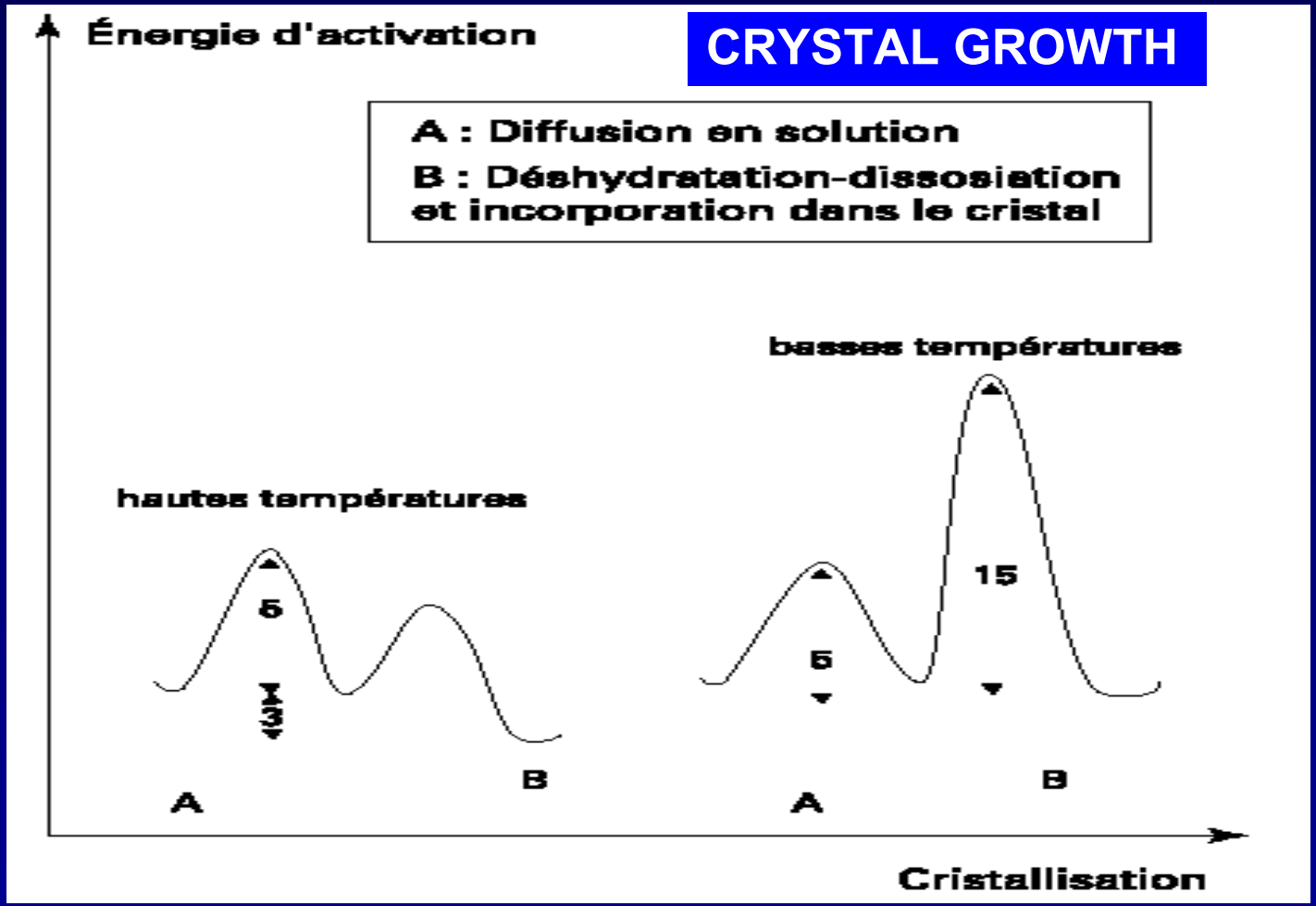


Figure 1. Average cluster size as a function of time.

