



ΔΙΕΡΓΑΣΙΕΣ ΔΙΑΧΩΡΙΣΜΟΥ

Μάθημα 11ο

Ακαδημαϊκό έτος 2017-2018

Separation Processes

Μηχανισμοί δράσης επιμολύνσεων

- 1. Περιορισμός μεταφοράς μάζας μορίων προς ή από την αναπτυσσόμενη επιφάνεια του κρυστάλλου. Πολλά μόρια, ιδιαίτερα τα πλέον ογκώδη παρεμποδίζουν τους συντελεστές μεταφοράς μάζας και τη δυνατότητα διάχυσης των δομικών μονάδων στα ενεργά κέντρα της κρυστάλλωσης. Αν η μεταφορά μάζας γίνει λόγω της παρουσίας επιμολύνσεως το καθορίζον την ταχύτητα στάδιο, η ταχύτητα ανάπτυξης μειώνεται.
- 2. Προσρόφηση επιμολύνσεων στην αναπτυσσόμενη κρυσταλλική επιφάνεια. Η προσροφημένη ουσία παρεμποδίζει την περαιτέρω ενσωμάτωση δομικών μονάδων. Για να γίνει κάτι τέτοιο θα πρέπει να εκτοπισθεί η επιμόλυνση. Εάν υπάρχει δε πολύ μεγάλη συνάφεια της μόλυνσης για τον κρύσταλλο, η ταχύτητα κρυσταλλικής ανάπτυξης επιβραδύνεται. Παράδειγμα: Παρεμποδιστές της κρυσταλλικής ανάπτυξης της ζάχαρης είναι το σιρόπι καλαμποκιού (corn syrup) και το ιμβερτοσάκχαρο. Οι απολήξεις γλυκόζης στις ουσίες αυτές, ροφούνται στο πλέγμα του καλαμοσακχάρου και αναστέλλουν την κρυσταλλική ανάπτυξη επειδή χρειάζεται πρόσθετη ενέργεια προκειμένου μόρια γλυκόζης να προστεθούν στον κρύσταλλο.

- 3. Ενσωμάτωση της επιμόλυνσης στο κρυσταλλικό πλέγμα της ουσίας. Η ενσωμάτωση αυτή προκαλεί διακοπή περαιτέρω προσθήκης δομικών μονάδων στον κρύσταλλο με αποτέλεσμα να αναστέλλεται η κρυσταλλική ανάπτυξη. Η ένταξη στο πλέγμα γίνεται συνήθως με μέρος του μορίου, ενώ το μέρος εκείνο που μένει εκτός παρεμποδίζει την κρυσταλλική ανάπτυξη με την ενσωμάτωση πρόσθετων ομάδων.
- Π.χ. η ραφφινόζη είναι αποτελεσματικός αναστολέας της κρυσταλλικής ανάπτυξης του καλαμοσακχάρου λόγω ομοιότητας δομής. Η Ραφφινόζη είναι τρισακχαρίτης ο οποίος περιέχει ένα δισακχαρίτη καλαμοσακχάρου συνδεδεμένο με ένα μόριο γαλακτοσακχάρου. Το μέρος του καλαμοσακχάρου είναι πλήρως συμβατό με τον κρύσταλλο του καλαμοσακχάρου αλλά το μόριο του γαλακτοσακχάρου μένει εκτός, στην επιφάνεια του κρυστάλλου αναστέλλοντας την περαιτέρω ανάπτυξή του.
- Για να μελετηθεί και συγκριθεί η επίδραση ορισμένων επιμολύνσεων είναι απαραίτητο να εξετασθεί η δράση τους σε συνθήκες σταθερού υπερκορεσμού, επειδή η παρουσία τους ενδέχεται να επηρεάζει την διαλυτότητα του άλατος ή το ΣΤ και ως εκ τούτου τον υπερκορεσμό.

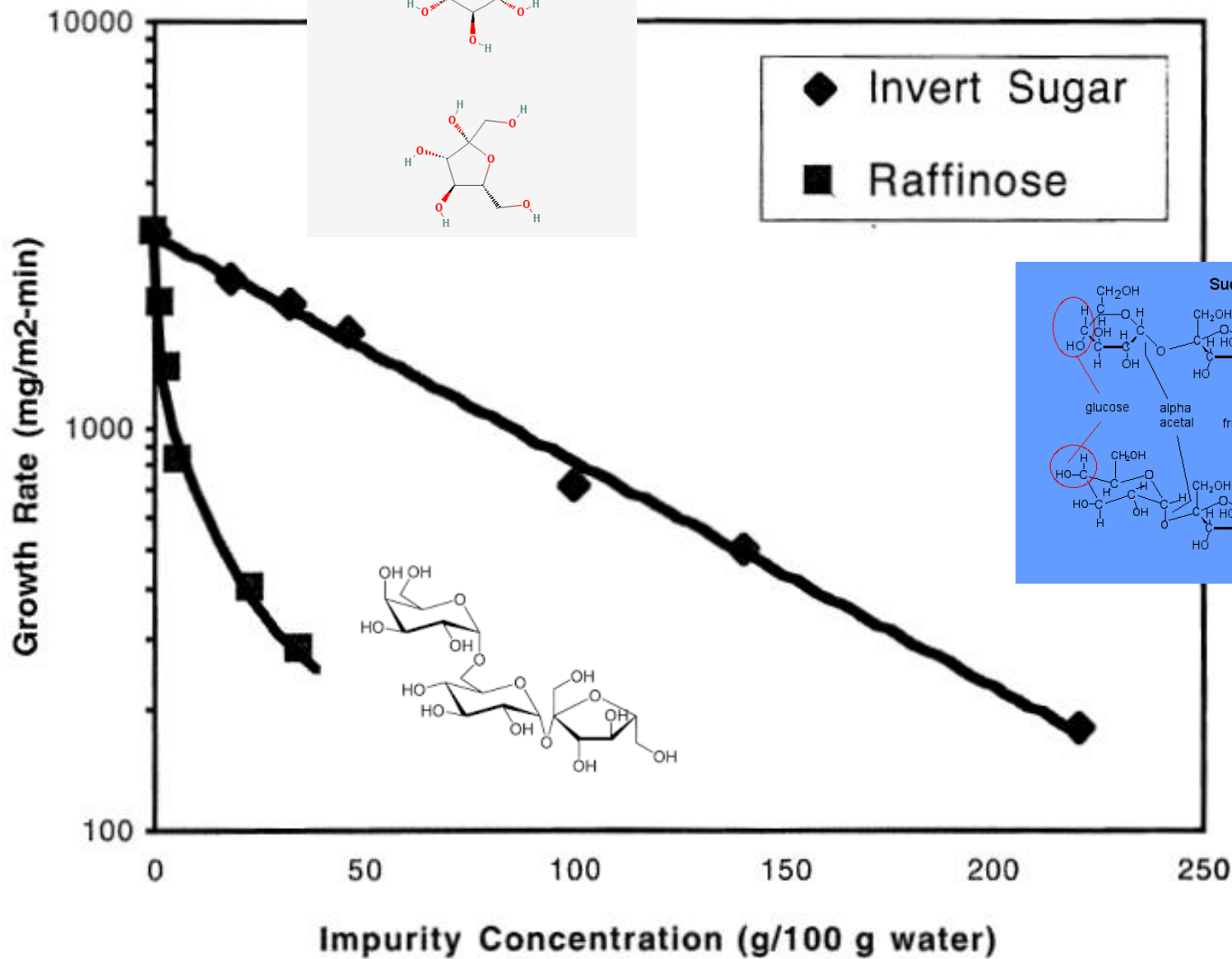


Figure 6-20 Effects of Invert Sugar and Raffinose on Sucrose Crystal Growth Rates at 41°C and **Constant** Supersaturation of $\Delta C = 40$ Sucrose/g Water.

The function of impurities

In general the presence of impurities (substances other than the crystallizing) results to:

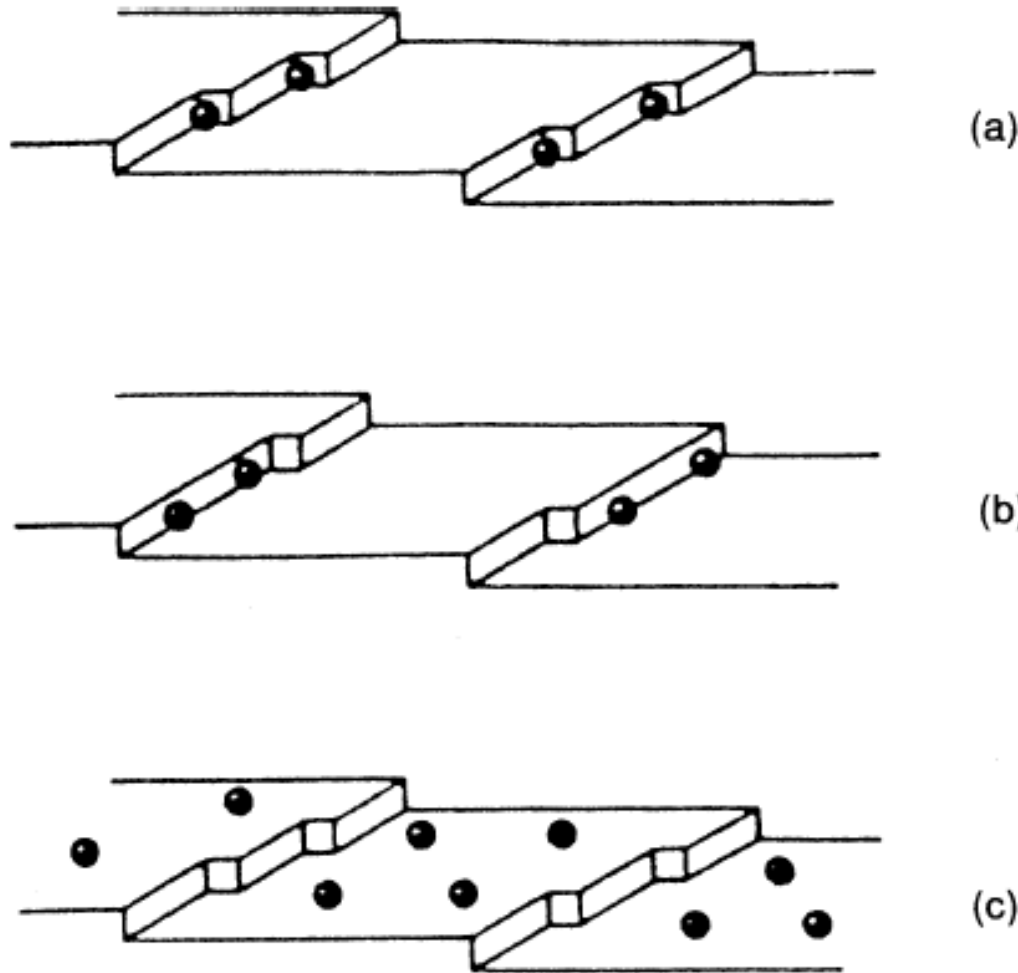
Acceleration of crystal growth

Inhibition of crystal growth

Change of crystal habit of the crystallizing substance

Impurities

- ❖ Impurities are incorporated into the active crystal sites and their extent of incorporation depends on the affinity (structural, chemical) with the substrate
- ❖ The affinity affects the mechanisms of incorporation (out of equilibrium)
- ❖ It is assumed that the affinity between the impurity and the substrate (at the molecular level) determines whether impurities shall be located at the surface, or in the bulk of the growing crystals
- ❖ The chemical and structural affinity between the substrate and the impurity affects the distribution of the impurity in the crystal lattice
- ❖ Impurities of similar size and chemical properties are uniformly distributed in the crystal lattice.
- ❖ Larger size molecules, less compatible with the substrate tend to accumulate in steps forming aggregates that may reach micrometer size



Depending on the type of sorption the efficiency of attachment is differentiated and so does the effectiveness of the additives in inhibiting the rate of growth of a crystal face

Figure 6.26. Sites for impurity adsorption on a growing crystal, based on the Kossel model: (a) kink; (b) step; (c) ledge (face). (After Davey and Mullin, 1974)

Single crystals are used for the investigation of the effect of impurities on the crystal habit of growing crystals

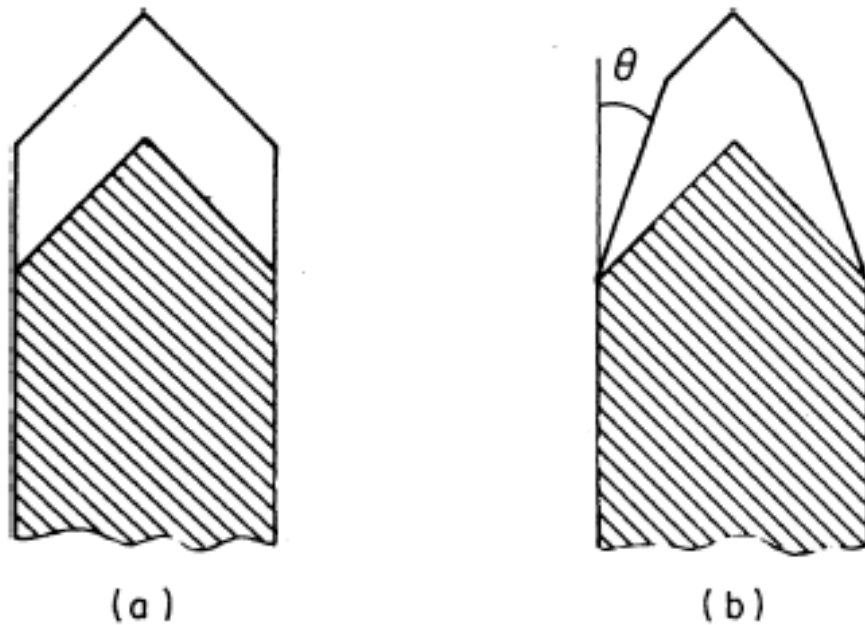



Figure 6.27. (a) Perfect 'capping' of an ADP crystal; (b) tapered growth caused by traces of Fe^{3+} (θ - angle of taper). (After Mullin, Amatavivadhana and Chakraborty, 1970)



(1) Adsorption (temporary attachment) of the impurity by diffusion from the supersaturated solution (Heat of adsorption Q_{ad}).

(2) Transport of the adsorbed impurity molecules to the surface-terrace (Energy: Q_{smig}).

(3) Adsorption of the impurity molecules, transported on the surface to steps without kinks, (Change of free energy, Q_{step}) and at kinks (Free energy Q_{kink}).

The relative values of the above energy quantities determine the sites at which adsorption shall take place

Possible situations:

(1) $Q_{ad} \approx Q_{smig}$ irrespective of the values of Q_{step} or Q_{kink} , adsorption takes place at the flat part of the crystal steps (terrace).

(2) $Q_{ad} > Q_{smig}$, The impurity molecules are mobile and could therefore be adsorbed at steps without kinks as well as in kinks with free energy change values Q_{step} and Q_{kink} , respectively. Since $Q_{step} < Q_{kink}$, the adsorption of mobile impurity molecules takes place preferably at kinks.

(3) $Q_{kink} < Q_{step}$, impurity molecules diffuse directly to the kinks and they are adsorbed there instead of the surface of the crystal step.

The relative rate of crystal growth in the presence of impurity with respect to the corresponding value of the rate in the absence of impurity is:

$$v/v_0 = 1 - \alpha\theta_{eq}$$

θ_{eq} = equilibrium surface coverage by the impurity, α the effectiveness of the impurity in the reduction of the rate of crystal growth.

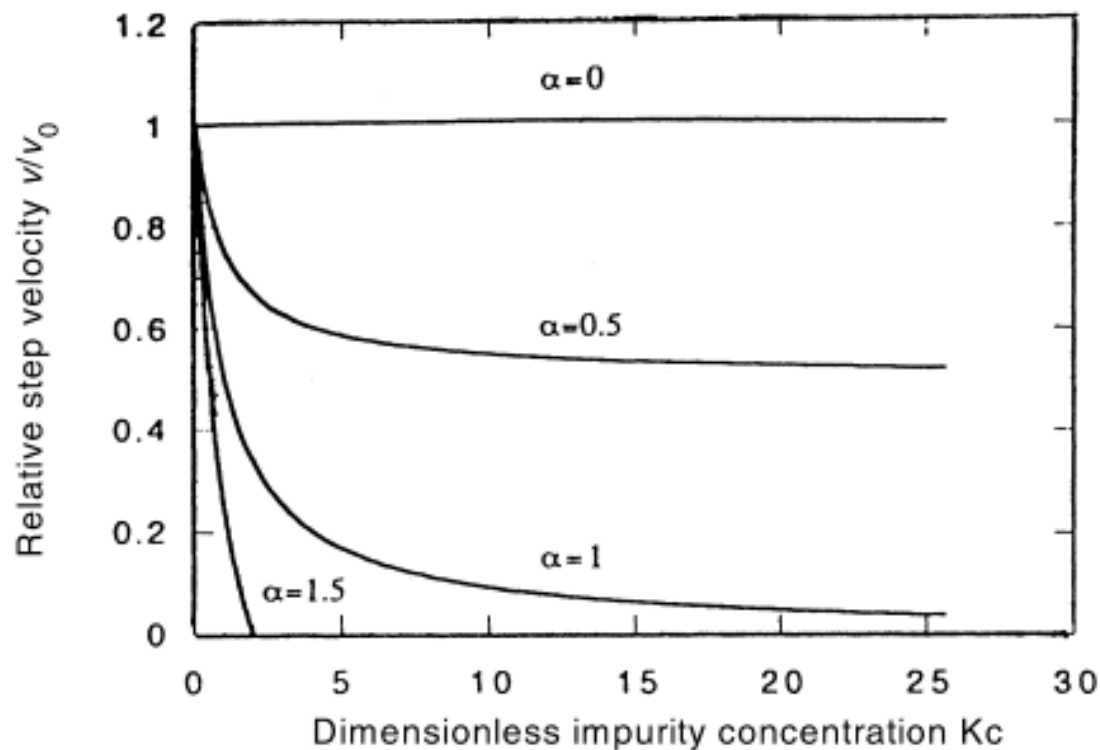
For $\alpha=1$, $\theta_{eq}=1$ the growth of the respective crystal face is 0. For $\alpha>1$, $\theta_{eq}<1$ (partial coverage), $v \rightarrow 0$, but when $\alpha<1$, v never becomes zero, even if $\theta=1$.

