1 Binding and Clustering

In these notes we will review the basic elements of binding, calling attention on the competition between the energetic gain of forming a bond and the loss of translational entropy. We will learn how to calculate theoretically the distribution of cluster sizes, in the hypothesis of an ideal gas of cluster, and discuss how the cluster partition functions can be calculated numerically. Building on the thermodynamic formalism, we will discuss some analytically soluble simple models of self-assembly: equilibrium and cooperative polymerisation and micelle formation.

The tendency of a system to spontaneously reach a well-defined structure is often named "self-assembly". Originally used in biology to describe the process that brings to the self organization of proteins into complex aggregates (like virus capsides), the word self-assembly has progressively permeated physics, chemistry and material science, becoming almost a substitute (despite its equivalence) for the more precise thermodynamic term, the minimization of the system free energy on going from a collection of disordered particles to the final (possibly ordered) structure. Crystallization of a metastable fluid can be properly considered as a well known example of self-assembly.

While the search for a minimum free energy state is ubiquitous, the word self-assembly, is commonly limited to the case in which the final structure is composed by (often ordered) aggregates of finite size: micelles, vesicles, filaments, ribbons, self-assembling spontaneously under the appropriate external conditions (density, temperature, salt concentration, pH and so on).

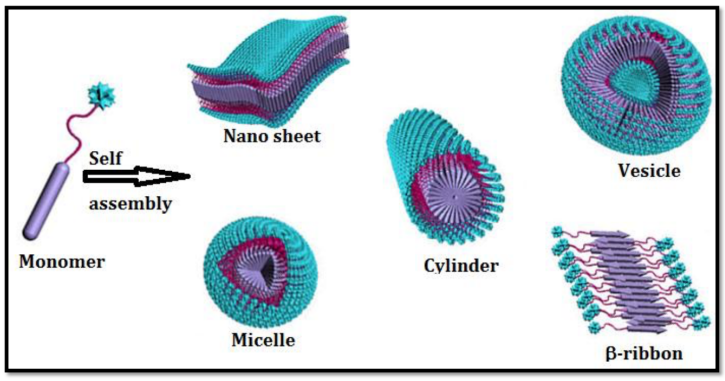

Figure 1: Examples of finite size aggregates

We start with some general consideration on self-assembly of one-component systems into finite size aggregates, and more specifically on its thermodynamic basis. Specifically, we will focus on particles whose interaction energy scale is indicated by ϵ and whose interaction range is indicated by Δ. We will use the generic word "particle", which according

to the context can refer to an atom, a molecule, a macromolecule, a colloidal particle.

To exploit self-assembly into finite size structures it is fundamental to develop a thermodynamic description of the clustering process, highlighting the role of the bonding volume compared to the volume per particle and the bonding energy. The competition between the entropic driving force disfavouring self-assembly and the energetic (or enthalpic) driving force favouring the formation of low energy aggregates is at the heart of self-assembly.

2 Thermodynamic description of the clustering process

The first step in the description of an aggregation process is the definition of the aggregate (or cluster). A cluster is commonly defined as the set of all particles mutually connected (e.g. via a continuous path of bonds). Hence, the definition of a cluster as an entity requires preliminarely the definition of "bond" between particles. In most of the cases, bonding can be defined geometrically or energetically. For example, two particles can be considered bonded if they are closer than a bonding distance and with a proper relative orientation or if their pair interaction energy is smaller than a threshold. In the case of square-well like interactions, a clear-cut definition of bond is provided by the relative energy of the two particles: if such energy is the square-well depth $-\epsilon$ a bond exists. Thus, differently from extended infinite size aggregates — which can be stabilised also by repulsive interactions (as in the paradigmatic case of hard-sphere crystallisation) — the formation of a stable aggregate of finite size requires attraction between the participating particles. For simplicity, I will assume generic interaction potentials, to highlight the relative role of the interaction range (bonding volume) and of the interaction strength. The simplest case is the square-well potential. In this case a "bond" of strength $\epsilon > 0$ sets in when the distance between two particles is within σ and $\sigma + \Delta$ (being σ the characteristic particle size). The values of Δ and ϵ enter in the evaluation of the partition function of the system (and hence in the free energy) determining the temperature T and density ρ conditions under which bonding becomes statistically relevant. Typically, Δ is a fraction of σ (as we will discuss later on, larger Δ values do not allow for self-assembly of finite size clusters).

The thermodynamic description of an aggregating system significantly simplifies if the hypothesis that clusters do not significantly interact among themselves is satisfied. (e.g. in the case in which the dominant contribution is excluded volume and the system packing fraction is small, so that clusters can be considered isolated). In this "ideal gas of cluster" approximation, the canonical partition function a system composed by clusters differing in the number n of bonded monomers, in the NVT ensemble (where N is the total number of monomers) can be written as

$$Q = \prod_{n=1}^{\infty} \frac{Q_n^{N_n}}{N_n!} \tag{1}$$

where Q_n is the partition function of the n-cluster and N_n is the number of clusters of

size n in the system. The sum if formally running to ∞ even if we will see that a constraint will control the total number of particles. For spherical particles interacting with isotropic potentials

$$Q_n = \frac{1}{n!\lambda^{3n}} \int' d\vec{r}_1 ....d\vec{r}_N \exp\left[-\beta V(\vec{r}_1, \vec{r}_2, ..., \vec{r}_N)\right] \tag{2}$$

where the $'$ sign in the integration limits indicates that only points in phase space $d\vec{r}_1 ....d\vec{r}_N$ for which the cluster does not break into disconnected smaller clusters should be considered.