Y.C. Chang & A.S. Meyerson, *AIChE J., 33(1987) 697-99*

SUCROSE CLUSTERS AND CRISTALLISATION
A MOLECULAR APPROACH



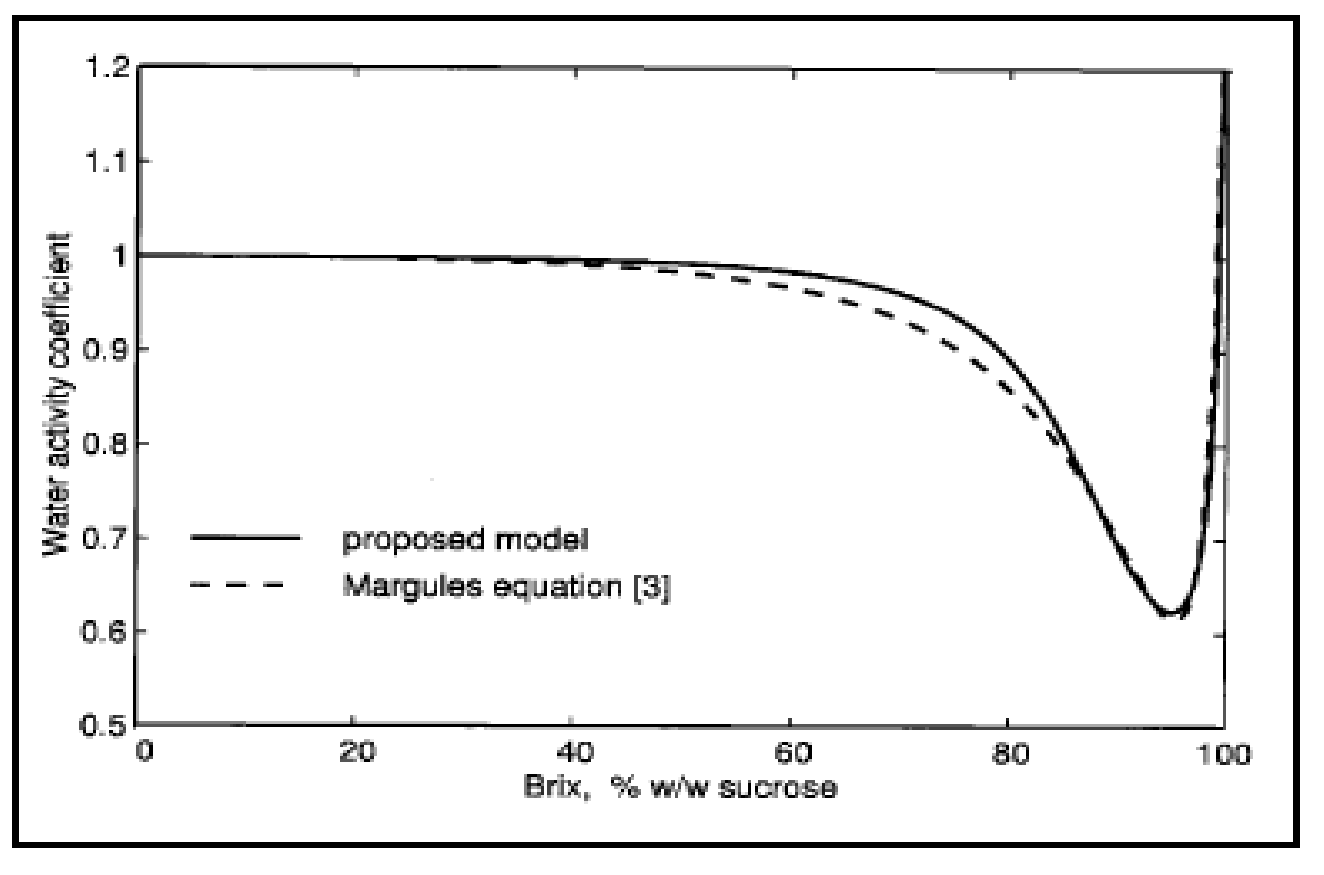
Removal of hydration water prior to incorporation: a limiting step

SUCROSE CLUSTERS AND CRISTALLISATION

A MOLECULAR APPROACH

- Conditions at the surface of growing crystal
  - sucrose molecules form hydrated clusters
  - water only hydrates the cluster surface
  - diffusivity tends towards zero
  - disassociation of hydration water
- Hypothesis for sucrose crystal growth
  - Destruction of clusters upon contact with dislocations at the surface of growing crystal
  - Disassociation of hydration water (fw > 1)
  - Release of monomeric sucrose molecules
  - Integration of sucrose molecules into crystal
  - Diffusion of free water to the bulk of solution