Assuming that the adsorption of the impurity is described by the Langmuir isotherm:

$$\theta_{eq} = Kc/(1 + Kc)$$

$$v/v_0 = 1 - [\alpha Kc/(1 + Kc)]$$

$$G/G_0 = 1 - [\alpha Kc / (1 + Kc)]$$



$$\alpha = \gamma a / kT \sigma L$$

α : size of the growth unit, γ edge surface energy, σ : supersaturation, L : separation of the adsorption active sites

Figure 6.28. Relationship between the relative step velocity v/v_0 and the dimensionless impurity concentration Kc for different values of the impurity effectiveness factor α . (After Kubota and Mullin, 1995)

Temkin Isotherm :

The heat of adsorption depends on surface coverage. For θ ca. 0.5

$$v/v_0 = 1 - \alpha_l Z (\ln C_0 + \ln c_i)$$

$$(v_0 - v)/v_0 = \alpha_l Z (\ln C_0 + \ln c_i)$$

Provided that

$$\ln(c_i/C_0) \approx (c_i/C_0) - 1,$$

$$\theta = Z \ln C_0 + Z \ln c_i$$

where

$$C_0 = \exp(Q_{\text{diff}}^0/R_G T)$$

and

$$Z = R_G T / b Q_{\text{diff}}^0 = 1/b \ln C_0$$

$$Q_{\text{diff}} = Q_{\text{diff}}^0 (1 - b\theta)$$

With $b < 1$

$$v/v_0 = 1 - (\alpha_l/b C_0) c_i$$

In most cases, the rate of adsorption decreases with increasing supersaturation. The rate constant increases from a value 0 until a critical supersaturation value, σ_0 below which adsorption is instantaneous. The respective rate of crystal growth shall increase from the value corresponding to instantaneous adsorption to the value of the rate corresponding to the pure solution.

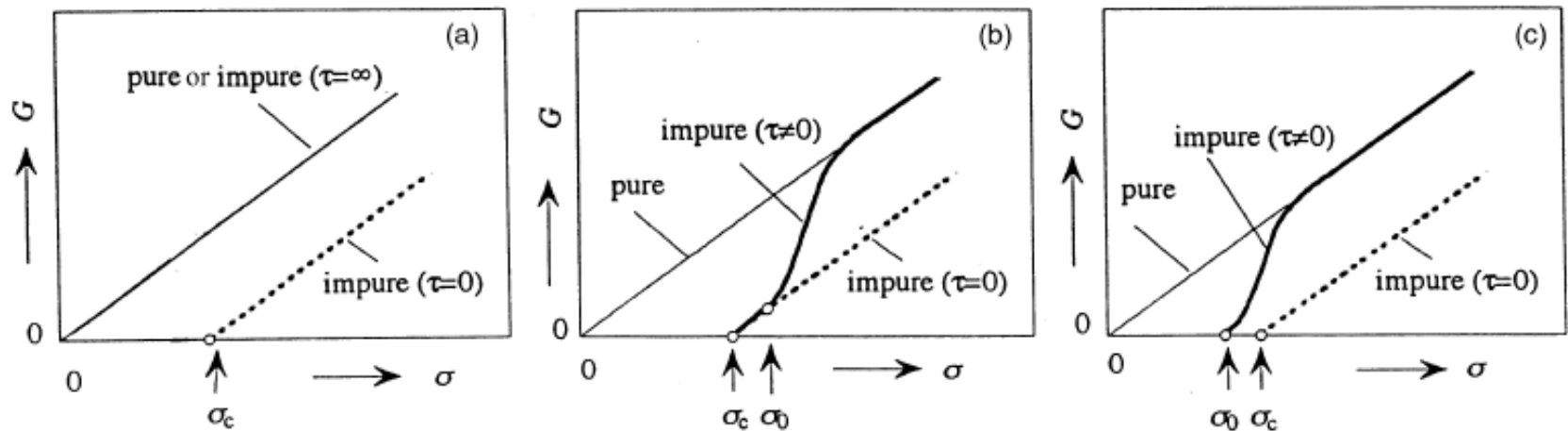


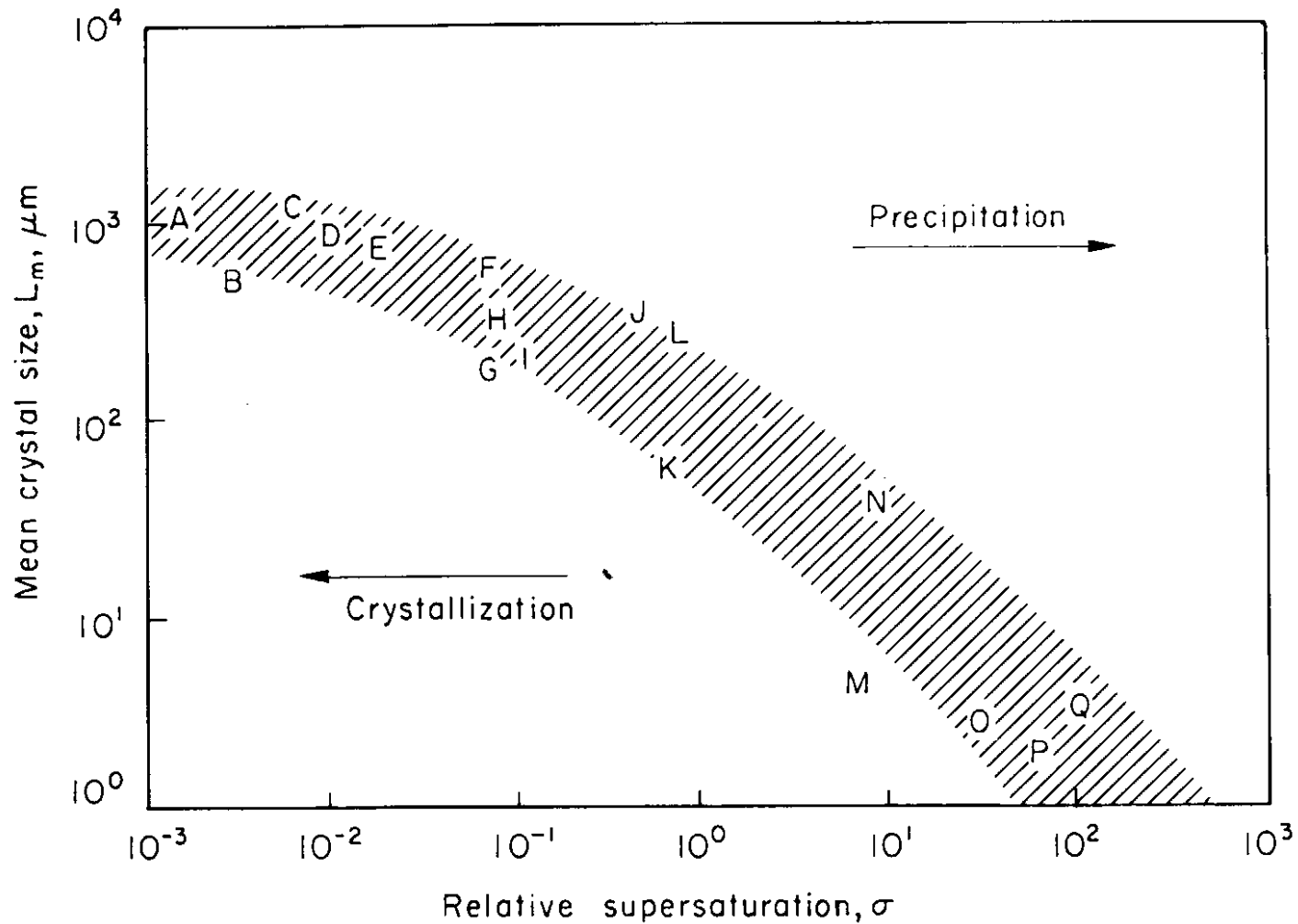
Figure 6.29. Face growth rate G as a function of supersaturation σ : (a) for instantaneous ($\tau = 0$) and very slow ($\tau = \infty$) adsorption, (b) and (c) for a continuous increase of τ from 0 to ∞ , (b) for $\sigma_0 > \sigma_c$ and (c) for $\sigma_0 < \sigma_c$. (After Kubota, Yokota and Mullin, 2000)

Hysteresis effect in crystal growth

Μέγιστο μέγεθος κρυσταλλιτών οι οποίοι αναπτύσσονται

- Βασικά, δεν υπάρχει όριο. Από πρακτική άποψη πάντως, πάντοτε υπάρχει ένα όριο. Σύμφωνα με την υπάρχουσα εμπειρία οι κρύσταλλοι δεν αναπτύσσονται σε βιομηχανικούς κρυσταλλωτήρες πέραν ενός ορίου.
- Μερικοί κρύσταλλοι έχουν τόσο μικρές ταχύτητες κρυσταλλικής ανάπτυξης ώστε να απαιτούνται υψηλοί χρόνοι παραμονής για να ληφθούν μεγάλου μεγέθους κρύσταλλοι.
- Π.χ. με γραμμική ταχύτητα 10^{-7}ms^{-1} ένας αρχικός κρυσταλλίτης αναμένεται να έχει μέγεθος ίσο με 2mm σε λιγότερο από 3 ώρες.
- Για γραμμική ταχύτητα 10^{-9}ms^{-1} ο ίδιος κρυσταλλίτης για να αναπτυχθεί στα 2mm χρειάζεται 3^{10} ημέρες [και οι δύο ταχύτητες είναι ρυθμοί που απαντώνται σε ανόργανους κρυστάλλους].
- Μόνο ο χρόνος παραμονής ενός κρυσταλλίτη στον κρυσταλλωτήρα δεν αρκεί για τον καθορισμό του μεγέθους λόγω της δευτερογενούς πυρηνογένεσης η οποία λαμβάνει χώρα, λόγω της οποίας αυξάνεται ο αριθμός των κρυσταλλιτών και περιορίζεται η αύξηση του μεγέθους των.
- Οι ρυθμοί είναι ευαίσθητες συναρτήσεις του υπερκορεσμού. Αύξηση του υπερκορεσμού ωστόσο αυξάνει την πυρηνογένεση.

- Η παρουσία επιμολύνσεων στο σύστημα επηρεάζει το μέγεθος των κρυσταλλιτών. Η κρυστάλλωση θειικού Cd και Cu από λεκάνες επιμετάλλωσης παρουσία ζελατίνης καταλήγει στο σχηματισμό κρυσταλλιτών οι οποίοι δεν ξεπερνούν το 1 μm. Απουσία της, οι κρύσταλλοι των αλάτων αυτών ξεπερνούν σε μέγεθος το 1 mm.
- Κάποιοι από τους κρυστάλλους τείνουν να θραύονται, όταν το μέγεθός τους υπερβεί μια κρίσιμη τιμή (αναδευτήρας ή σημείο έναρξης πολυκρυσταλλικής ανάπτυξης).
- Ανάπτυξη πολυκρυσταλλικών στερεών όχι μόνο μειώνει τις μηχανικές ιδιότητες των κρυστάλλων (ψαθυρές) αλλά τις κάνει και ασταθέστερες (διάλυση λόγω Gibbs-Thomson, διάλυση ακμών).
- Οι αδιαφανείς ωειδείς κρύσταλλοι, οι οποίοι παράγονται σε πολλούς βιομηχανικούς κρυσταλλωτήρες, πιθανώς προκύπτουν από αλληλουχίες κρυστάλλωσης-διάλυσης-απότριψης.

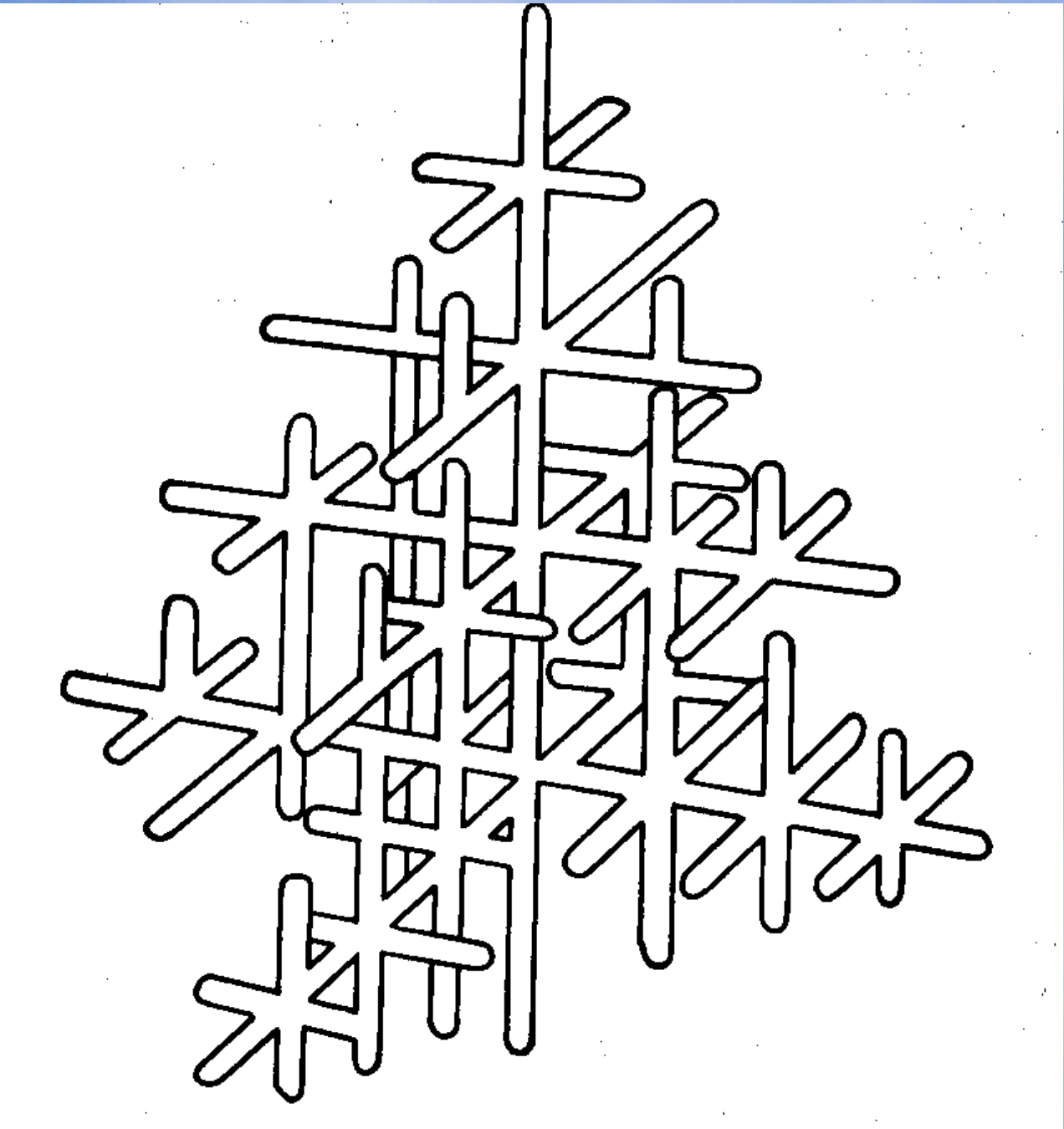


Maximum mean crystal sizes obtained in an MSMPR crystallizer: A, KCl; P, NaCl; C, $(\text{NH}_2)_2\text{CS}$; D, $(\text{NH}_4)_2\text{SO}_4$; E, KNO_3 ; F, Na_2SO_4 ; G, K_2SO_4 ; $\text{NH}_4\text{Al}(\text{SO}_4)_2$; I, $\text{K}_2\text{Cr}_2\text{O}_7$; J, $\text{KAl}(\text{SO}_4)_2$; K, KClO_3 ; L, $\text{NiSO}_4(\text{NH}_4)_2\text{SO}_4$; M, BaF_2 ; N, CaCO_3 ; O, TiO_2 ; P, CaF_2 ; Q, BaSO_4 . (After Mersmann and Kind, 1988)

The background of the slide is a photograph of an industrial facility, likely a refinery or chemical plant. It features a complex network of large, silver-colored metal pipes and structures. The pipes are arranged in various orientations, some running horizontally and others vertically. The sky is a clear, bright blue with a few wispy white clouds. The overall scene is brightly lit, suggesting a sunny day.