For the monomer (assumed as a spherical rigid body, e.g. no internal fluctuations)

$$Q_1 = \frac{V}{\lambda^3}$$

For directional interactions, one need to integrate over all Euler angles of the particles Ω_j and the partition function becomes

$$Q_n = \frac{1}{n!\lambda^{3n}} \int' d\vec{r}_1 ....d\vec{r}_n d\Omega_1 ...d\Omega_n \exp\left[-\beta V(\vec{r}_1, \vec{r}_2, ..., \vec{r}_n, \Omega_1, ...\Omega_n)\right] \tag{3}$$

where now λ includes the rotational component of the integral over the kinetic energy. In these cases it is convenient to redefine $\Lambda^3 = \lambda^3 / \int d\Omega_1$ and define a spherically averaged partition function

$$Q_n = \frac{1}{n!\Lambda^{3n}} \frac{\int' d\vec{r}_1 ....d\vec{r}_N d\Omega_1 ...d\Omega_n \exp -\beta V(\vec{r}_1, \vec{r}_2, ..., \vec{r}_n, \Omega_1, ...\Omega_n)}{\int d\Omega_1 ...d\Omega_n} \tag{4}$$

The Helmholtz free energy F, the logarithm of the partition function, is then given by

$$\beta F = -\ln Q = -\sum_{n=1}^{\infty} [N_n \ln Q_n - N_n \ln N_n + N_n] = \sum_{n=1}^{\infty} N_n [\ln Q_n - \ln N_n + 1] \tag{5}$$

The cluster size distribution N_n is still undefined. To evaluate it, we require the free energy to be a minimum respect to all possible variation of N_n. Still, we must satisfy the constraint $\sum_n nN_n = N$. Introducing a Lagrange multiplier α to include the constraint we write

$$\frac{\partial(\beta F + \alpha \sum_k kN_k)}{\partial N_n} = 0 \tag{6}$$

$$\ln \frac{N_n}{Q_n} - n\alpha = 0 \tag{7}$$

or

$$N_n = Q_n(\exp\alpha)^n \tag{8}$$

Since $N_1 = Q_1 \exp\alpha$, the same expression can be written as

$$N_n = Q_n \frac{N_1^n}{Q_1^n} \tag{9}$$

or equivalently in a more symmetric form

$$\frac{N_n}{Q_n} = \left(\frac{N_1}{Q_1}\right)^n \tag{10}$$

In an ideal gas, $\ln(N/Q)$ is the chemical potential (in units of k_BT). Then, Eq. 10 essentially states that

$$\mu_n = n\mu_1$$

or equivalently that each monomer has the same chemical potential, independently from the cluster it belongs to. Eq. 9 shows also that the probability of observing an aggregate of size n is proportional to the strength of the partition function Q_n.

Knowing the cluster size distribution is now possible to write a close expression for the system free energy in the ideal gas of cluster approximation as

$$\beta F = -\sum_{n=1}^{\infty}\left[N_n \ln Q_n - N_n \ln Q_n \frac{N_1^n}{Q_1^n} + N_n\right] = -\sum_{n=1}^{\infty}\left[nN_n \ln\frac{N_1}{Q_1} + N_n\right] = N\ln\frac{N_1}{Q_1} - \#_c \tag{11}$$

where $\#_c$ is the total number of clusters in the system. Considering that $\ln\frac{N_1}{Q_1}$ is the chemical potential of the monomer in the ideal gas approximation, the free energy, can be written as

$$\beta F = N\beta\mu - \#_c \tag{12}$$

It is interesting to note that, being an ideal gas, the pressure is proportional to the number of clusters ($\#_c = \beta PV$) and that the monomer concentration (which fix the value of μ) and the total number of clusters are the only information requested to write down the system free energy. This geometric way of writing the free-energy is particularly useful when analyzing confocal images of self-assembling systems. Indeed by measuring the number of aggregates in the field of view as well as the number of monomer (two structural properties) one obtain an experimental measure of the system free energy.

2.1 on the chemical potential

For further use (and to make contact with other disciplines) we note that the chemical potential can be split into two parts, introducing a "mass" concentration $X_n \equiv (nN_n)/V$ ($X_n/n = \rho_n$)

$$\beta\mu_n = -\ln\frac{Q_n V}{N_n V} = \ln\frac{N_n}{V} - \ln\frac{Q_n}{V} = \ln\frac{X_n}{n} - \ln\frac{Q_n}{V} = \ln\rho_n - \ln\frac{Q_n}{V}$$

The first part is the classical concentration term, while the second part is the chemical potential of the cluster at fixed center of mass (the so-called standard part) and indicated as $\beta\mu_n^0$, such that

$$\beta\mu_n = \beta\mu_n^0 + \ln\frac{X_n}{n} = \beta\mu_n^0 + \ln\rho_n$$

2.2 Dimer formation: what controls association

Before applying the formalism previously derived, it is useful to comment on the conditions which allow clusters to form for a very simple case in which we limit ourselves for simplicity to monomers and dimers. The formation of a dimer (e.g. the formation of a bond between two monomers) is proportional to Q_2. For a square-well interaction potential

$$Q_2 = \frac{1}{2!\Lambda^6}\int' d\vec{r}_1 d\vec{r}_2 e^{-\beta V(\vec{r_1},\vec{r_2})} = \frac{V}{2!\Lambda^6} e^{\beta\epsilon}\frac{4\pi}{3}[(\sigma+\Delta)^3 - \sigma^3] \tag{13}$$

Again, let's stress that Q_2 has three contributions. A V term, associated to the center of mass (entropic), an energy Boltzmann term (proportional in general to the number of bonds in the cluster, one in this case), and an entropic bonding volume term V_b, counting the number of microstates in which a bond exists.

Defining V_b as the volume that allows for a bond (e.g. $V_b = \frac{4\pi}{3}[(\sigma+\Delta)^3 - \sigma^3]$)

$$N_2 = Q_n(\rho_1\Lambda^3)^2 = \frac{VV_b}{2}\frac{N_1^2}{V^2}e^{\beta\epsilon} = N_1^2\frac{V_b}{2V}e^{\beta\epsilon} \tag{14}$$

The condition such that half of the particles are dimers ($N_2 = N/4$ and $N_1 = N/2$) is reached when $\rho V_b \exp(\epsilon/k_BT) \approx 1$. This expression clearly show how the probability of forming bonds results from the competition of an entropic term (bonding volume compared to total volume per particle ρ^{-1}) and an energetic term (the Boltzmann factor). Assuming typical values for $\Delta \approx 0.1\sigma$ and for the packing fraction $\phi \equiv \frac{\pi}{6}\sigma^3\rho \approx 0.1$ this condition already teach us that the probability that the bond is formed in not negligible only if k_BT is smaller than ϵ ($k_bT/\epsilon \approx 0.2$) It is also important to consider the lifetime of the bonds, i.e. their persistence. As a first approximation, the lifetime of a bond is proportional to $\exp(\epsilon/k_BT)$. Thus at the typical temperature when fifty per cent of the particles are clustered (i.e. $\exp(\epsilon/k_BT) \approx 100$) the bonds are generally still very intermittent and the

aggregates are to be considered as transient clusters with significant exchange of particles between aggregates. This immediately clarifies that to form a stable aggregate, i.e. an aggregate in which the relative position of the constituent particles is persistent in time, one need to go to $k_BT \ll \epsilon$. Requiring that $10^8 - 10^9$ attempts are needed before breaking a bond (this estimate of course depend on the attempt rate and the experimental observation time) implies $k_BT/\epsilon \approx 0.045 - 0.05$.