WATER ACTIVITY COEFFICIENT f_w IN SUPERSATURATED SUCROSE SOLUTIONS

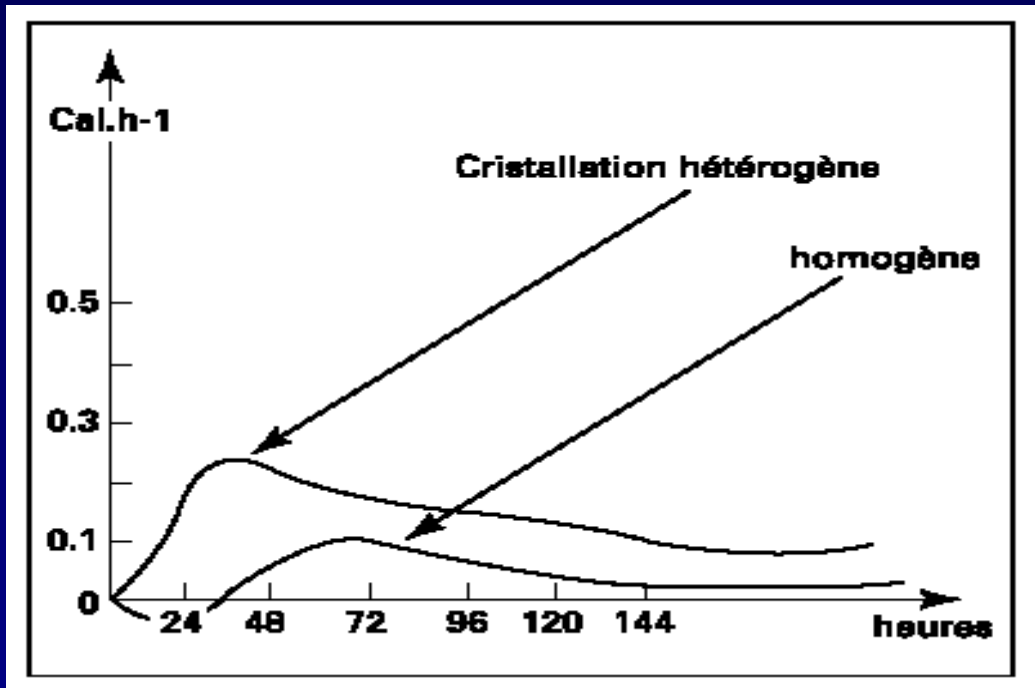


Increase of f_w at C > 95% to reach f_w > 1 at C ~ 100%

(M. Starzak, M. Mathlouthi, *Zuckerindustrie,127(2002) 175-185)*

SUCROSE CLUSTERS AND CRISTALLISATION

A MOLECULAR APPROACH



Endothermic start of homogeneous nucleation corresponds to cluster hydration water disassociation