Dendrites

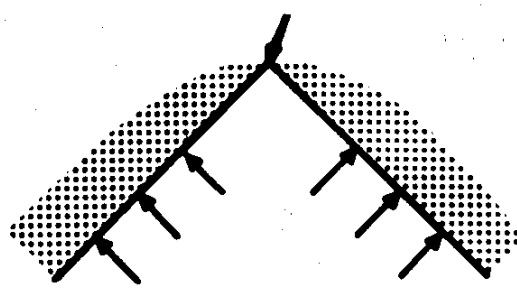
- In crystal growth from melts the rate determining step is heat transfer.
- If the crystal growing cannot dissipate heat sufficiently fast is forced to modify its surface in such a way that heat may be dissipated.
- The result is the formation of **dendrites**



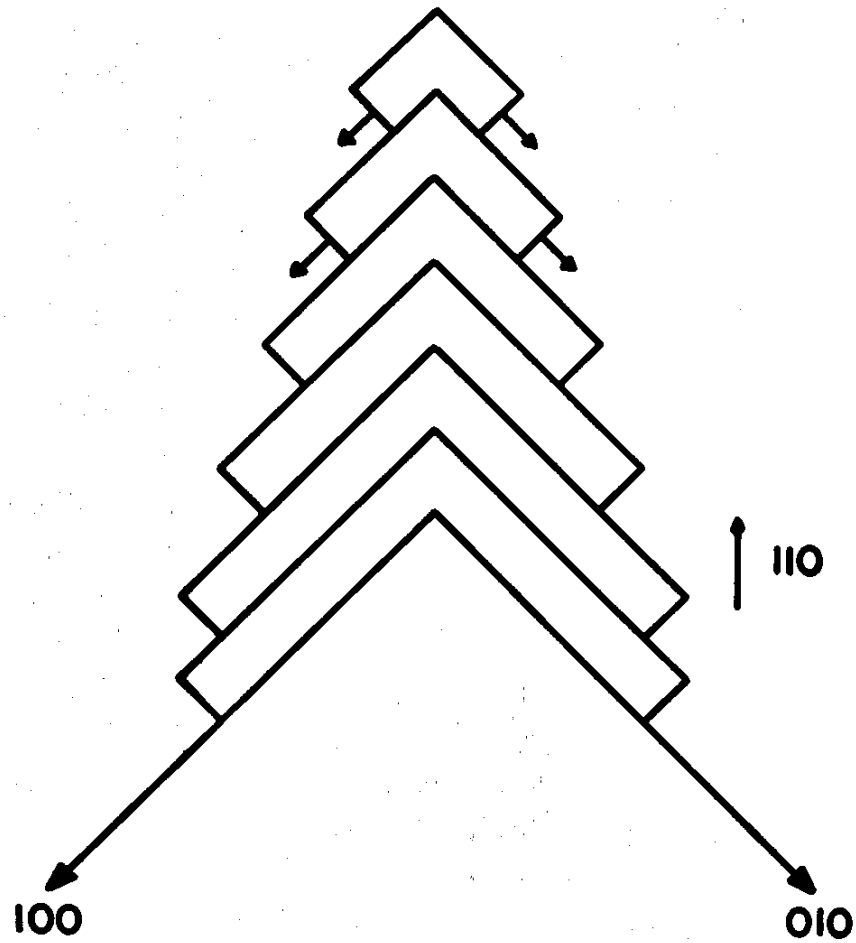


Another explanation

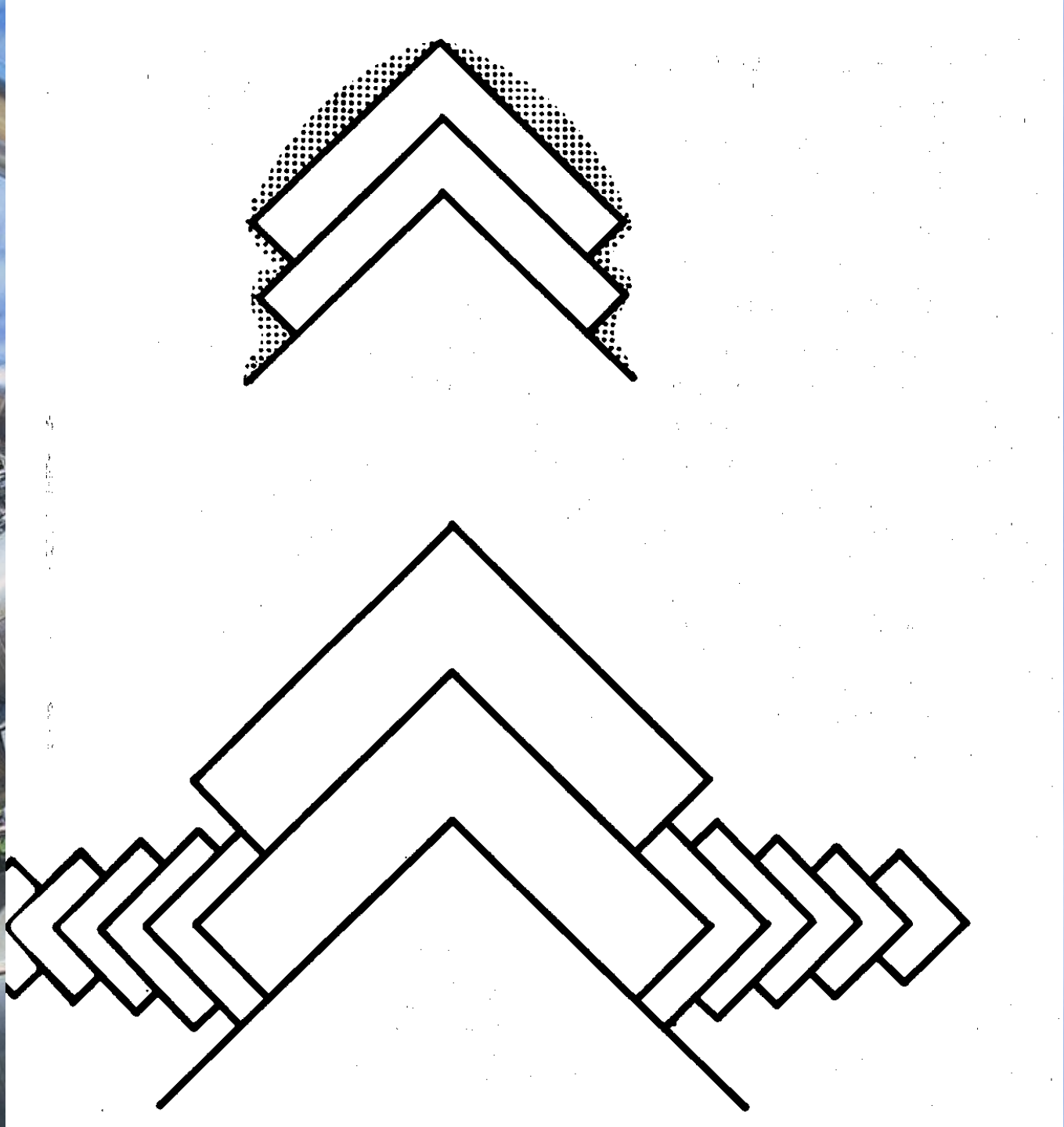
- There is traffic congestion between water molecules surrounding ions and the crystal
- The solvent molecules «block» the fast growing crystal faces and as a result, the corners which are less hindered grow faster



(a)



(b)



The background of the slide features a photograph of industrial infrastructure, including large, shiny metal pipes and scaffolding, set against a clear blue sky with some light clouds. The pipes are arranged in a complex, vertical and horizontal pattern, suggesting a refinery or chemical processing plant.

Inclusion

- Solid, liquid and gas impurities included at the interior of the crystals and are due to the inclusion of the mother fluid in the growing crystal
- Up to 0.5% κ.β. In liquid inclusions in industrially obtained crystals
 - Primary inclusions
 - Secondary inclusions
- Large crystals or fast growing crystals have more chances to develop inclusions

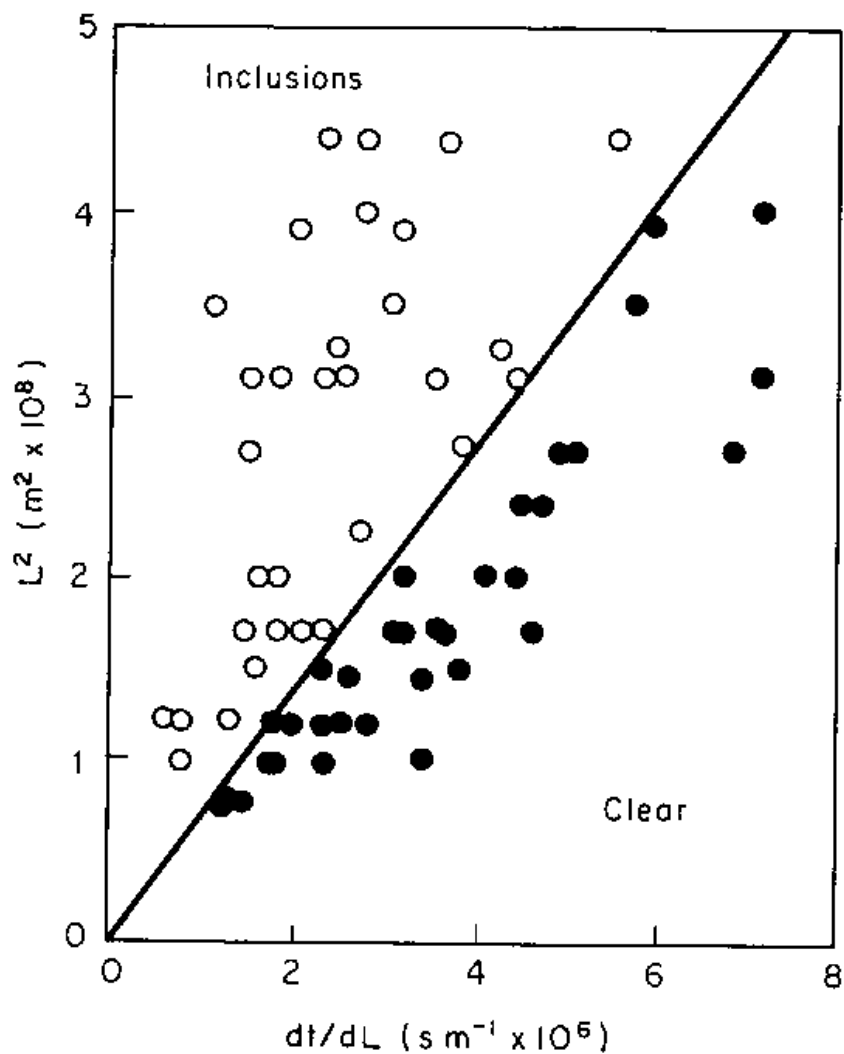
Ρυθμός και εξωτερική εμφάνιση κρυστάλλων NaCl

<i>Crystal size</i> <i>L</i> (10^{-4} m)	<i>Growth velocity</i> dL/dt (10^{-7} m s $^{-1}$)	<i>Volumetric growth rate</i> † dV/dt (10^{-15} m 3 s $^{-1}$)	<i>Crystal appearance</i>
1.0	2.9	9	transparent
1.2	2.9	13	transparent
1.2	3.8	16	transparent
2.0	1.4	17	transparent
1.7	2.6	23	opaque
1.5	3.7	25	opaque
1.8	4.1	40	opaque
2.0	3.7	44	opaque
3.0	1.8	49	opaque

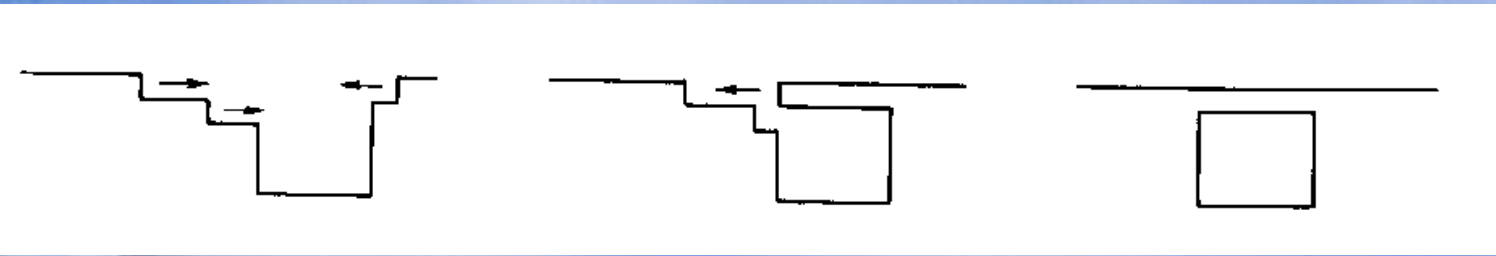
* Calculated from data of Yamamoto (1939)

† Volumetric rate increase $dV/dt = 3L^2 \cdot dL/dt$

Κριτήρια αποφυγής σχηματισμού εγκλεισμών



Criteria for the avoidance of mother liquor inclusions in sodium chloride crystals. (After Yamamoto, 1939)

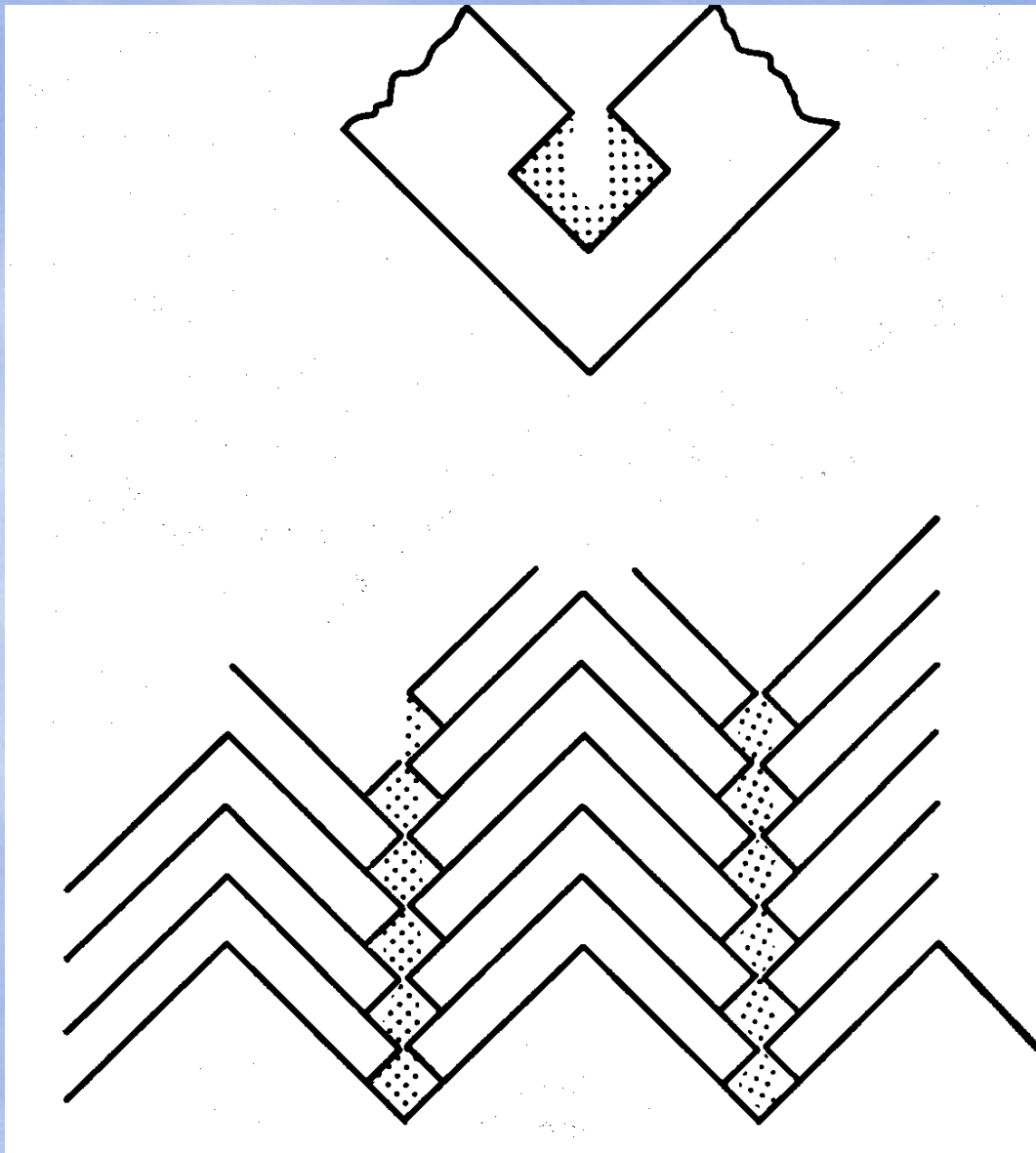


❖ In the fluid surrounding small crystals there is a diffusion field leading to spherical symmetry and as a result the component of the concentration gradient is larger close to the center of the face rather than the edges