3 Dissociation Equilibrium

A salt in a solvent (commonly water) dissociates into ions. The process can be schematized as a chemical reaction

$$AB \longleftrightarrow A + B$$

We can write the three partition functions as

$$Q_A = \frac{V}{\lambda_A^3} e^{-\beta f_A} \qquad Q_B = \frac{V}{\lambda_B^3} e^{-\beta f_B}$$

Here βf_A and βf_B indicates any free-energy contribution in the case the association-dissociation process takes place in a solvent, not in a gas phase.

$$Q_{AB} = \frac{V^2}{\lambda_A^3 \lambda_B^3} e^{-\beta f_{AB}}$$

where $e^{-\beta f_{AB}}$ now includes both the association term and the interaction with the solvent $e^{-\beta f_{AB}} = \frac{V_b}{V} e^{-\beta \epsilon_{AB}} e^{-\beta f_{AB}^{solvent}}$. Note that here we split the volume contribution in such a way that $e^{-\beta f_{AB}}$ is a pure number.

The free energy is

$$-\beta F = \ln \frac{Q_A^{N_A}}{N_A!} \frac{Q_B^{N_B}}{N_B!} \frac{Q_{AB}^{N_{AB}}}{N_{AB}!}$$

which has to be minimized (respect to N_A) with the constraints ($N_A = N_B$) and $N_{AB} = N_0 - N_A$, where N_0 is the number of salt molecules initially dissolved in the solvent. So

$$-\beta F = \ln \frac{(Q_A Q_B)^{N_A}}{(N_A!)^2} \frac{Q_{AB}^{N_0 - N_A}}{(N_0 - N_A)!} =$$

$$N_A \ln(Q_A Q_B) + (N_0 - N_A) \ln Q_{AB} - 2(N_A \ln N_A - N_A) - (N_0 - N_A) \ln(N_0 - N_A) + (N_0 - N_A)$$

Minimizing respect to N_A and equating to zero, we find

$$\ln(Q_A Q_B) - \ln Q_{AB} - 2 \ln N_A + \ln(N_{AB}) = 0$$

or

$$\frac{N_A^2}{N_{AB}} = \frac{Q_A Q_B}{Q_{AB}} = \frac{e^{-\beta(f_A + f_B)}}{e^{-\beta f_{AB}}}$$

Recall that in the ideal gas state, the chemical potential μ is $-\ln \frac{Q}{N}$. Here we note that the found relation is such that

$$\ln \frac{Q_{AB}}{N_{AB}} = \ln \frac{Q_A}{N_A} + \ln \frac{Q_B}{N_B} \quad \rightarrow \quad \mu_{AB} = \mu_A + \mu_B$$

hence, one can also formulate chemical equilibrium as equality of the chemical potential for each species. The sum of the chemical potential of A and B in dissociated state must be equal to the chemical potential of the associated complex.

Dividing by the volume, to transform number of particles in number density (concentration)

$$\frac{n_A n_B}{n_{AB}} = \frac{1}{V} \frac{Q_A Q_B}{Q_{AB}} = \tilde{K}_{AB}$$

where $\tilde{K}_{AB}$ has the name of dissociation constant (in units of number density). If we convert in mole/liter (mol/dm^3),

$$\frac{[A][B]}{[AB]} = K_{AB} \quad [\text{mol dm}^{-3}]$$

To grasp the meaning of K_{AB} note that when $[A] = [AB]$, $[B] = [A] = K_{AB}$. Hence K_{AB} indicated the molarity corresponding to an equal number of intact and dissociated salt molecules.

3.1 Water dissociation

Water is a small molecule. Its dissociation reaction is

$$H_2O \rightleftarrows H^+ + OH^-$$

In pure water the concentration of H^+ and OH^- is equal to 10^{-7} M. Since the concentration of H_2O is essentially fixed, the dissociation constant is, since $[H_2O] = 1000/18 = 55.5$ mol/dm^3

$$\frac{[H^+][OH^-]}{[H_2O]} = \frac{10^{-7} \cdot 10^{-7}}{55.5}$$

This is the same to say that one out of 55 10^7 water molecules are dissociated at ambient temperature. Indeed, indicating with N_A the Avogadro number and with V 1 dm^3,

$$\frac{N_{H^+} N_{OH^-}}{N_{H_2O}} = \frac{10^{-7} \cdot 10^{-7}}{55.5} N_A V$$

$$N_{H^+}^2 = \frac{10^{-7} \cdot 10^{-7}}{55.5} N_A V N_{H_2O}$$

As we have seen, in 1 dm^3 $N_{H_2O} = 55.5N_A$, such that

$$N_{H^+} = 10^{-7}N_A \qquad \frac{N_{H^+}}{N_{H_2O}} = \frac{10^{-7}N_A}{55.5N_A} = \frac{1}{55.5\ 10^7}$$

Commonly, the concentration of $[H^+]$ is indicated by the relation

$$\mathrm{p}H = -log_{10}[H^+]$$

Electrolytes are classified in three types: acid, which produces H^+; base which produces OH^{-1} and salt which does produce neither H^+ nor OH^{-1}. A solution is said acid when the pH is larger than 7 and basic otherwise.

In summary

- The pH of pure water equals 7. This value is also called neutral pH.
- Adding HCl lowers the pH. A solution with pH less than 7 is called acidic. We will call an acid any neutral substance that, when dissolved in pure water, creates an acidic solution. (There are more sophisticated definitions of an acid than this one.)
- Adding NaOH raises the pH. A solution with pH greater than 7 is called basic. We will call a base any neutral substance that, when dissolved in pure water, creates a basic solution.