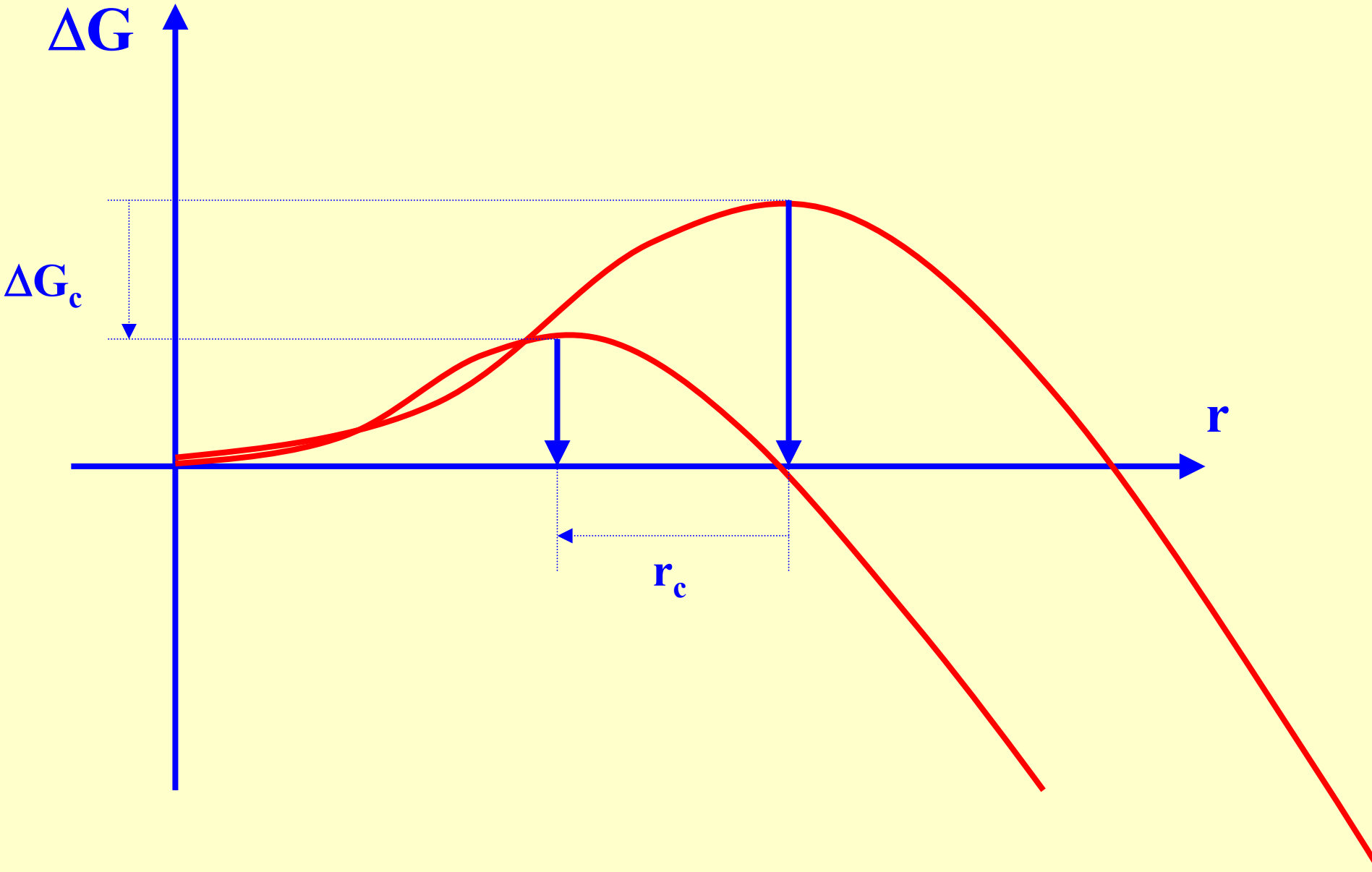
Secondary nucleation (false grain) at the surface of growing crystals due to clusters

Secondary nucleation is due to transitional boundary layer of partially integrated clusters into the growing crystal : These clusters are stripped off the surface to give nuclei

The movement of a sucrose crystal in the supersaturated solution or the flow of solution over stationary crystal produces nuclei (Powers, 1963)

$\Delta G' < \Delta G$: Free energy change associated with secondary nucleation lower than that associated with homogeneous nucleation because of lower surface tension due to contact angle between crystal and nuclei

Secondary nucleation (false grain) at the surface of growing crystals due to clusters



Summary of the role of clustering in crystal growth and secondary nucleation

- Driving force of crystal growth can be assumed to depend on free water diffusion backwards from integration layer at the surface of crystal to bulk solution rather than the classical sucrose diffusion from solution to crystal surface.

- Such a hypothesis is based on the fact that sucrose molecules in supersaturated solutions exist as clusters with diffusivity near 0. Contact of clusters with dislocations at crystal surface allows release of sucrose monomers which integrate the crystal structure.

-Secondary nucleation is thermodynamically easier than homogeneous nucleation because of lower surface tension and lower size needed for transforming embryo (cluster) into nucleus.