❖ More solvent is transported to the center

❖ When the crystal has grown sufficiently the edges develop faster than the center thus forming cavities

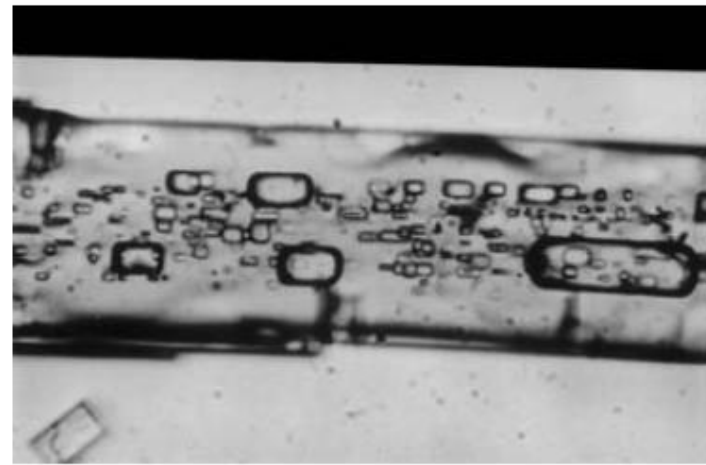
❖ Cavities are plugged with the advancement of the steps



The growth of dendrites favors the formation of inclusions of foreign substances



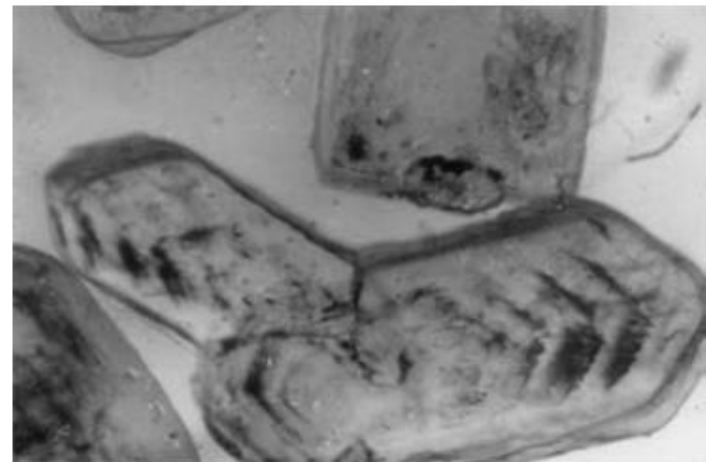
(a)



(b)

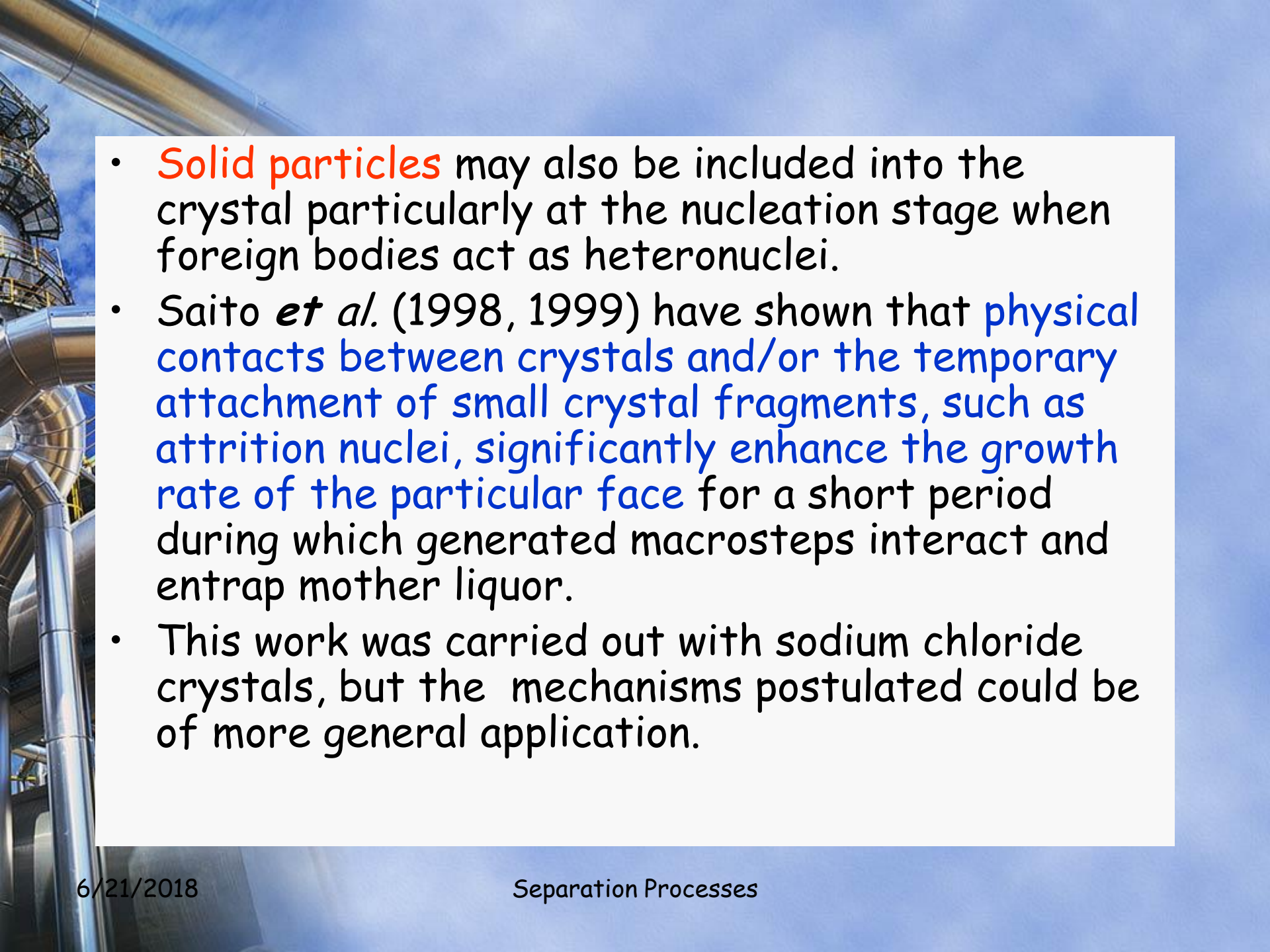



(c)



(d)

Figure 6.46. *Some examples of liquid inclusions in crystals: (a) a regular pattern in ammonium perchlorate, (b) random aligned inclusions in potassium iodide, (c) an 'hour-glass' pattern in sucrose and (d) 'herring-bone' inclusions in sucrose*

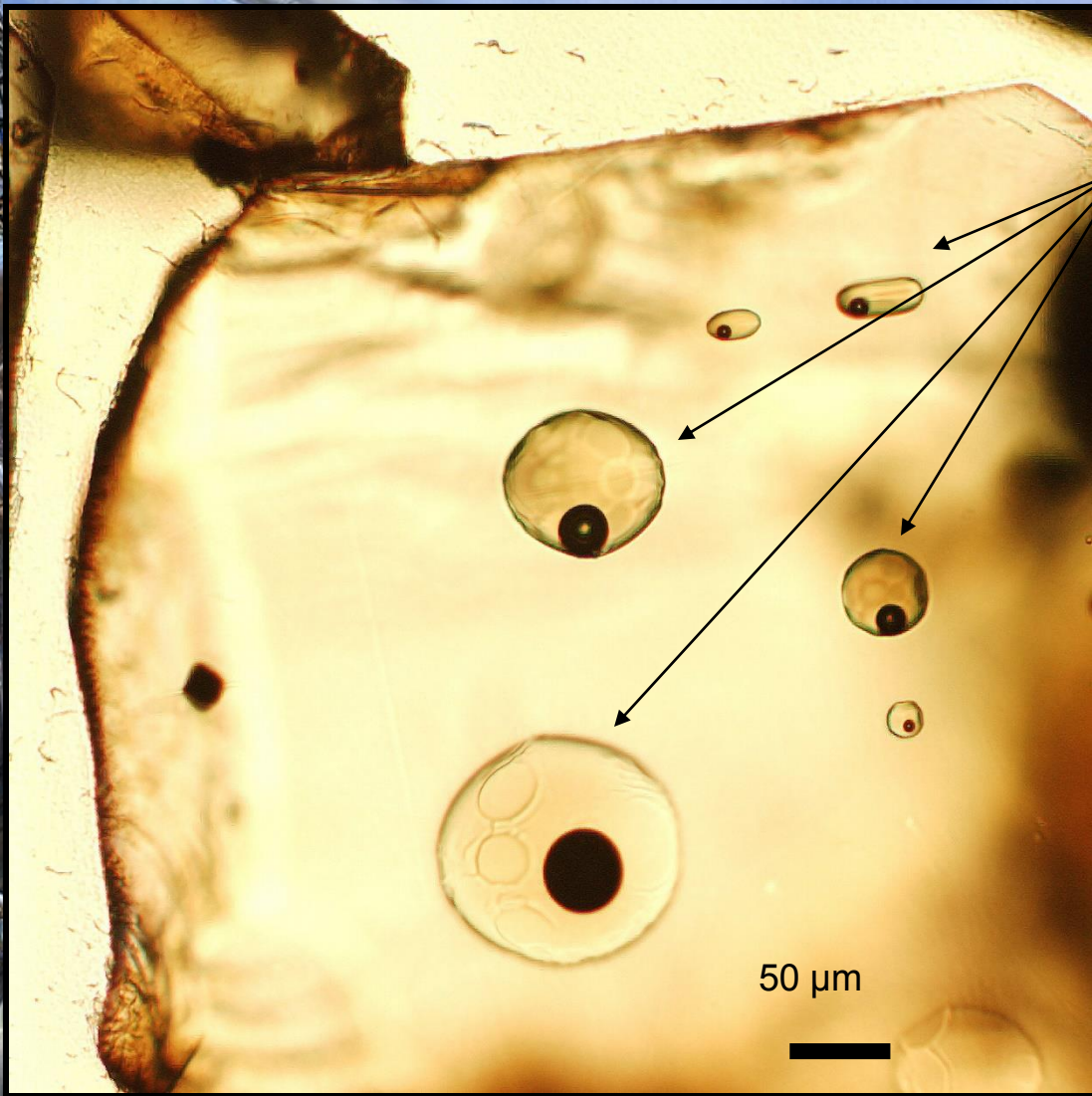
- 
- The background of the slide features a photograph of industrial infrastructure, including large, curved metal pipes and scaffolding, set against a clear blue sky. The pipes are made of a reflective material, likely stainless steel, and are arranged in a complex, vertical and horizontal pattern. The overall scene suggests a chemical or pharmaceutical processing plant.
- **Solid particles** may also be included into the crystal particularly at the nucleation stage when foreign bodies act as heteronuclei.
 - Saito *et al.* (1998, 1999) have shown that **physical contacts between crystals and/or the temporary attachment of small crystal fragments, such as attrition nuclei, significantly enhance the growth rate of the particular face** for a short period during which generated macrosteps interact and entrap mother liquor.
 - This work was carried out with sodium chloride crystals, but the mechanisms postulated could be of more general application.

- 
- A vertical image on the left side of the slide showing industrial pipes and structures, likely part of a chemical or pharmaceutical plant. The pipes are metallic and have various fittings and valves. The background is a clear blue sky.
- Inclusions may sometimes be prevented if the crystals are grown in the presence of certain **ionic impurities**, e.g. traces of Pb^{2+} and Ni^{2+} allow near-perfect crystals of ADP (ammonium dihydrogen phosphate) to be grown for piezoelectric use; traces of Pb^{2+} help good crystals of NaCl to be grown.
 - **Anionic surfactants** are particularly effective for eliminating inclusions in ammonium perchlorate growth from aqueous solution (Hiquily and Laguerie, 1984).
 - A **change of solvent** may have a significant effect:
 - Hexamine, which readily develops inclusions when grown from aqueous solution, contains none when grown from methanol or ethanol.
 - An increase in the **viscosity** of the mother liquor may also help; small amounts of carboxymethyl cellulose added to the solution have been known to have a beneficial effect.
 - **Ultrasonic vibrations** have also been tried with moderate success.

- Under isothermal conditions **inclusions may change shape or coalesce** as the internal system adjusts itself towards the condition of minimum surface energy.
- If the **temperature is raised**, negative crystals (faceted inclusion cavities) may be formed by a process of **recrystallization**.
- Fluid inclusions cannot be removed by heating alone. In fact even heating to decrepitation frequently fails to destroy all the inclusions.
- liquid inclusions can move under the influence of a temperature gradient. Since **solubility is temperature dependent**, crystalline material dissolves on the high solubility side of the inclusion, diffuses across the liquid and crystallizes out on the low solubility side (Wilcox, 1968).
- Henning and Ulrich (1997) measured migration rates of water inclusions in crystal layers of captolactam induced by temperature gradients. Migration progressed towards the warm surface at rates proportional to the temperature gradient while inclusions increased in size and changed their shape. Large inclusions moved faster than small ones.

- A general review of inclusions has been written by Deicha (1955). Deicha, G. (1955) *Lacunes des Cristeaux et leurs Inclusions Fluides*, Masson, Paris.
- Powers (1969-70) and Mantovani *et al.* (1985) give comprehensive accounts of inclusions in sugar crystals, and a world-wide coverage of research on inclusions, although mainly of geological interest,
- Powers, H.E.C. (1969/70) Sucrose crystals: inclusions and structure. *Sugar Technology Reviews*, 1, 85.
- Mantovani, G., Vaccan, G., Squaldino, G., Aquilano, D. and Rubbo, M. (1985) Sucrose crystal colour as a function of some industrial crystallization parameters. *L'Industria Saccarrifera Italiana*, 78, 7-14 and 79-86.
- A practical guide to fluid inclusion studies, with a geological bias, has been written by Shepherd, Rankin and Alderton (1985).
- Shepherd, T.J., Rankin, A.H. and Alderton, D.H.M. (1985) *A Practical Guide to Fluid Inclusion Studies*, Blackie, Glasgow.

Melt inclusions: An introduction



"Parcels" of melt
trapped in igneous
crystals

≡ Fluid inclusions

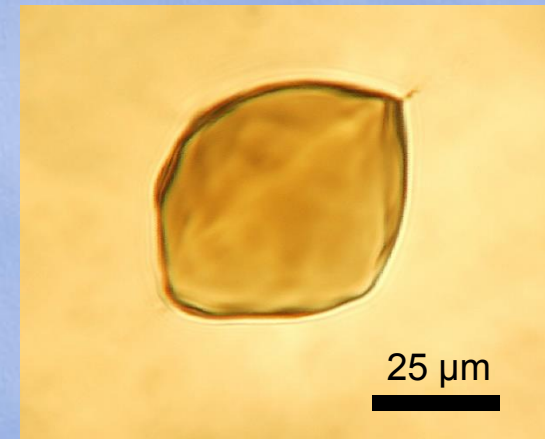
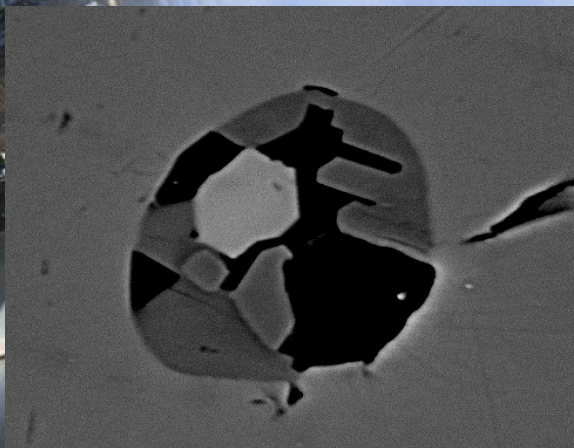
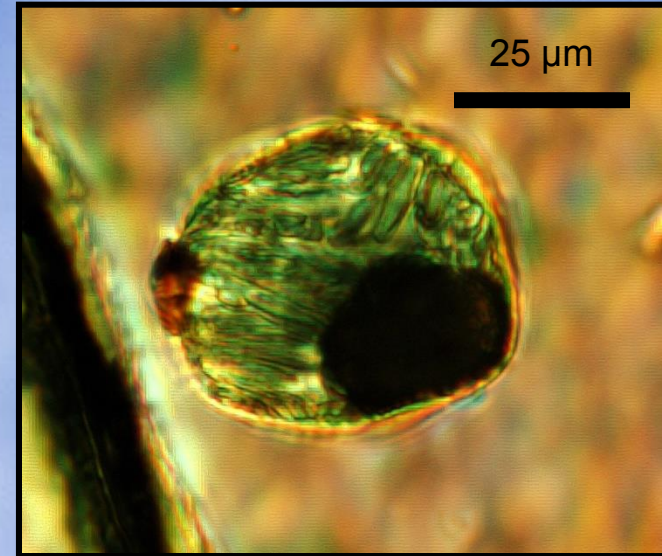
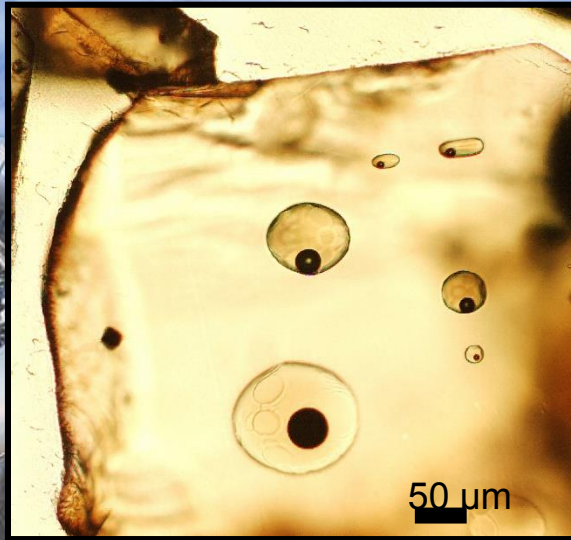
Occur in basaltic and
related rocks wherever
they are found:

Silicic and Plutonic Rocks

Xenoliths

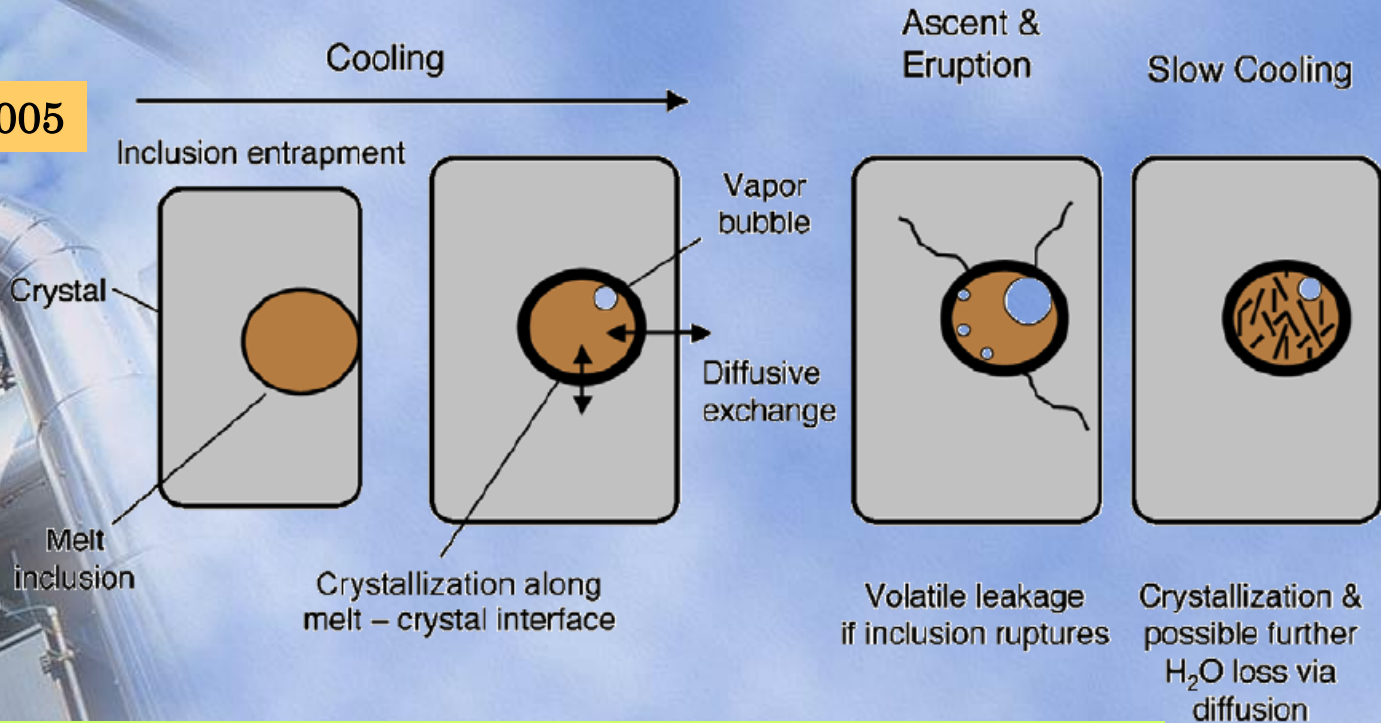
Evolution of melt inclusions after trapping

Important impact on physical appearance and chemical compositions



Evolution of melt inclusions after trapping

Wallace, 2005



1. Venting/breaching/alteration
2. Post-entrapment crystallization
3. Diffusive exchange

Μετατροπές φάσεων

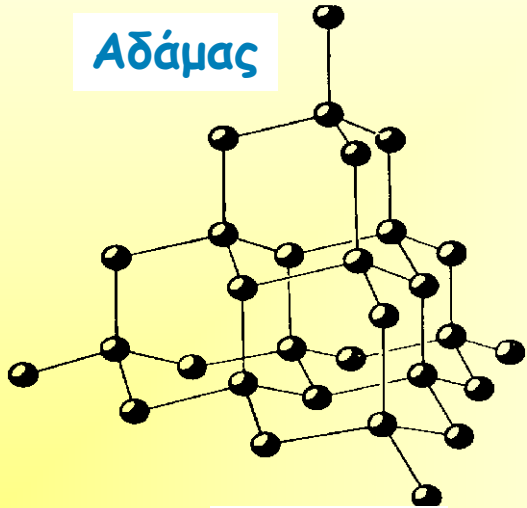
- Σε πολλές περιπτώσεις κατά την κρυστάλλωση, η πρώτη κρυσταλλική φάση η οποία σχηματίζεται είναι μετασταθής δηλ. είναι μια πολυμορφική φάση ή ένα ένυδρο άλας (κανόνας Ostwald)
- Κάποιες από τις μετασταθείς φάσεις μετατρέπονται προς τις σταθερότερες ταχύτατα, ενώ άλλες εμφανίζουν εξαιρετική σταθερότητα στο χρόνο.
- Κάποιες πάλι από τις μετατροπές φάσεων είναι αντιστρεπτές (εναντιοτροπικές) ενώ άλλες μη αντιστρεπτές (μονοτροπικές)

Πολυμορφισμός

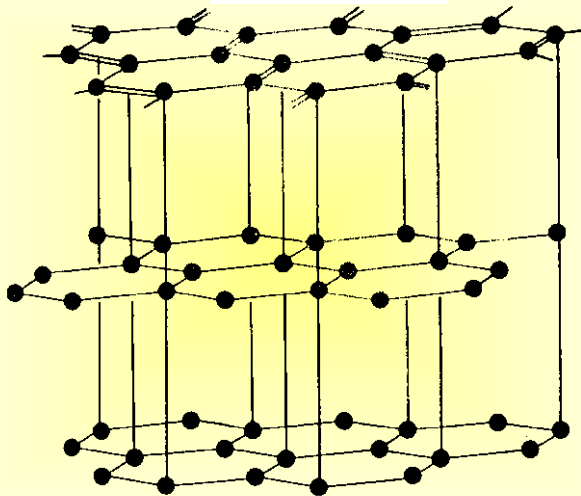
Η αυτή χημική ουσία- διαφορετικές κρυσταλλικές δομές

Αλοτροπισμός

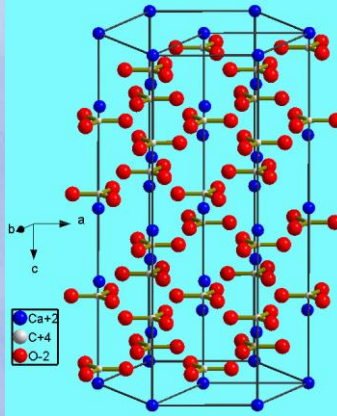
Αδάμας



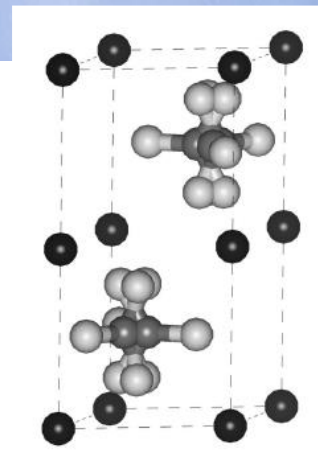
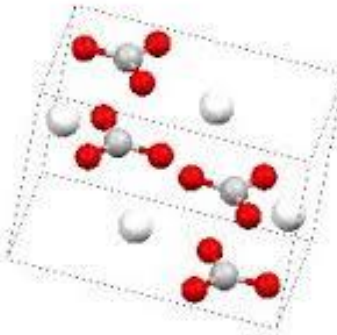
Γραφίτης



διατήρηση
βιοδιαθεσιμότητα
Αξιόπιστη επεξεργασία
Προστασία ΠΙ



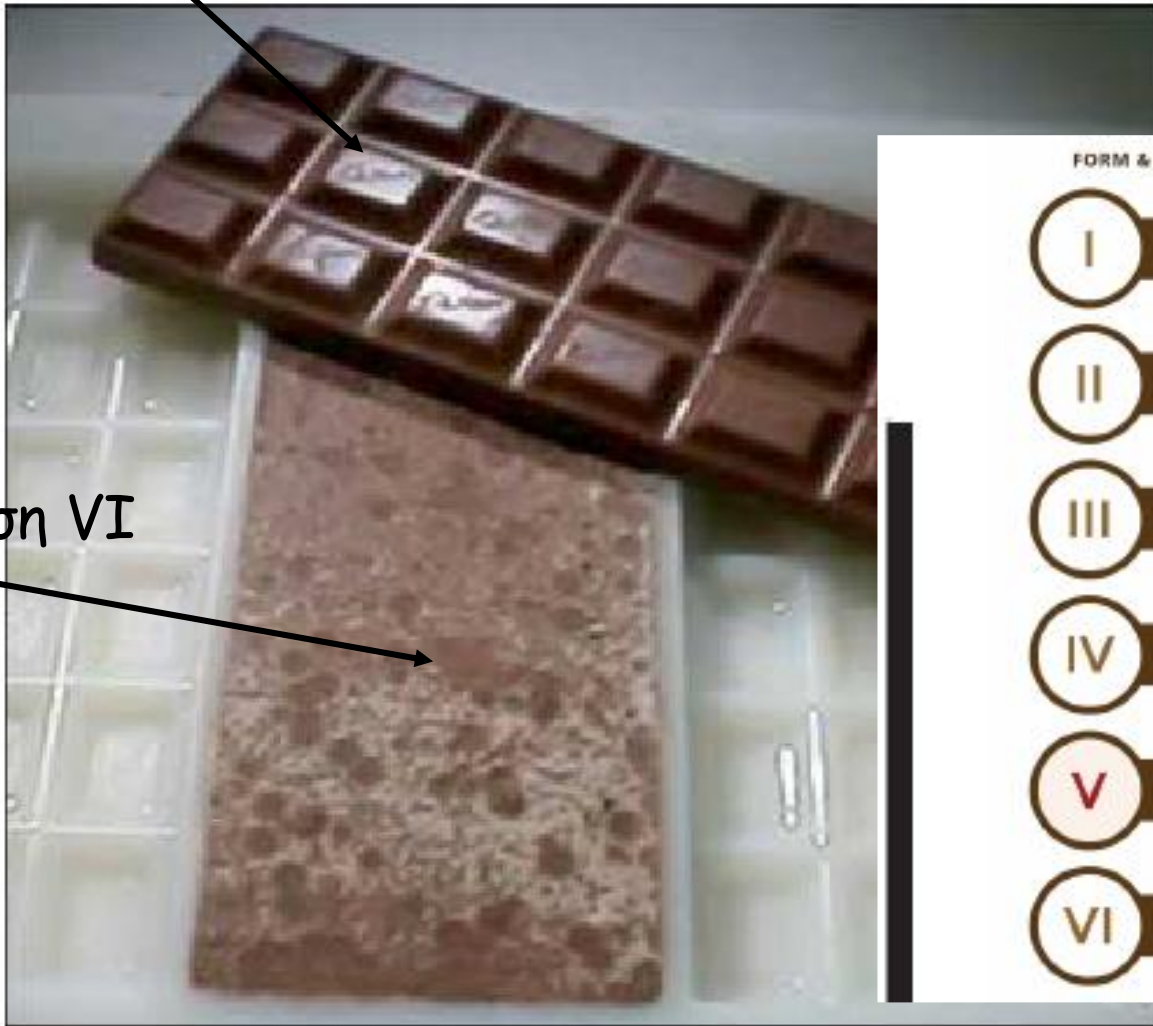
CaCO₃



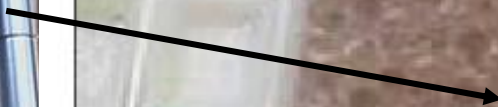
Διαφορετικές
ιδιότητες, π.χ.:
πυκνότητα
υγροσκοπικότητα
ΣΤ, διαλυτότητα,
σταθερότητα
Ταχύτητα
διάλυσης
Επιφανειακές
ιδιότητες
Σκληρότητα,
συμπιεστότητα
Αντοχή στην τάση

Πολυμορφισμός - Σοκολάτα

Φάση V



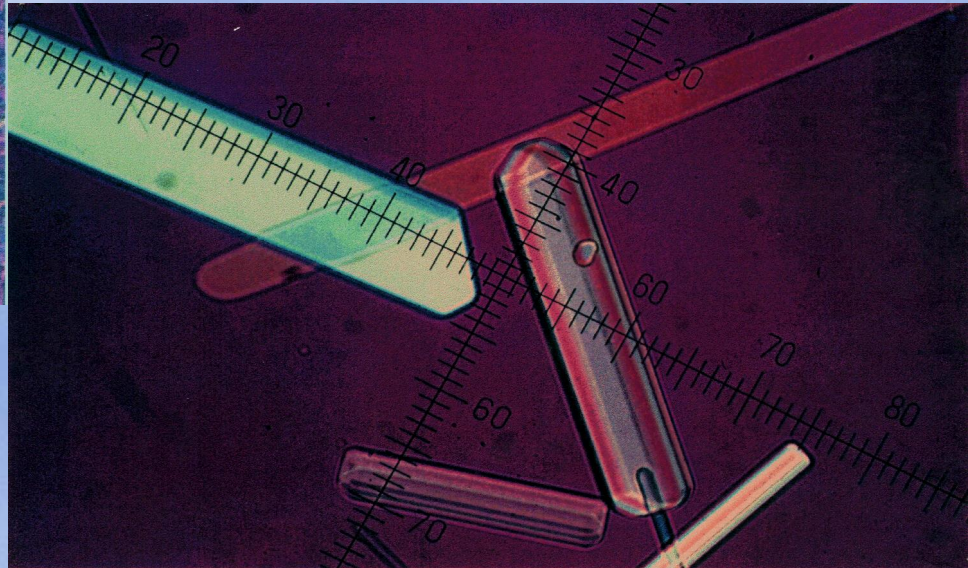
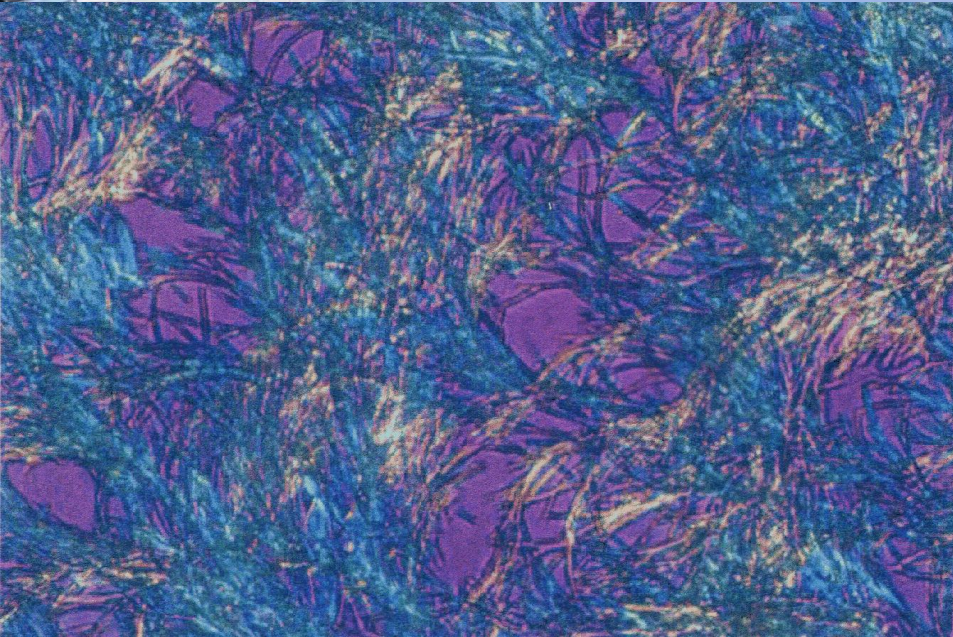
Φάση VI