Many organic molecules behave like HCl above and so are called acids. For example the carboxyl group -COOH dissociates via

$$-COOH \rightarrow -COO^- + H^+$$

Familiar examples of this sort of acid are vinegar (acetic acid), lemon juice (citric acid), and DNA (deoxyribonucleic acid). DNA dissociates into many mobile charges plus one big macroion, with 2 net negative charges per basepair. Unlike hydrochloric acid, however, all these organic acids are only partially dissociating. For example, the pK for dissociation of acetic acid is 4.76; compare the corresponding value of 2.15 for a strong acid like phosphoric (H_3PO_4). Dissolving a mole of acetic acid in a liter of water will thus generate a lot of neutral CH_3COOH and only a modest amount of H^+. We say acetic acid is a weak acid. Any molecule that gobbles up H^+ will raise the pH. This can happen directly or indirectly. For example, another common motif is the amine group, -NH_2, which directly gobbles protons by the equilibrium

$$-NH_2 + H^+ \rightarrow -NH_3^+$$

A special case is ammonia, NH_3, which is simply an amine group attached to a hydrogen atom. We have already seen how other bases (such as lye) work by gobbling protons indirectly, liberating hydroxyl ions which push the equilibrium to the left. Bases can also

be strong or weak, depending on the value of their dissociation equilibrium constant (for example, NaOH $\rightarrow$ Na^+ + OH^-) or association constant. Now suppose we add equal quantities of both HCl and NaOH to pure water. In this case the number of extra H^+ from the acid equals the number of extra OH^- from the base, so we still have $[H^+] = [OH^-]$. The resulting solution has still pH=7. What happened is that the extra H^+ and OH^- gobbled each other, combining to become water. The other ions remain, leaving a solution of table salt, Na^++Cl^-. You could also get a neutral solution by mixing a strong base, NaOH, with a weak acid, CH_3COOH, but you would need a lot more acid than base.

3.1.1 The charge on a protein varies with its environment (Nelson)

proteins can be described as linear chains of monomers, the amino acids. Each amino acid (except proline) contributes an identical group to the protein chain's backbone, -NH-CH-CO-, with a variable group (or side chain) covalently bonded to the central carbon. The resulting polymer is a chain of residues, in a precise sequence specified by the message in the cell's genome coding for that protein. The interactions of the residues with one another and with water determine how the protein folds; the structure of the folded protein determines its function. In short, proteins are horrendously complicated. How can we say anything simple about such a complex system? Some amino acids, for example aspartic or glutamic acid, liberate H^+ from their own carboxyl groups, like any organic acid. Others, including lysine and arginine, pull H^+ out of solution onto their basic side chains. The corresponding dissociation reactions thus involve transfer of a proton:

$$\text{Acidic side chain:} \quad -COOH \rightarrow -COO^- + H^+$$

$$\text{Basic side chain:} \quad -NH_3^+ \rightarrow -NH_2 + H^+.$$

The species on the left are the **protonated** forms; those on the right are **deprotonated**. Each residue of type α has a characteristic equilibrium constant $K_{eq,\alpha}$ for its deprotonation reaction. We find these values tabulated in books. The range of actual values is about $10^{-4.4}$ for the most acidic (aspartic acid) to about 10^{-12} for the most basic (arginine). The actual probability that a residue of type α will be protonated will then depend on$K_{eq,\alpha}$, and on the pH of the surrounding fluid. Denoting this probability by P_α, the average charge on an acidic residue in solution will then be $(-e)(1 - P_\alpha)$. Similarly, the average charge on a basic residue will be eP_α. In both cases the average charge goes down as pH goes up. Actually, in a protein uncharged and charged residues will affect each other instead of all behaving independently. Hence the degree of dissociation of a residue is a universal function of the pH in its protein environment, shifted by the pK of that residue. A residue is protonated half the time when the ambient pH just equals its dissociation pK.

3.1.2 A historic note

Not only does every protein have its characteristic isoelectric point; each variant of a given protein will too. A famous example is the defect responsible for sickle-cell anemia. In a historic discovery, Linus Pauling and coauthors showed in 1949 that the red blood cells of sickle-cell patients contained a defective form of haemoglobin. Today we know that the defect lies in parts of haemoglobin called the $\beta-$globin chains, which differ from normal $\beta-$globin by the substitution of a single amino acid, from glutamic acid to valine in position six. This tiny change ($\beta-$globin has 146 amino acids in all) is enough to create a sticky (hydrophobic) patch on the molecular surface. The mutant molecules clump together, forming a solid fiber of fourteen interwound helical strands inside the red cell and giving it the sickle shape for which the disease is named. The deformed red cells in turn get stuck in capillaries, then damaged, and destroyed by the body, with the net effect of creating pain and anemia. In 1949, the sequence of $\beta-$globin was unknown. Nevertheless, Pauling and coauthors pinpointed the source of the disease in a single molecule. They reasoned that a slight chemical modification to haemoglobin could make a correspondingly small change in its titration curve, if the differing amino acids had different dissociation constants. Isolating normal and sickle-cell haemoglobin, they indeed found that while the corresponding titration curves look quite similar, still their isoelectric points differ by about a fifth of a pH unit. The sign of this difference is just what would be expected for a substitution of valine for glutamic acid: The normal protein is consistently more negatively charged in the range of pH shown than the defective one, because it has one more acidic (negative) residue, and that residue (glutamic acid) has pK=4.4, so it is dissociated throughout the range of explored pH. In other physical respects the two molecules are alike; for example, Pauling and coauthors measured that both had the same sedimentation and diffusion constants. Nevertheless, the difference in isoelectric point was enough to distinguish the two versions of the molecule. Most strikingly, at pH 6.9, the normal and defective proteins have opposite signs of their charges, and so migrate in opposite directions under an electric field.