From Clusters to Nanoparticles

Conditions for performance of a coarse drug carrier:

- **spherical shape and small particle size < 5 µm**
- **ease of aerosolization**
- **very high specific area to adsorb or fix drug**
- **very high dissolution rate**

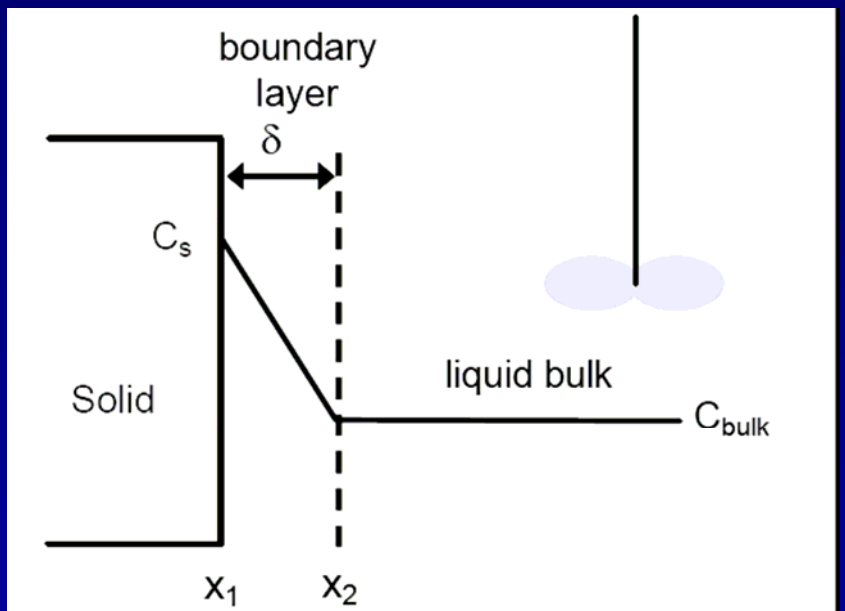
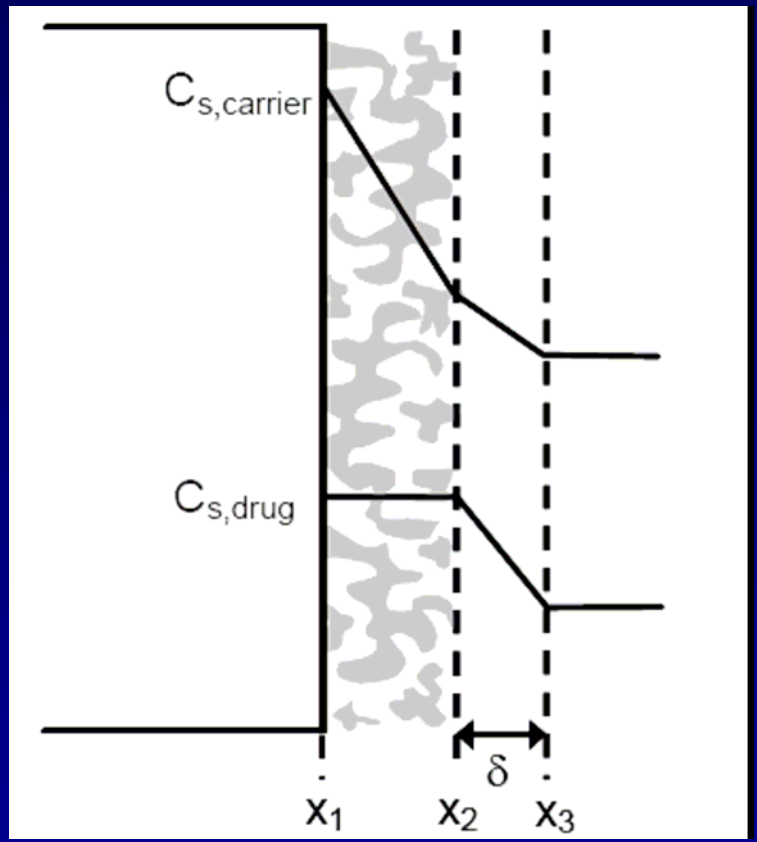