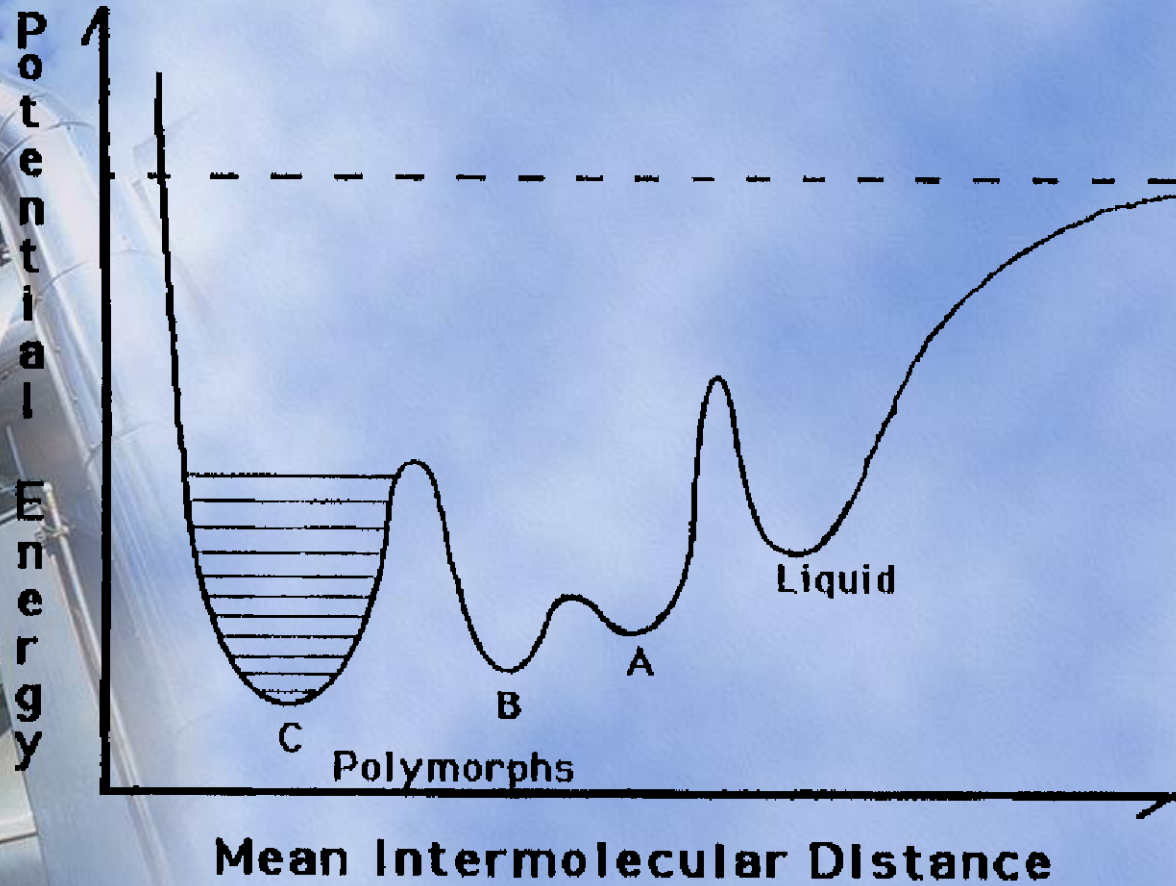
FORM & MELTING POINT	DESCRIPTION & PROPERTIES
I 17.3°C	BOTH SOFT AND CRUMBLY WITH NOTICEABLE BLOOMING Form I is produced by cooling melted chocolate rapidly (e.g. by putting it in the freezer). Form II is produced by cooling melted chocolate at 2°C per minute. Form I crystals also gradually become Form II after a short time of freezing temperature storage.
II 23.3°C	
III 25.5°C	BOTH FIRM, BUT DON'T GIVE A GOOD 'SNAP', & SHOW SOME BLOOMING Form III is produced by cooling at 5-10°C. Form II becomes Form III after storage at low temperatures above freezing.
IV 27.3°C	Form IV is produced by allowing melted chocolate to cool at room temperature. Form II also becomes Form IV after storage at room temperature for some time.
V 33.8°C	SHINY, SMOOTH TEXTURE, GOOD 'SNAP', AND MELTS IN THE MOUTH Formed by tempering chocolate slowly at room temperature. Most desirable!
VI 36.3°C	HARD AND MELTS SLOWLY IN THE MOUTH, SHOWS SOME BLOOMING Can't be formed from melted chocolate - can only be formed after solid, tempered chocolate has rested for at least 4 months.

INCREASED STABILITY & DENSITY

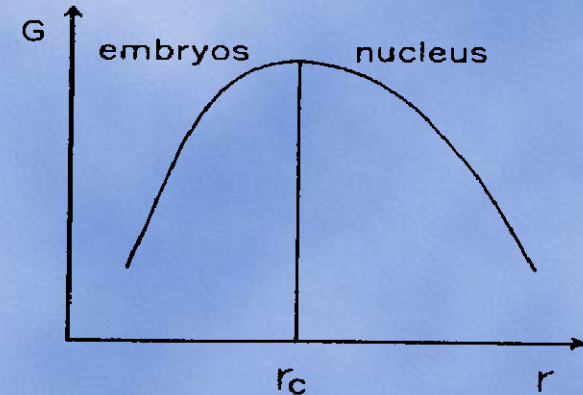
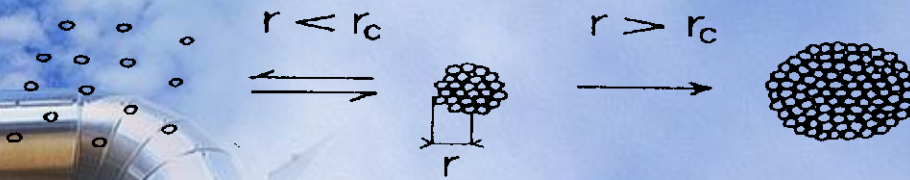
Πολυμορφικές φάσεις μετά καλίου άλατος του *p*-αμινο βενζοϊκού οξέος



Πολυμορφισμός

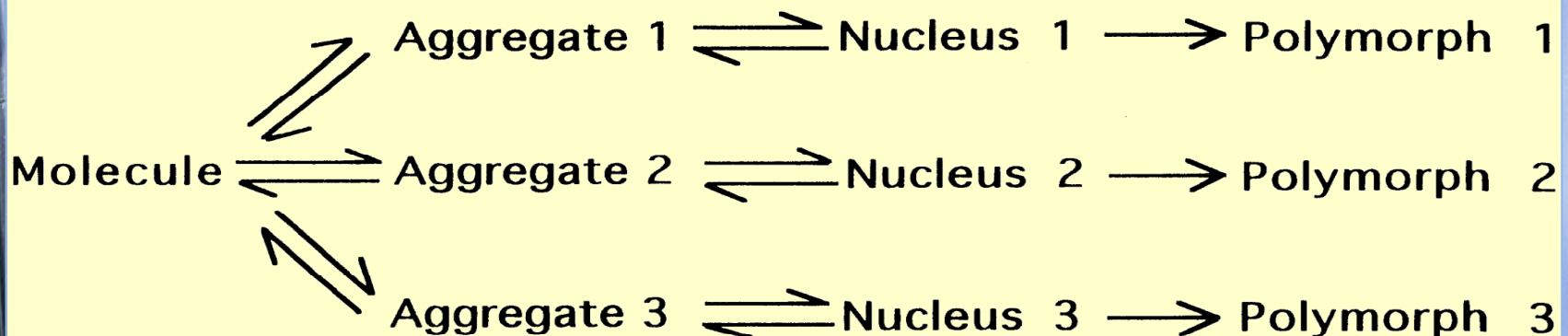


Πυρηνογένεση πολυμορφικών φάσεων




$$J = J_0 \exp \left[-\frac{\Delta G_{crit}}{kT} \right]$$

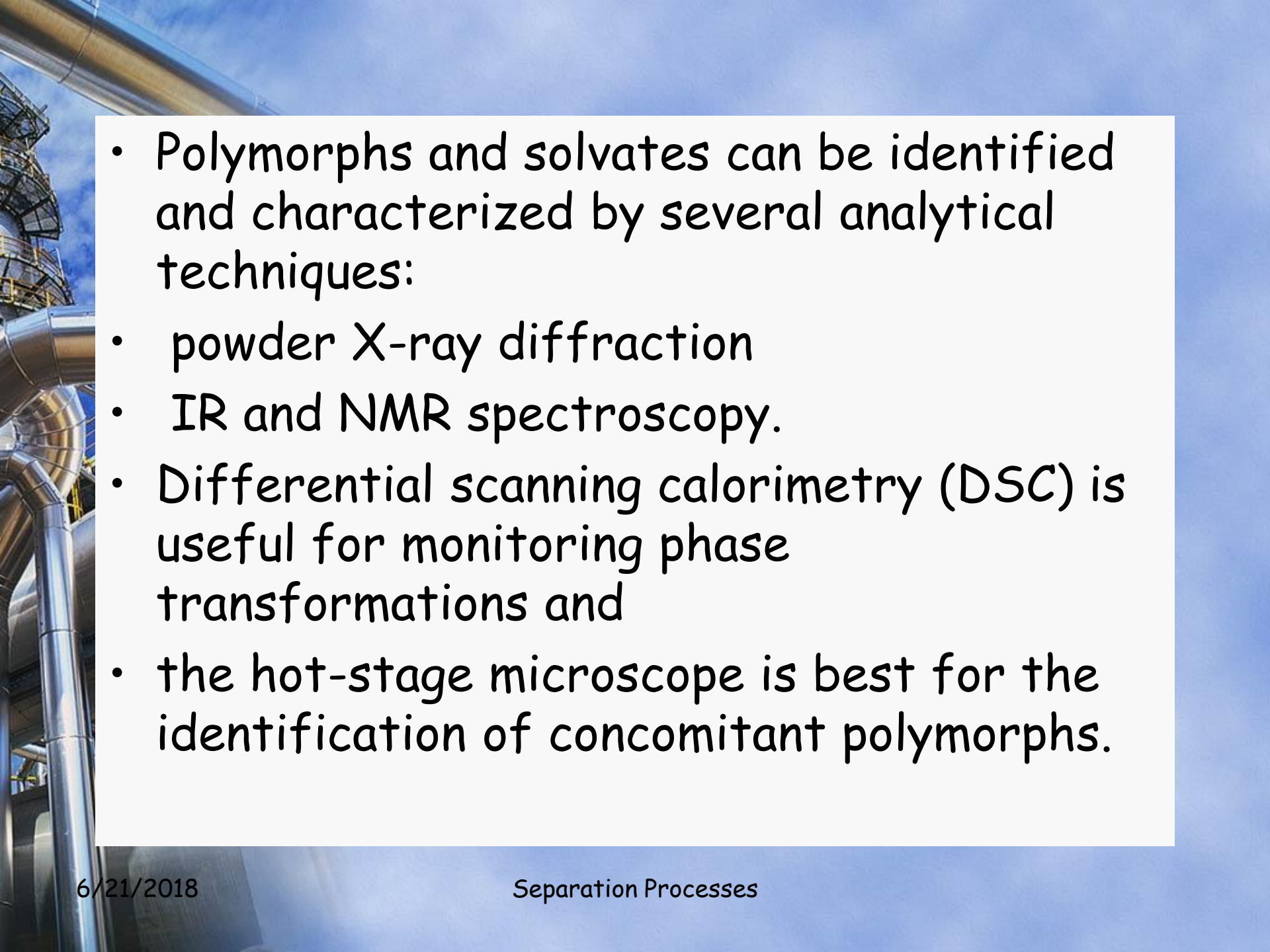
$$\Delta G_{crit} = F \frac{\gamma_{SL}^3 \mathcal{G}_m^2}{(\Delta\mu)^2} = F \frac{\gamma_{SL}^3 \mathcal{G}_m^2}{(kT \ln S)^2}$$



- Η μετασταθής φάση η οποία κρυσταλλώνεται πρώτη, προκειμένου να ταυτοποιηθεί πρέπει να απομονωθεί γρήγορα και να ξηρανθεί με τον κατάλληλο τρόπο πριν μετατραπεί
- Σε ξηρή μορφή μπορεί να είναι σταθερή για μακρό χρονικό διάστημα
- Αν είναι επιθυμητή η κρυστάλλωση της πλέον σταθερής πολυμορφικής φάσης πρέπει να διασφαλισθούν οι κατάλληλες συνθήκες και να δοθεί ο κατάλληλος χρόνος στον κρυσταλλωτήρα προκειμένου να γίνει η μετατροπή στην επιθυμητή σταθερή φάση.

- Polymorphs differ in the type of lattice or in the spacing of the points in the crystal lattice, may exhibit different shapes which allow their differentiation by microscopic observation
- **These changes should not be confused with crystal habit modifications** which are due only to changes of growth of different crystal faces and do not affect physical properties of the crystals
- The different polymorphs, which may also differ in habit, **have distinctively different physical properties** (density, hardness, mp, solubility, reactivity, thermal properties, optical and electrical behavior etc)
- Each polymorph of a substance constitutes a separate phase in the Gibbs phase rule sense. However crystals of different habit they are one and the same phase
- **Polymorphs may transform in the solid state but crystals of different habit they cannot**
- **Hydrates and other solvates are not- strictly speaking- polymorphs**
- Enantiomorphs are not true polymorphs

- 
- A vertical industrial distillation column with multiple trays and a complex network of pipes and ladders, set against a clear blue sky.
- Bernstein, Davey and Henk (1999) have drawn attention to a little appreciated phenomenon of the **simultaneous crystallization of different polymorphs**.
 - They use the term '**concomitant polymorphs**' to describe these mixtures that can occur and cause problems in industrial processes since the product crystals may show erratic variations in habit, colour, melting point, dissolution rates, etc. despite any evidence of process changes or impurity contamination.

- 
- The background of the slide features a photograph of industrial infrastructure, including large, shiny metal pipes and complex scaffolding structures against a clear blue sky. The pipes are arranged in a vertical and horizontal pattern, with some showing signs of wear and rust.
- Polymorphs and solvates can be identified and characterized by several analytical techniques:
 - powder X-ray diffraction
 - IR and NMR spectroscopy.
 - Differential scanning calorimetry (DSC) is useful for monitoring phase transformations and
 - the hot-stage microscope is best for the identification of concomitant polymorphs.

Hot stage microscopy

- Fluid stage transformation as a function of temperature is observed
- Silicon oil stage microscopy is used for detection of pseudopolymorph.

APPLICATION:

- in the study of solid-state active pharmaceutical ingredients (APIs), EXCIPIENTS and pharmaceutically relevant polymers and lipids.





x ray diffraction method

- It provide the most complete information about solid state (identification & description)
- This method is based on the scattering of x-ray by crystals
- By this method one can identify the unit cell dimensions & conclusively establish the crystalline lattice system & provide specific differences between crystalline forms of given compound.
- In an X-ray diffraction measurement, a crystal is mounted on a goniometer and gradually rotated while being bombarded with X-rays, producing a diffraction pattern of regularly spaced spots known as **reflections**.
- It is tedious time consuming so it is not used or unsuitable for routine use.



Application:-

- many materials can form crystals—such as salts, metals, minerals, semiconductors, as well as various inorganic, organic and biological molecules—X-ray crystallography has been fundamental in the development of many scientific fields

Differential Thermal Analysis (DTA)

- The advantage is that the sample size required is only 2-5mg .
- DTA measures the tempt difference between sample and reference as a function of temperature or time when heating at constant rate.
- A DTA consists of a sample holder comprising thermocouples, sample containers and a ceramic or metallic block; a furnace; a temperature programmer; and a recording system.
- The key feature is the existence of two thermocouples connected to a voltmeter.
- One thermocouple is placed in an inert material such as Al_2O_3 , while the other is placed in a sample of the material under study.
- As the temperature is increased, there will be a brief deflection of the voltmeter if the sample is undergoing a phase transition.



Differential Scanning Calorimetric (DSC)

- DSC is also like to DTA except that the instrument measures the amount of energy required to keep the sample at the same temperature as the reference i.e. it measures the enthalpy of transition.
- When no physical or chemical changes is occurring within the sample then there is neither a temperature change nor the need to input energy to maintain an isotherm.
- Samples that may be studied by DSC or DTA are: Powders, fibers , single crystals, polymer films, semi-solids.
- DSC measures endothermic and exothermic transitions as a function of temperature.
 - -Endothermic heat flows into a sample.
 - -Exothermic heat flows out of the sample.



Differential
Scanning
Calorimeter (TA
Instruments
Q10, Q 100, Q
1000)

Applications of DTA / DSC in preformulation studies

1. To determine the purity of a sample
2. To determine the number of polymorphs and to determine the ratio of each polymorph
3. To determine the heat of solvation .
4. To determine the thermal degradation of a drug or excipients .
5. To determine the glass-transition temperature(t_g) of a polymer.

The background of the slide is a photograph of an industrial facility, likely a refinery or chemical plant. It features a complex network of large, silver-colored metal pipes and structures. The pipes are arranged in various orientations, some running horizontally and others vertically. The sky is a clear, bright blue with a few wispy white clouds. The overall scene is brightly lit, suggesting a sunny day.

Thermo Gravimetric Analysis (TGA)

- is a type of testing that is performed on samples to determine changes in weight in relation to change in temperature.
- Such analysis relies on a high degree of precision in measurements: weight and temperature change.
- As many weight loss curves look similar, the weight loss curve may require transformation before results may be interpreted.