4 The simplest self-assembly process. Equilibrium polymerization

The simplest case of self-assembly refers to particles that can form two bonds each (e.g. particles with functionality $f = 2$). To evaluate the partition function we assume that particles interact with two attractive sites. We consider that the surface of the particle is decorated with two patches on the poles, and that a bond is present between the two patches when the relative distance between the particles is within $\sigma + \Delta$ and when the orientation of both patches involved in the bonds is within a cone of semi-amplitude θ. For example, for a dimer we have

$$Q_2 = \frac{1}{2!\Lambda^6} \int' d\vec{r}_1 d\vec{r}_2 d\Omega_1 d\Omega_2 e^{-\beta V(\vec{r_1},\vec{r_2},\Omega_1,\Omega_2)} / \int d\Omega_1 d\Omega_2 \tag{15}$$

With the simple model selected, the Boltzmann factor $\exp(\beta\epsilon)$ is constant in all points in space where a bond is present. Changing variable to $\vec{r}_1$ and $\vec{r}_2 - \vec{r}_1$, the integration over $\vec{r}_1$ is immediate and results in a V term. The integration over $\vec{r}_2 - \vec{r}_1$ is limited for relative distances between σ and $\sigma + \Delta$ and so it gives $\frac{4}{3}\pi[(\sigma+\Delta)^3 - \sigma^3)]$ times the integration over the bonding angles. Normalized by the $(4\pi)^2$ factor, the angular part results in a contribution $(\frac{1-\cos\theta}{2})^2$. This last term correspond to the so-called coverage χ (the fraction of the sphere surface associated to bonding) squared. The resulting partition function is thus

$$Q_2 = \frac{V}{2\Lambda^6} f^2 \frac{4}{3}\pi[(\sigma+\Delta)^3 - \sigma^3)]\chi^2 \exp(\beta\epsilon)$$

where the term f^2 counts the four ways a bond can be formed between two particles with two patches each. Using the previously introduced bonding volume definition,

$$Q_2 = 2\frac{VV_b}{\Lambda^6}\exp(\beta\epsilon) = \frac{V}{\Lambda^3}Q_{bond} \qquad Q_{bond} = 2\frac{V_b}{\Lambda^3}\exp(\beta\epsilon) \tag{16}$$

where the term V/λ^3 indicates the contribution to the partition function associated to the exploration of the system volume of the cluster center of mass, while the remaining part is the bond partition function in which the term $2V_b/\lambda^3$ counts the number of microstates associated to the existence of the bond and $\exp(\beta\epsilon)$ is the Boltzmann term, which depends on the ratio between the bond energy and the thermal energy.

Generalization to the case of a cluster of size n (neglecting self-avoiding contributions and under the assumption that there is no change in the bonding energy on clustering, the so-called isodesmic hypothesis, implicit in the simple classical potential we are using) the partition function can be written as

$$Q_n^{f=2} = \frac{\omega_n}{n!\lambda^{3n}} V [V_b^{11}\exp(\beta\epsilon)]^{\#_b} \tag{17}$$

with the number of bonds $\#_b = n - 1$ and

$$\frac{\omega_n}{n!} = 2^{n-1} \tag{18}$$

where ω_n counts the number of distinct bonded chains that can be formed by n distinguishable particles. To calculate ω_n one considers that the first particle can be selected in n ways and that it has two possible bonding configurations. The second one among the $n-1$ remaining particles, always with two bonding possibilities. Hence

$$\omega_n = 2n \times 2(n-1) \times 2(n-2) \times ..... \times 2 = n!\ 2^{n-1}$$

(the missing 2 arises from the left-right symmetry of the polymers) and

$$Q_n^{f=2} = 2^{n-1}\frac{V}{\lambda^3}\left[\frac{V_b}{\lambda^3}\exp(\beta\epsilon)\right]^{n-1} = \frac{V}{\lambda^3}\left[2\frac{V_b}{\lambda^3}\exp(\beta\epsilon)\right]^{n-1} = \frac{V}{\Lambda^3}Q_{bond}^{n-1} \tag{19}$$

which can be interpreted as the center of mass partition function (V/Λ^3) and the bonds $(n-1)$ partition function Q_{bond}^{n-1}.

The cluster size distribution is then given by

$$N_n = \frac{N_1^n}{Q_1^n}Q_n = \left(\frac{N_1\lambda^3}{V}\right)^n \frac{V}{\lambda^3}Q_{bond}^{n-1} = \rho_1 V\left(\rho_1\lambda^3 Q_{bond}\right)^{n-1} = N_1\left(\rho_1\lambda^3 Q_{bond}\right)^{n-1} = N_1 e^{(n-1)\ln(\rho_1\lambda^3 Q_{bond})}$$

e.g. an exponential distribution of polymer lengths, with characteristic decay $\bar{n} = -[\ln(\rho_1\lambda^3 Q_{bond})]^{-1}$.

The functional dependence of the cluster free energy in linear polymerization,

$$\ln Q_n^{f=2} = \ln\frac{V}{\Lambda^3} + (n-1)\ln Q_{bond}$$

scales with n. This is typical of all one-dimensional aggregates (rods), for which the standard part of the chemical potential is

$$\beta\mu_n^0 \equiv -\ln\frac{Q_n}{V} = -(n-1)\ln Q_{bond}$$

4.1 Geometrical description

In the bifunctional particle system, the maximum number of possible bonds $\#_{bonds}^{max}$ is equal to the total number of particles. The number of bonds in the system can instead be calculated from the cluster size distribution as

$$\#_{bonds} = \sum_{n=1}^{\infty}(n-1)N_n = N - \#_{clusters}$$

where the last equality is based on the fact that $N = \sum_{n=1}^{\infty} nN_n$ and we have defined $\#_{clusters}$ the total number of cluster in the system. Thus, the probability that a bond exists is

$$p_b = \frac{\#_{bonds}}{\#_{bonds}^{max}} = 1 - \frac{\#_{clusters}}{N}$$

Since

$$N_n = N_1 x^{n-1} \qquad x = e^{\ln(\rho_1\lambda^3 Q_{bond})}$$

we find

$$N = \sum_{n=1}^{\infty} nN_n = \frac{N_1}{x}\sum_{n=1}^{\infty} nx^n = \frac{N_1}{x}x\frac{d}{dx}\sum_{n=1}^{\infty} x^n = N_1\frac{d}{dx}\frac{x}{1-x} = N_1\frac{1}{(1-x)^2}$$

and

$$\#_{clusters} = \sum_{n=1}^{\infty} N_n = \frac{N_1}{x} \sum_{n=1}^{\infty} x^n = N_1 \frac{1}{1-x}$$

and, as a result,

$$p_b = 1 - N_1 \frac{1}{1-x} \frac{(1-x)^2}{N_1} = 1 - (1-x) = x$$

Thus, x has the meaning of bond probability and we can rewrite

$$N_n = N_1 p_b^{n-1} \qquad N_n = N(1-p_b)^2 p_b^{n-1}$$

The number of monomers N_1 is $N(1-p_b)^2$ which can be interpreted as both reactive sites un-bonded. Then each additional particle is connected with probability p_b.