Figure 4. Schematic representation of dissolution of a solid

The dissolution rate of a solid is given by

$$\frac{dm}{dt} = A\frac{D}{\delta}(C_s - C_{bulk})$$

From Clusters to Nanoparticles

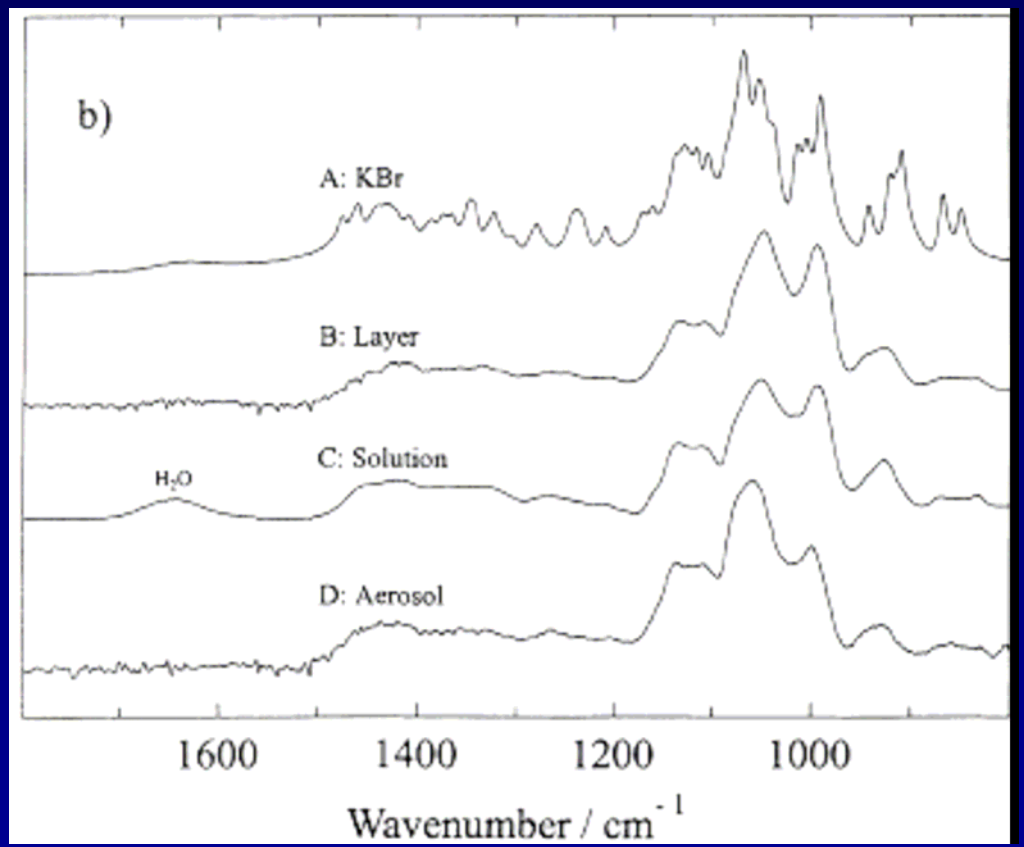


Schematic representation of the simultaneous and instantaneous dissolution of drug and nanoparticles of coarse drug carrier

Drug carrier particles can be obtained with amorphous sucrose which consits in agglomerated nuclei originating from clusters.

From Clusters to Nanoparticles

Physical state of Sucrose nanoparticles



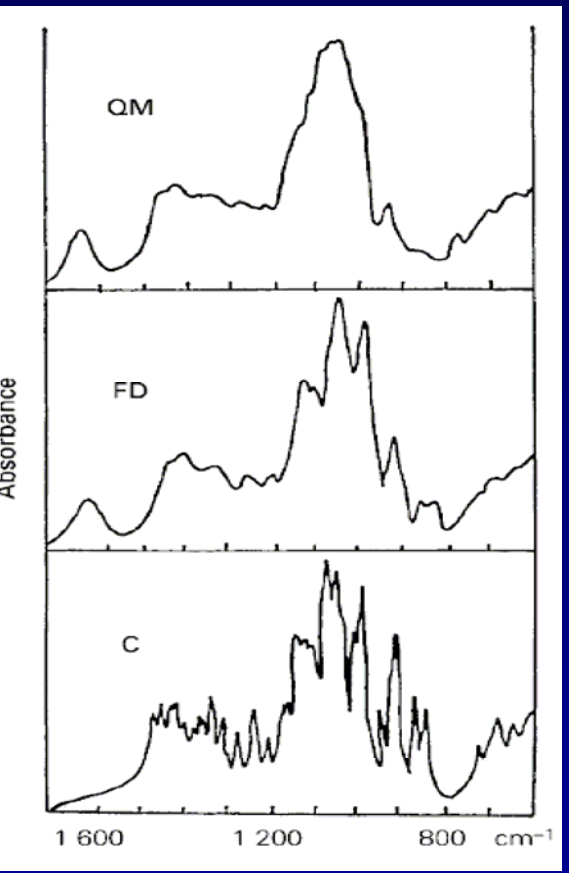
Sucrose electrospray nanoparticles (82 nm) : D have a structure different from crystal (KBr pellet) : A dried thin layer : B and saturated solution : C