Θερμοσταθμική Ανάλυση (TGA)

- TGA is commonly employed in research and testing to determine characteristics of materials such as polymers, to determine degradation temperatures, absorbed moisture content of materials, the level of inorganic and organic components in materials, decomposition points of explosives, and solvent residues.
- It is also often used to estimate the corrosion kinetics in high temperature oxidation.
- TGA Q 500.

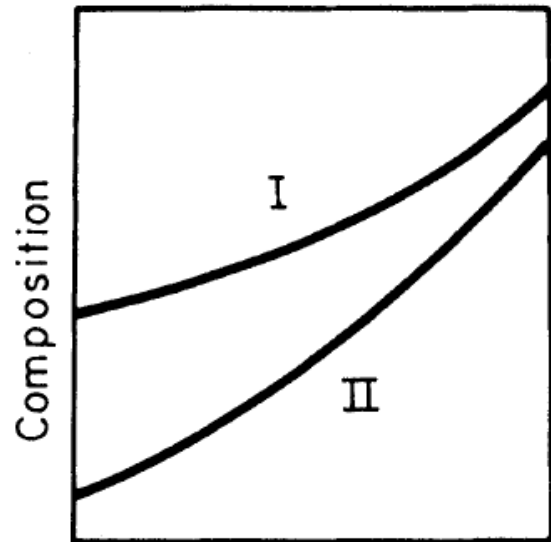


Dilatometry

- Measure change in volume caused by thermal or chemical effect.
- Using dilatometry the melting behaviour of Theobroma Oil was studied.
- Extremely accurate but tedious , time consuming and not widely used.

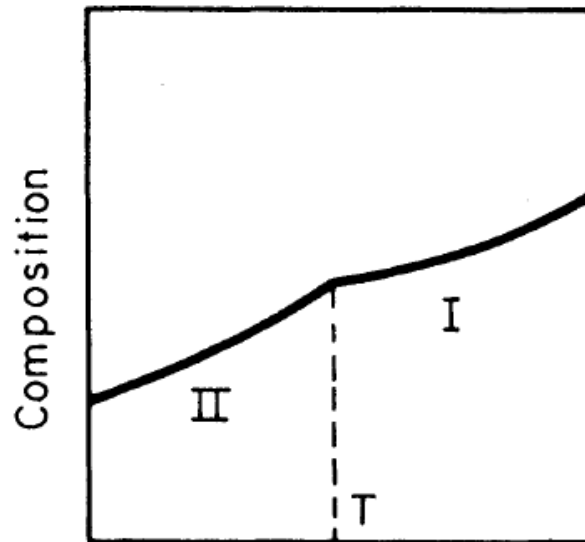


Πολυμορφισμός



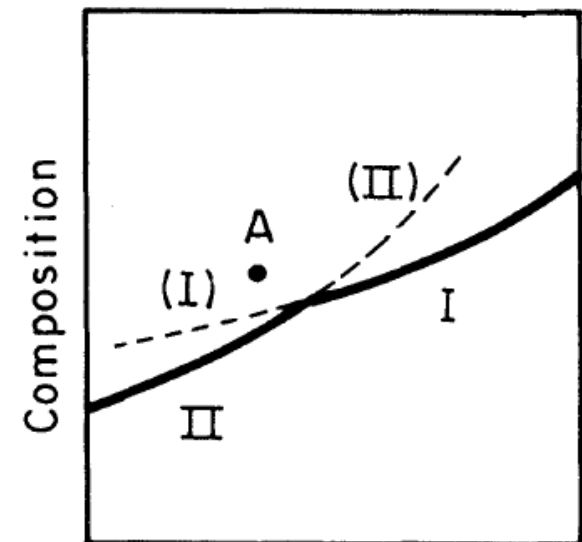
Temperature

(a)



Temperature

(b)



Temperature

(c)

A: Μονοτροπικό σύστημα (β) Εναντιοτροπικό σύστημα (γ) εναντιοτροπικό σύστημα με μετασταθείς φάσεις

- In *a*, form **II**, having the lower solubility, is more stable than form **I**. These two non-interchangeable polymorphs are **monotropic** over the whole temperature range depicted.
- In *b*, form **II** is stable at temperatures below the transition temperature T and form **I** is stable above T . At the transition temperature both forms have the same solubility and reversible transformation between these two **enantiotropic** forms **I** and **II** can be effected by temperature manipulation.
- In *c*, however, the intervention of **metastable** phases is shown (the broken line extensions to the two solubility curves) which bear evidence of the **importance of kinetic factors** which for a time may override thermodynamic considerations.

Under specified conditions of temperature and pressure, **except at a transition point**, only one polymorph is thermodynamically stable. All others are unstable and potentially capable of transforming to the stable polymorph. Whether they will do so, however, is another matter entirely. The more stable polymorph has the lower free energy at a given temperature. If polymorph I is more stable than polymorph II then the chemical potential of the species in the solid phase I is lower than that in solid phase II, i.e.

$$\mu_{\text{II}} < \mu_{\text{I}}$$

At equilibrium (solid phase in contact with the saturated solution)

$$\mu_0 + \mathbf{RT} \ln a_{\text{II}} < \mu_0 + \mathbf{RT} \ln a_{\text{I}}$$

From the relationship between the chemical potentials of polymorphs I and II:

$$a_{II} < a_I$$

and, since activity a and concentration c are related,

$$c_{II} < c_I$$

At a given temperature the more stable polymorph shall have the lower solubility in **any given solvent**

Similarly at any given pressure the more stable phase shall have a higher melting point

Difference between enantiotropy and monotropy.

Enantiotropic pair	monotropic pair
Reversible phase transition	Irreversible phase transition
Metastable \longleftrightarrow stable	Metastable \rightarrow stable
Transition is endothermic	Transition is exothermic
Lower melting form is thermodynamically stable below the transition temp.. And higher m.p . form is stable above the transition temp..	Higher melting form is always thermodynamically stable form.
lower m.p. has lower heat of fusion.	Higher m.p. has high heat of fusion.

Precipitation in systems dominated by crystal growth

- Nucleation may be limited either at the very initial stages or it may be eliminated
- Very rapid nucleation or crystal growth in crystal seeds
- Constant number of crystals during precipitation and the same morphology
- The size is characterized by a length r
- The rate of crystallization is independent both on the crystal size and on the crystal shape

Factors influencing crystal growth

- McCabe's ΔL law (1929)
- Growth dispersion
 - Varying distribution of dislocations
 - Stress effects
 - Crystal growth rates decrease with decreasing crystal size (NaCl, NaClO₃, K₂SO₄, CaC₂O₄·H₂O)
 - Even for sparingly soluble salts with crystal sizes < 1 μ m

Growth rate dispersion

- For diffusion controlled growth of small crystals, small crystals will grow faster than large
- Surface integration controlled: small crystals grow slower if mononuclear mechanism or as the result of varying activities of dislocation groups in screw dislocation growth

Growth of AgBr

- Diffusion mechanism
 - Small crystals grow faster at high supersaturations
 - At low supersaturation small crystals grow slower due to the Gibbs-Thomson effect
 - Intermediate supersaturations: the growth is size independent

Role of admixtures (impurities) very important: Kinetics-morphology

Co-precipitation

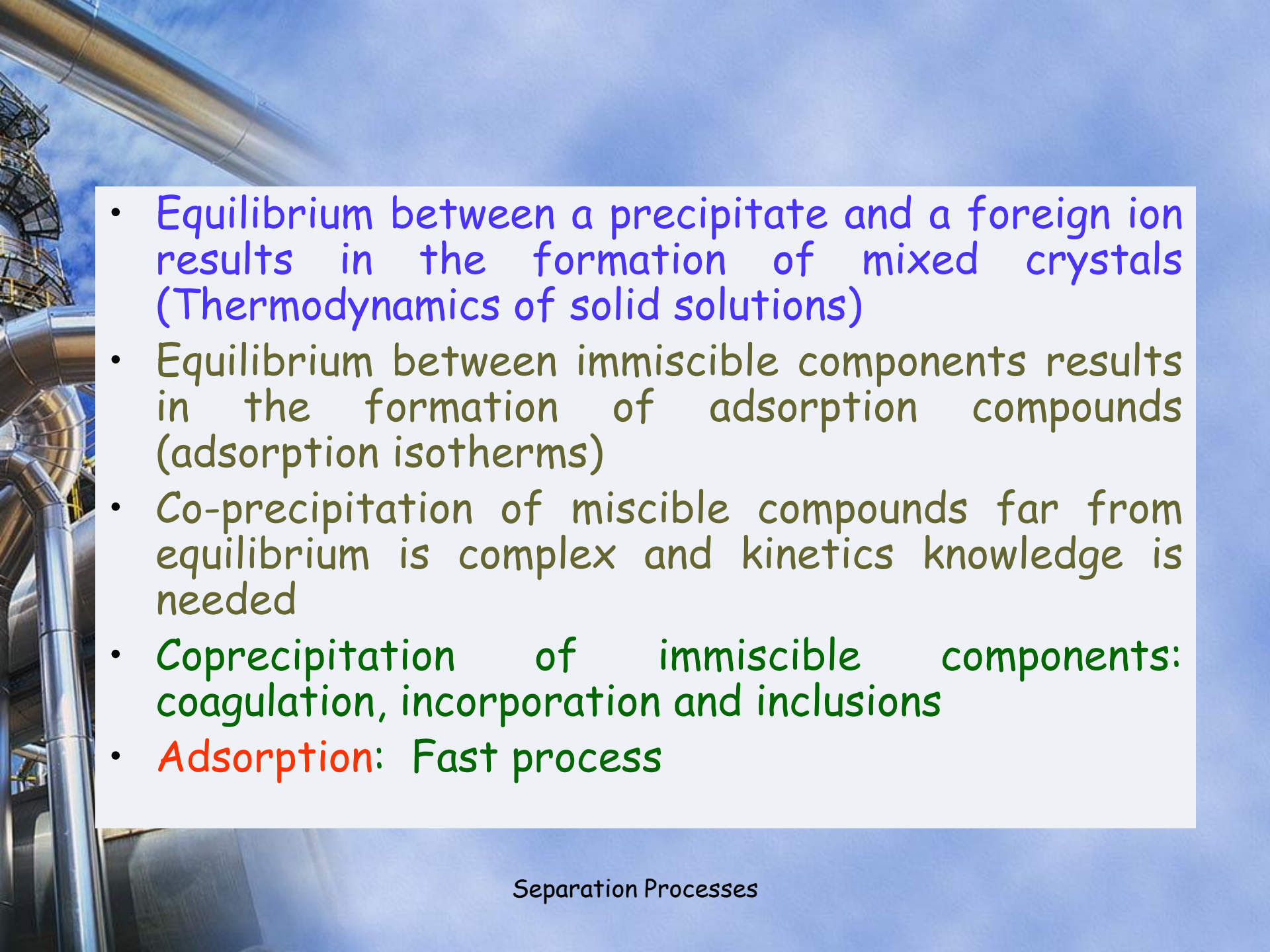
- Very important process for substance concentration [The chemist's dream: obtain gold from seawater ...] and separation.

May be achieved:

- By adsorption of one substance on another
- By the formation of solid solution
- combination
- Modification of the co-precipitation through the control of precipitation kinetics, coagulation and mutual miscibility of the components (as determined by ion size, polarizability and the electric charge)


Co-precipitation modes

- Equilibrium reactions
- Reactions out of equilibrium
- Miscible
- Imiscible components

- 
- Equilibrium between a precipitate and a foreign ion results in the formation of mixed crystals (Thermodynamics of solid solutions)
 - Equilibrium between immiscible components results in the formation of adsorption compounds (adsorption isotherms)
 - Co-precipitation of miscible compounds far from equilibrium is complex and kinetics knowledge is needed
 - Coprecipitation of immiscible components: coagulation, incorporation and inclusions
 - **Adsorption:** Fast process

Equilibrium systems-miscible components

- The solubility of one solid into another depends on the mutual ion compatibility in the respective crystal lattices
- For equilibrium, the component of the lower proportion should be able to diffuse freely to the substrate (lattice) of the other component

- 
- Ion diffusion in solid state depends on the defects mobility
 - Schottky and Frenkel defects are most common

Historically, **point defects** in crystals were first considered in ionic crystals, not in the much simpler metal crystals. The reason was that some known properties of ionic crystals (e.g. their conduction mechanism by ion migration at high temperatures) could be understood for the first time in terms of point defects, while no special properties of metals (in the twenties) were in desperate need of an explanation.

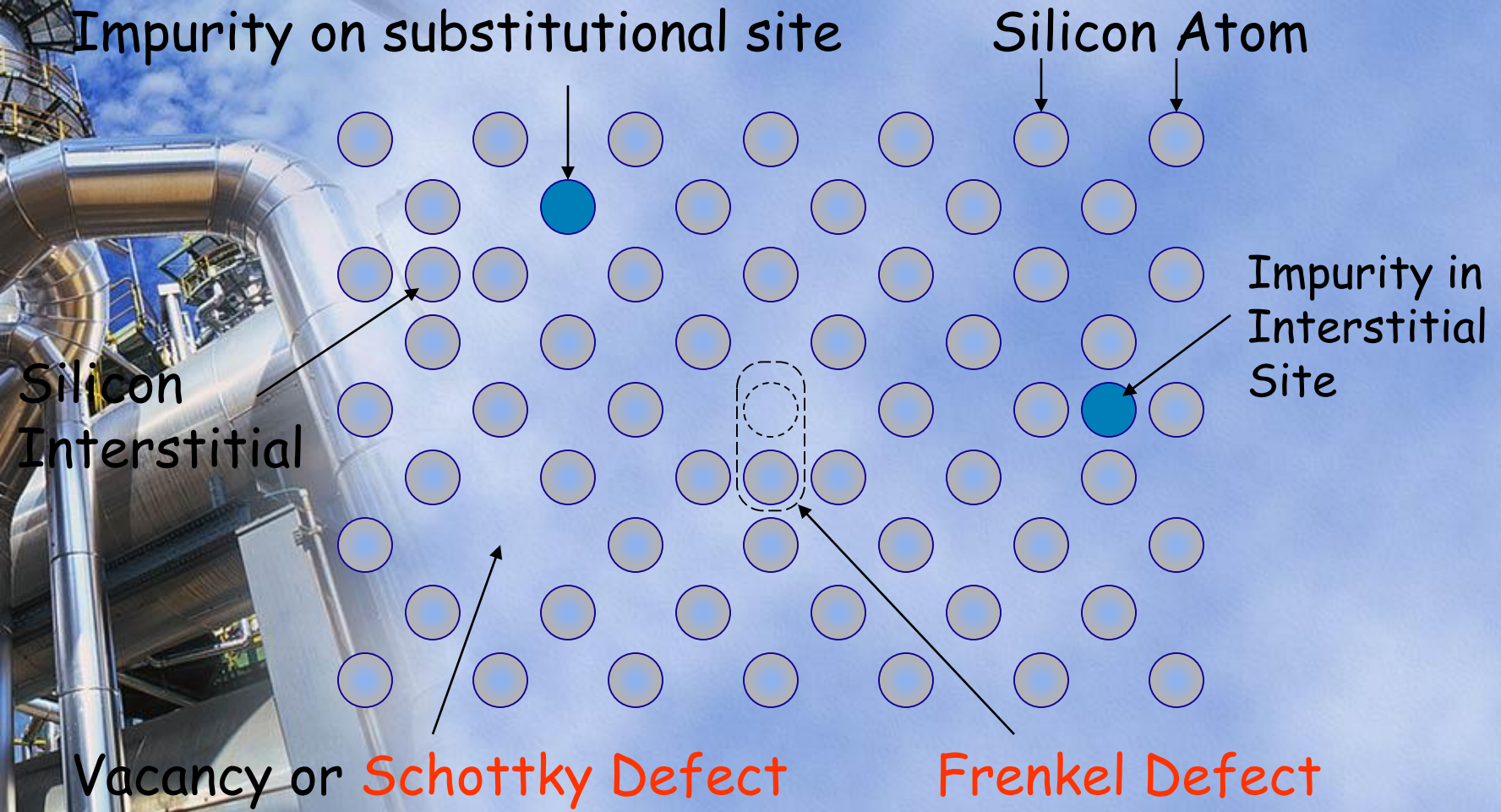
Frenkel defects then are charged interstitial - vacancy pairs carrying automatically different charge, e.g. a vacancy on a Na^+ site and a Na^+ interstitial

Schottky defects then are differently charged pairs of vacancies, i.e. missing Na^+ and Cl^- ions in the NaCl crystal

- **Generation**

- Schottky-process (from surface to crystal)
- Frenkel process (out of lattice to interstitial)