5 Surfactants. (Nelsen)

Emulsions form when amphiphilic molecules reduce the oil-water interface tension Section 7.5 discussed why salad dressing separates into oil and water, despite the superficial increase in order which such separation entails. Water molecules are attracted to oil molecules, but not as much as they are attracted to each other: The oil-water interface disrupts the network of hydrogen bonds, so droplets of water coalesce in order to reduce their total surface area. But some people prefer mayonnaise to vinaigrette. Mayonnaise, too, is mostly a mixture of oil and water, and yet it does not separate. What is the difference? One difference is that mayonnaise contains a small quantity of egg. An egg is a complicated system, including many large and small molecules. But even very simple, pure substances can stabilize suspensions of tiny oil droplets in water for long periods. Such substances are generically called emulsifiers or surfactants; a suspension stabilized in this way is called an emulsion. Particularly important are a class of simple molecules called detergents, and the more elaborate phospholipids found in cell membranes. The molecular architecture of a surfactant shows us how it works. Figure 8.3a shows the structure of sodium dodecylsulfate (SDS), a strong detergent. The left side of this molecule is hydrophobic: It is a hydrocarbon chain. The right side, however, is highly polar: In fact it is an ion. This fusion of unlike parts gives the class of molecules with this structure the name amphiphiles. These two parts would normally migrate (or partition) into the oil phase and water phase, respectively, of an oil-water mixture. But such an amicable separation is not an option— the two parts are handcuffed together by a chemical bond. When added to an oil-water mixture, though, surfactant molecules can simultaneously satisfy both of their halves by migrating to the oil-water interface.

In this way the polar head can face water while the nonpolar tails face oil. Given enough surfactant to make a layer one molecule thick (that is, a monolayer) over the entire interface, the oil and water phases need not make any direct contact at all. In mayonnaise,

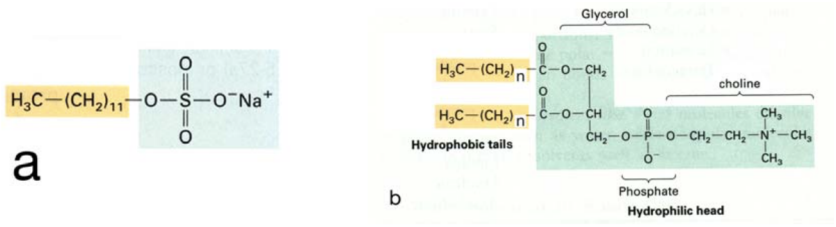

Figure 8.3: (Structural diagrams.) (a) Structure of sodium dodecyl sulfate (SDS), a strong detergent. A nonpolar, hydrophobic, tail *(left)* is chemically linked to a polar, hydrophilic head *(right)*. In solution the Na^+ ion dissociates. Molecules from this class form micelles (see Figure 8.5). (b) Structure of a typical phosphatidylcholine, a class of phospholipid molecule. Two hydrophobic tails *(left)* are chemically linked to a hydrophilic head *(right)*. Molecules from this class form bilayers (see Figure 8.4).

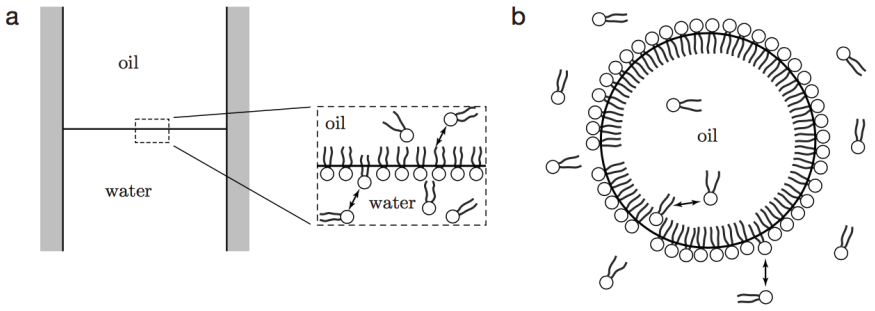

Figure 8.4: (Schematics.) (a) An oil-water interface stabilized by the addition of a small amount of surfactant. Some surfactant molecules are dissolved in the bulk oil or water regions, but most migrate to the boundary as shown in the inset. (b) An oil-water emulsion stabilized by surfactant: The situation is the same as (a), but for a finite droplet of oil.

the relevant component of the egg is a phospholipid (lecithin), which migrates to the oil-water interface to minimize its own free energy, and at the same time also lowers the interfacial energy to the point where rapid coalescence of droplets does not occur. (Other delicacies, for example sauce Béarnaise, also work this way.) Since a monolayer can be only a couple of nanometers thick, a small quantity of surfactant can stabilize an enormous area of interface.

5.0.1 Historical Note

Around 1773, Franklin's attention turned to, of all things, oil slicks. What intrigued him was the fact that a certain quantity of oil could spread only so far on water. Attempting to spread it farther caused the film to break up into patches. Franklin noticed that a given quantity of olive oil always covered about the same area of water; specifically, he found that a teaspoon of oil ($\approx 5cm^3$) covered half an acre of pond ($\approx 2000m^2$). Franklin reasoned that if the oil were composed of tiny irreducible particles, then it could only spread until these particles formed a single layer, or "monolayer", on the surface of the water. It is easy to go one step farther than Franklin and find the thickness of the layer, and hence the size scale of a single molecule. Dividing the volume of oil by the area of the layer, we find the size of one oil molecule to be about 2.5 nm. Remarkably, Franklin's eighteenth-century experiment gives a reasonable estimate of the molecular size scale!

You can observe the vast reduction in surface tension brought about by a tiny amount of dissolved soap in a simple experiment. Carefully float a loop of fine sewing thread on water. Now touch a bar of soap to the part of the water surrounded by the rubber band. Explain what happens. You can also see for yourself just how large an area can be covered by one drop of detergent, or equivalently, just how much that drop can be diluted and still change the surface tension over several square centimetres of water. In the same way, a small amount of detergent can clean up a big oily mess by encapsulating oil into stable, hydrophilic droplets small enough to be flushed away by running water.