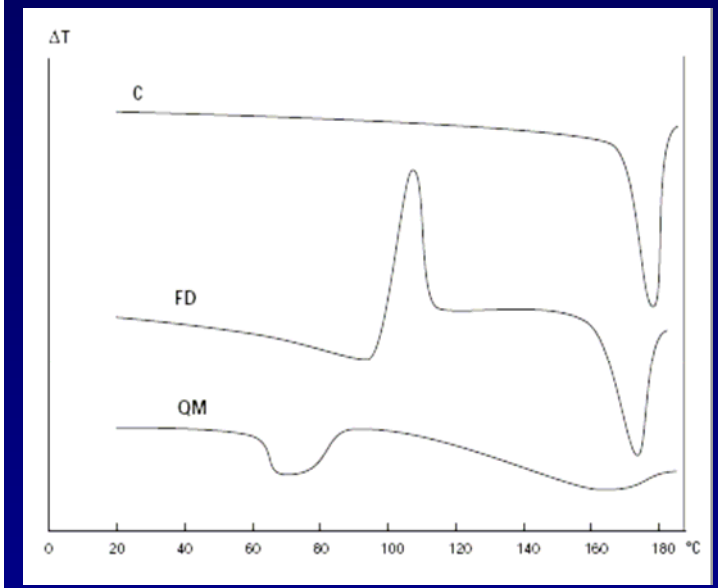
Signorell et al., *Chem. Phys. Letters, 329(2000) 52-60*

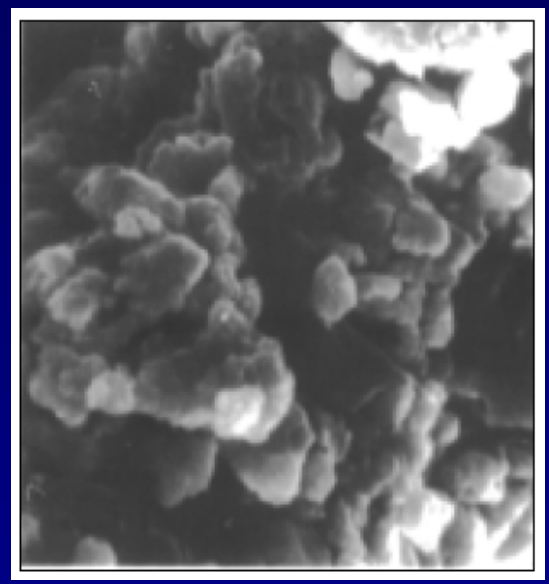
From Clusters to Nanoparticles

Physical state of Freeze dried Sucrose

Mathlouthi et al. (1986), *Carbohydr. Res.,147, 1-9.*







Freeze dried particles (FD) different from glassy QM (Quenched Melt) and crystalline Sucrose (C) can be considered as nanoparticles.

CONCLUSION

Among molecular interactions in water-sucrose solutions, the clustering of sucrose molecules remains the less studied

However numerous evidences for cluster existence in sucrose supersaturated solutions are reported in literature

Sucrose Clustering in supersturated solution plays an important role in nucleation (it accounts for a pre-nucleation stage)

A method for the estimation of the size of clusters is proposed

A new approach of crystal growth is suggested in which the release of cluster hydration water and its diffusion to the bulk of solution is the real driving force of crystal growth

Secondary nucleation explained by cluster behavior at crystal surface

Sucrose nanoparticles used in drug release originate from the clustering of sucrose in amorphous sugar particles

EURO FOOD'S WATER

Thank you for your attention