Illustration of the Defects



- Experimentally equilibrium co-precipitation may be achieved if after a fast precipitation the precipitate is peptized with the co-precipitating ions

$$D = \frac{(AY / AX)_{solid}}{(Y^- / X^-)_{solution}}$$

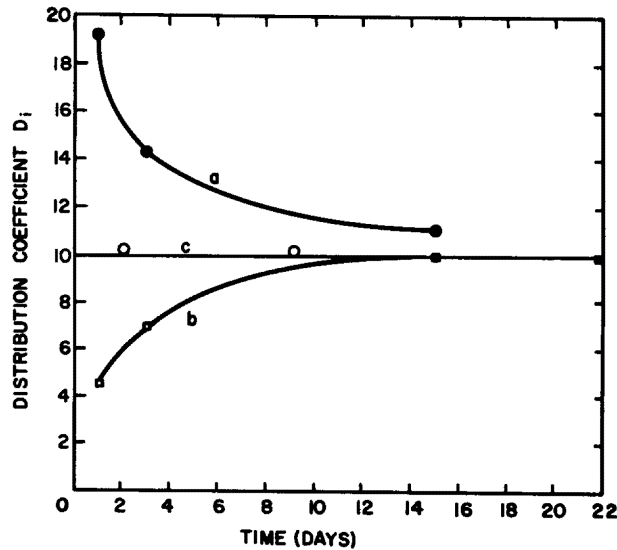
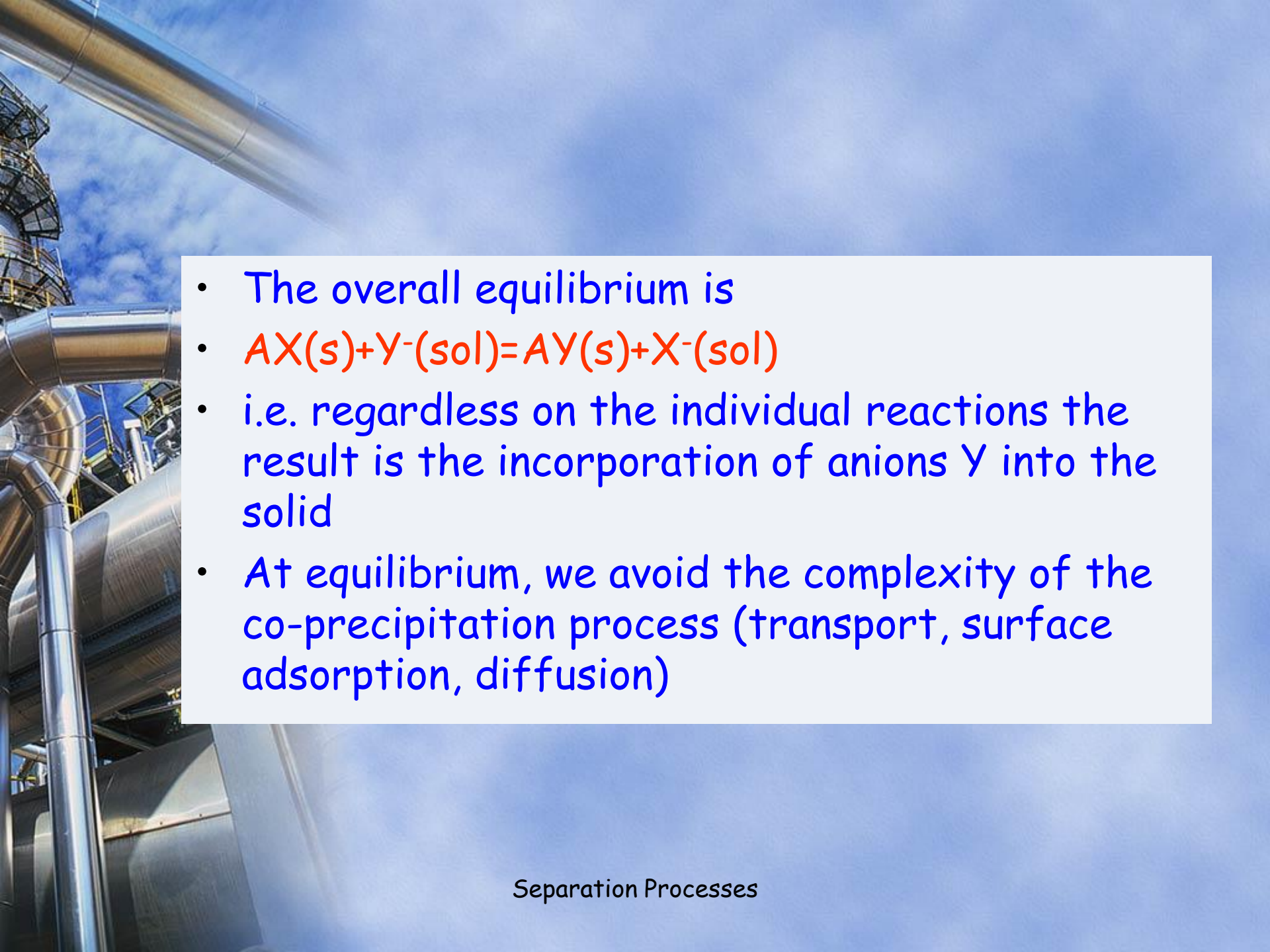


Fig. 3-1. Approach to equilibrium in the radium-barium bromide system as a function of time, at 35°C: curve a, activity initially in solid; curve b, activity initially in solution; curve c, entire system initially in liquid state. (After Chlopin, ref. 1)

Distribution of Ra in BaBr₂ crystals. Suspension in a saturated solution-cooling-precipitation

- Mixed ionic crystals consist of the substrate and a cation or anion associated with the co-precipitating ion
- Substitution of an anion in a solid may be considered as a two step process :
 - Surface adsorption
 - Lattice incorporation with diffusion
- $X^-(ads) + Y^-(sol) = Y^-(ads) + X^-(sol)$
- $Y^-(ads) + AX(s) = AY(s) + X^-(sol)$

- 
- The overall equilibrium is
 - $AX(s)+Y^-(sol)=AY(s)+X^-(sol)$
 - i.e. regardless on the individual reactions the result is the incorporation of anions Y into the solid
 - At equilibrium, we avoid the complexity of the co-precipitation process (transport, surface adsorption, diffusion)

- The distribution coefficient is given by the **Henderson-Kracek equation**:

$$D = \frac{(AY / AX)_{solid}}{(Y^- / X^-)_{solution}}$$

- $D_i > 1$: the relative concentration of component Y in the solid is larger than the respective value in the solution and the method is recommended as a separation method for this component from the solution
- Systems in which $D_i > 1$ are called **enrichment systems** (**συστήματα εμπλουτισμού**)

- $D_i < 1$ **depletion systems** for one component
- In aqueous and solid solutions:

$$\mu_{AY} = \mu_{AY}^0 + RT \ln(\alpha_{AY})_{soln}$$

$$\mu'_{AY} = \mu_{AY}^{0'} + RT \ln(\chi_{AY} f_{AY})$$

At equilibrium $\mu_{\delta i \alpha \lambda} = \mu_{\sigma \tau}$

$$\ln \left[\frac{\chi_{AY} f_{AY}}{\alpha_{AY}} \right] = - \frac{\mu_{AY}^{0'} - \mu_{AY}^0}{RT}$$

Similarly, for AX

$$\ln \left[\frac{\chi_{AX} f_{AX}}{\alpha_{AX}} \right] = - \frac{\mu_{AX}^{0'} - \mu_{AX}^0}{RT}$$

Therefore

$$\ln \left[\frac{(\chi_{AY} f_{AY})(\alpha_{AX})}{(\chi_{AX} f_{AX})(\alpha_{AY})} \right] = \frac{[(\mu_{AY}^0 - \mu_{AY}^{0'}) - (\mu_{AX}^0 - \mu_{AX}^{0'})]}{RT}$$

At equilibrium between pure AY and its solution

$$\mu_{AY}(0) = \mu_{AY}^0 + RT \ln(\alpha_{AY})_0 = \mu_{AY}^{0'}(\text{solid}) \equiv \mu_{AY}^{0'}$$

similarly

$$\mu_{AX}(0) = \mu_{AX}^0 + RT \ln(\alpha_{AX})_0 = \mu_{AX}^{0'}(\text{solid}) \equiv \mu_{AX}^{0'}$$

Combination of the last two equations yields:

$$\frac{(\chi_{AY} f_{AY})(\alpha_{AX})}{(\chi_{AX} f_{AX})(\alpha_{AY})} = \frac{(\alpha_{AX})_0}{(\alpha_{AY})_0} = K_0$$

K_0 is the solubilities ratio

In most cases of co-precipitation the concentration of the microcomponent (Y or AY) in the solid is $\chi_{AY} \ll 1$ and consequently the coefficient f_{AY} is constant, hence:

$$\chi_{AY} \left(\frac{\alpha_{AX}}{\alpha_{AY}} \right) f_{AX} \cong \frac{K_0}{f_{AY}} \cong K'_0$$

And because $\chi_{AX} \approx 1$

$$f_{AX} = \exp \frac{\mu'_{AX} - \mu^0_{AX}}{RT}$$

$K \alpha 1$

$$\chi_{AY} \left(\frac{\alpha_{AX}}{\alpha_{AY}} \right) = K'_0 \exp \left[- \frac{\Delta G'_{AX}}{RT} \right]$$

Hence

$$D_i = \frac{\chi_{AY} c_{AX}}{c_{AY}} = K'_0 \left(\frac{\gamma_{AX}}{\gamma_{AY}} \right)^2 \exp \left[-\frac{\Delta G'_{AX}}{RT} \right]$$

with

$$\Delta G'_{AX} = \mu_{AX}^{0'} - \mu'_{AX}$$

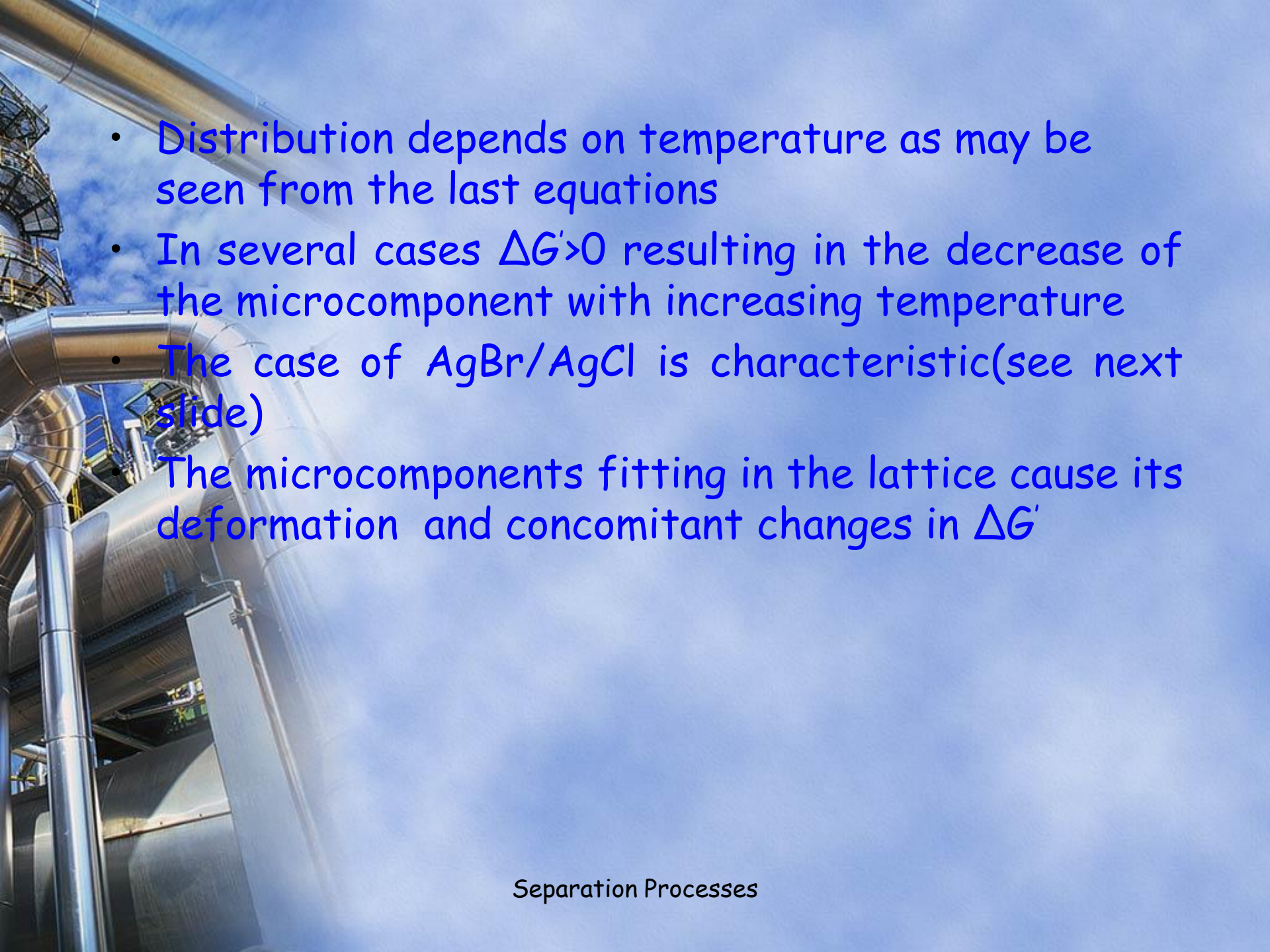
i.e. the change in chemical potential of the solid solvent because of the dissolution of the component Y

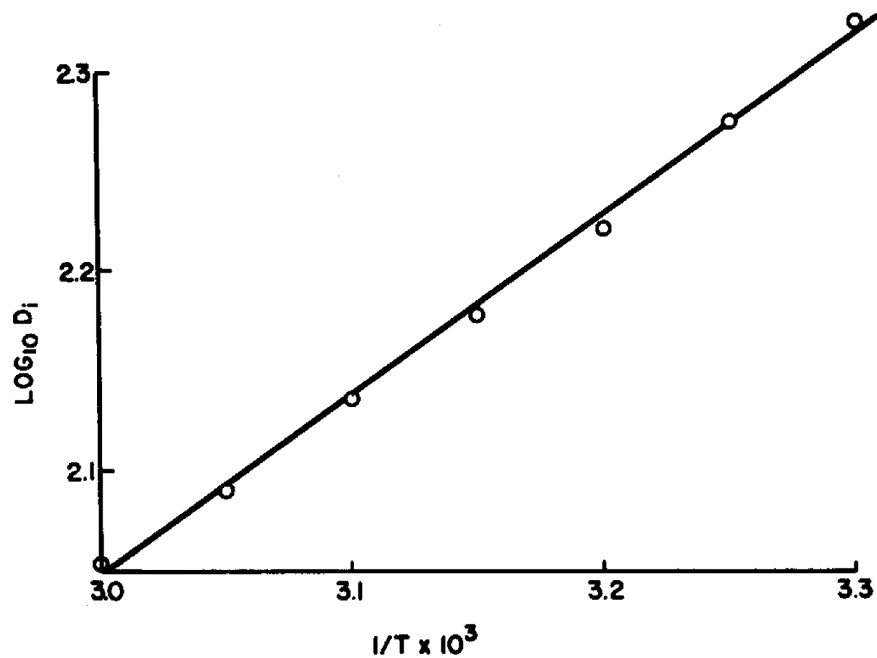
Vaslow, Boyd suggested a similar relationship with $f_{AX}=1$

$$f_{AY} = \exp \frac{\mu_{AY} - \mu_{AY}^{i\delta}}{RT}$$

$$D_i = \frac{\chi_{AY} c_{AX}}{c_{AY}} = K_0 \left(\frac{\gamma_{AX}}{\gamma_{AY}} \right)^2 \exp \left[\frac{-\Delta G'_{AX}}{RT} \right]$$

In ideal solid solutions, where there is no change in the substrate lattice and the activity coefficients are the same the distribution coefficient coincides with the solubilities ratio in the solution phase

- 
- A photograph of an industrial distillation plant. Several large, vertical stainless steel distillation columns are visible, connected by a network of horizontal and vertical pipes. The scene is set against a clear blue sky with some light clouds. The lighting suggests a bright, sunny day.
- Distribution depends on temperature as may be seen from the last equations
 - In several cases $\Delta G' > 0$ resulting in the decrease of the microcomponent with increasing temperature
 - The case of AgBr/AgCl is characteristic (see next slide)
 - The microcomponents fitting in the lattice cause its deformation and concomitant changes in $\Delta G'$



The homogeneous distribution coefficient D_1 as a function of $1/T$ for the Br^-/AgCl system. (After Vaslow and Boyd, ref. 3)

TABLE 3-1
The Homogeneous Distribution Coefficient D_1 for Different Solid Solutions with the Solubility Ratio K_0 and the Excess Free Energy Function $\overline{\Delta G}$ Calculated from Eq. 3-18

Solid solution	Temp., °C	D_{obs}	K_0	$\overline{\Delta G}$, cal/ mole	Ref.
AgBr in AgCl	30	211.4	315.7	+287	2
AgCl in AgBr	30	0.0036	0.0031	-70	2
AgCl in TiCl	40	4.2	7.2×10^5	+7500	2
$\text{Pb}(\text{IO}_3)_2$ in $\text{Ba}(\text{IO}_3)_2$	25	25	3.2×10^8	+2800	4
$\text{Ra}(\text{IO}_3)_2$ in $\text{Ba}(\text{IO}_3)_2$	25	1.42	1.32	-39	5
RaSO_4 in BaSO_4	20	1.8	5.9	+700	6
SrSO_4 in BaSO_4	25	3.010	1.81×10^{-2}	+2480	7
PbSO_4 in BaSO_4	25	2.55×10^{-2}	9.61×10^{-2}	+805	8

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