5.1 Micelles self-assemble suddenly at a critical concentration

A mixture of stabilized oil droplets in water may be delicious or useful, but it hardly qualifies as a "self-assembled" structure. The droplets come in many different sizes (that is, they are poly- disperse), and just generally have little structure. Can entropic forces drive the construction of anything more closely resembling what we find in cells? To answer the above question we begin with another: It may seem from Section 8.4.1 that surfactant molecules in pure water (or pure oil) would be stymied: With no interface to go to, won't they just have to accept the hydrophobic cost of exposing their tails to the surrounding water? Figure 8.5 shows that the answer to the second question is "no." Surfactant molecules in solution can assemble into a micelle, a sphere consisting of a few dozen molecules. In this way the molecules can present their nonpolar tails to each other,

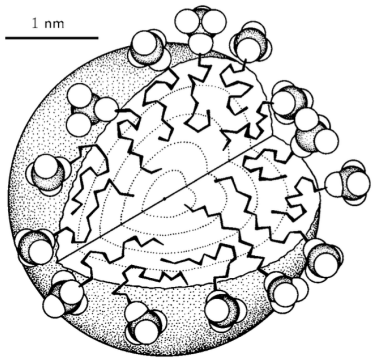

Figure 8.5: (Sketch.) A micelle of sodium dodecyl sulfate (SDS). The micelle consists of 60 SDS molecules. The hydrocarbon chains pack in the core at a uniform density roughly the same as that of liquid oil. [From Israelachvili, 1991.]

and not to the surrounding water. This configuration can be entropically favorable, even though by choosing to associate in this way each molecule loses some of its freedom to be located anywhere, oriented in any way (see Section 7.5 on page 240). A remarkable feature of Figure 8.5 is that there is a definite "best" size for the resulting micellar aggregate. If there were too many amphiphile molecules, then some would be completely in the interior, where their polar heads would be cut off from the surrounding water. But with too few amphiphiles (for example, just one molecule), the tails would not be effectively shielded. Thus amphiphilic molecules can spontaneously self-assemble into objects of fixed, limited, molecular- scale size. The chemical force driving the assembly is not the formation of covalent bonds, but something gentler: the hydrophobic effect, an entropic force.

5.1.1 Historical Note

As early as 1913 J. McBain had deduced the existence of well-defined micelles from his quantitative study of the physical properties of soap solutions. One of McBain's arguments went as follows. We know how many total molecules are in a solution just by measuring how much soap we put in, and making sure that none of it precipitates out of solution. But we can independently measure how many independently moving objects the solution contains, by measuring its osmotic pressure and using the van 't Hoff relation. For very dilute solutions McBain and others found that the osmotic pressure faithfully tracked the total number of amphiphilic ions (solid symbols on the left of Figure 8.6), just as it would for an ordinary salt like potassium chloride (open symbols in Figure 8.6). But the similarity ended at a well-defined point, now called the critical micelle concentration or CMC. Beyond this concentration, the ratio of independently moving objects to all ions dropped sharply (solid symbols on the right of the graph). McBain was forced to conclude that beyond the CMC his molecules didn't stay in an ordinary solution, dispersed through the sample. Nor, however,

did they aggregate into a separate bulk phase, as oil does in vinaigrette. Instead, they were spontaneously assembling into intermediate- scale objects, bigger than a molecule but still microscopic. Each type of amphiphile, in each type of polar solvent, had its own characteristic value of the CMC. This value typically decreases at higher temperature, pointing to the role of the hydrophobic interaction in driving the aggregation. McBain's results were not immediately accepted. But eventually, as a large number of physical quantities were all found to undergo sharp changes at the same critical concentration as the osmotic pressure (for instance, electrical conductivity), the chemical community realized that he was right.

6 How to predict the cluster distribution from the free-energy per particle

We have seen that (assuming $\Lambda = 1$ in the following)

$$\rho_n = \frac{N_n}{V} = \frac{Q_n}{V}\left(\frac{N_1}{Q_1}\right)^n$$

The term $\frac{Q_n}{V}$ indicates the free energy associated to the aggregate, excluding the center of mass translational degrees of freedom (V). If we define a free energy $F_{aggregate}(n) = -k_B T \ln \frac{Q_n}{V}$ of the cluster of size n and as $f_b(n) = \frac{F_{aggregate}(n)}{n}$

$$\frac{Q_n}{V} = e^{-\beta F_{aggregate}(n)} = e^{-\beta n f_b(n)}$$

then, writing for retaining generality $Q_1 = V e^{-\beta n f_b(1)}$

$$\rho_n = \left(\rho_1 e^{-\beta f_b(n)} e^{+\beta f_b(1)}\right)^n$$

This expression shows that if $f_b(n) < f_b(1)$, i.e. that if the free energy per particle goes down on increasing n, then $\rho_n \gg \rho_1$. Oppositely, if $f_b(n) > f_b(1)$, small finite clusters will dominate.

7 Critical Micelle Concentration (CMC)

We have seen that the probability of observing a cluster of size n is proportional to its partition function times the monomer concentration to the power n. This simple expression already reveals that, even at constant T (i.e. without changing the cluster partition function) aggregation can be stimulated by the increase in the density.

The thermodynamic equilibrium condition results in

$$\rho_n = \left(\rho_1 e^{-\beta f_b(n)} e^{+\beta f_b(1)}\right)^n$$

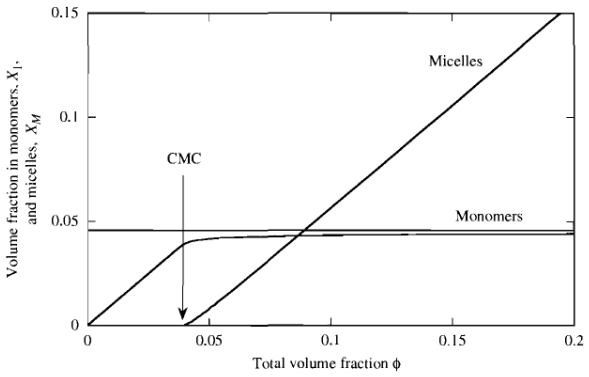

Fig. 9.4 The volume fraction in monomers and micelles as a function of total volume fraction of amphiphile, in the approximation in which all micelles are taken to have the same aggregation number M. Below the CMC, almost all the amphiphile is present as monomers. Above the CMC, as extra amphiphile is added to the solution almost all goes into micelles, with the concentration of monomers rising only very slowly.

7.1 What do we need to have finite size clusters (micelles)

We have seen that when $f_b(n)$ decreases with n clusters do form but keep growing on increasing density (or decreasing T). Different is the case when $f_b(n)$ shows a minimum in its n dependence. In this case finite size clusters can result from the aggregation process.

Let us assume that we can expand the bonding free energy around its minimum M,

$$\beta f_b(n) = \beta f_b(M) + \frac{1}{2}\frac{d^2 \beta f_b(m)}{dn^2}|_M (n-M)^2 = \beta f_b(M) + \frac{1}{2} I (n-M)^2$$

To start, let's now compare ρ_n for a generic n and for $n = M$

$$\rho_n = \left[\rho_1 e^{-\beta f_b(n)} e^{+\beta f_b(1)}\right]^n \quad \text{and} \quad \rho_M = \left[\rho_1 e^{-\beta f_b(M)} e^{+\beta f_b(1)}\right]^M$$

then

$$\rho_n^{\frac{1}{n}} = \left[\rho_1 e^{-\beta f_b(n)} e^{+\beta f_b(1)}\right] \quad \text{and} \quad \rho_M^{\frac{1}{M}} = \left[\rho_1 e^{-\beta f_b(M)} e^{+\beta f_b(1)}\right]$$

and dividing member by member

$$\frac{\rho_n^{\frac{1}{n}}}{\rho_M^{\frac{1}{M}}} = \frac{\left[\cancel{\rho_1} e^{-\beta f_b(n)} \cancel{e^{+\beta f_b(1)}}\right]}{\left[\cancel{\rho_1} e^{-\beta f_b(M)} \cancel{e^{+\beta f_b(1)}}\right]}$$

which can also be expressed as

$$\frac{\rho_n^{\frac{1}{n}}}{\rho_M^{\frac{1}{M}}} = \frac{\left[e^{-\beta f_b(n)}\right]}{\left[e^{-\beta f_b(M)}\right]}$$

or

$$\rho_n^{\frac{1}{n}} = e^{-\beta f_b(n) + \beta f_b(M)} \rho_M^{\frac{1}{M}} = e^{\frac{(\beta f_b(M) - \beta f_b(n))M}{M}} \rho_M^{\frac{1}{M}} = \left[\rho_M e^{M(\beta f_b(M) - \beta f_b(n)}\right]^{\frac{1}{M}}$$

or

$$\rho_n = \left[\rho_M e^{M(\beta f_b(M) - \beta f_b(n)}\right]^{\frac{n}{M}}$$

If we assume that the n dependence of the bond free energy has a minimum for $n = M$, then

$$\rho_n = \left[\rho_M e^{M\Gamma(n-M)^2)/2}\right]^{\frac{n}{M}}$$

When M is large, for all cluster sizes close to M, $n/M \approx 1$ and

$$\rho_n = \left[\rho_M e^{M\Gamma(n-M)^2)/2}\right]$$

e.g. a gaussian distribution with variance $\sigma^2 = k_B T/(2M\Gamma)$.

It is also interesting to look how the density affects the micellization process. To do so in a simplified way, let's lump all micelles in just one size M and consider only the equilibrium between monomers and micelles.

In this case

$$\rho_M = \left[\rho_1 e^{-\beta(f_b(M) - f_b(1))}\right]^M$$

It is important to notice that, being M large, it acts in the exponent as a selector. Since the total number density is $\rho = \rho_M + \rho_1$, three cases are relevant. When

- $\rho_1 e^{-\beta(f_b(M) - f_b(1))} < 0$. In this case $\rho_M \approx 0$ and $\rho \approx \rho_1$.
- $\rho_1 e^{-\beta(f_b(M) - f_b(1))} > 0$. In this case ρ_M is much larger than ρ_1 and $\rho_M \approx \rho$
- The density for which $\rho_1 e^{-\beta(f_b(M) - f_b(1))} = 1$ defines the critical micelle concentration (CMC).

Note that on increasing ρ beyond the CMC, ρ_1 remains fixed at the CMC value. ρ_1 can not decrease, since else there would be no larger clusters. It also can not really increase, since all density is concentrated in the micelles.

8 Micelles (once more)

The same calculation can be done retaining the partition functions. As before, particles can only exist in monomeric state or in a cluster of $M >> 1$ particles (the micelle)

As we have demonstrated previously, in the case of an ideal gas of non-interacting clusters

$$N_M = Q_M \frac{N_1^M}{Q_1^M}$$

Then, indicating with N the original number of particles in the system

$$N = N_1 + MN_M = N_1 + MQ_M \frac{N_1^M}{Q_1^M}$$

or

$$\frac{N_1}{N} = 1 - MQ_M \frac{N_1^M}{NQ_1^M}$$

Now we can write, assuming that a micelle has a well defined energy E_M in all of its configurations, the partition function of the micelle as

$$Q_M = \frac{V}{\lambda^3} \left(\frac{V_b}{\lambda^3} \right)^{M-1} \exp(-\beta E_M)$$

to emphasise the entropy and energy (or enthalpy) contributions and the partition function of the monomer $Q_1 = \frac{V}{\lambda^3}$. Then

$$\frac{N_1}{N} = 1 - M \frac{V}{\lambda^3} \left(\frac{V_b}{\lambda^3} \right)^{M-1} \exp(-\beta E_M) \frac{N_1^M}{N(\frac{V}{\lambda^3})^M}$$

and after some algebra

$$\frac{N_1}{N} = 1 - M \left(\frac{N_1}{N} \right)^M \left(\frac{NV_b}{V} \right)^{M-1} \exp(-\beta E_M) \tag{20}$$

which can be written symbolically defining x as the fraction of particles in monomeric state $x = 1 - M(Ax)^M$, with $A^{1/M} = \left(\frac{NV_b}{V} \right)^{M-1} \exp(-\beta E_M)$. Fixing the properties of the micelle (M and the model parameters V_b and E_M) it is possible to solve Eq. 20 for all densities and temperatures. The solution for N_1/N depends on the value of A. For values of Ax smaller than one, $N_1/N \approx 1$ and the system is a monomeric state. For Ax greater than 1, $\rho_1 \equiv N_1/V$ reaches a constant value. Note also that both the entropic and the energetic contributions scale with M. Hence, the cross-over from values smaller than one to values larger than one is extremely fast. The concentration for which $Ax = 1$ is commonly indicated critical micelle concentration (cmc).

8.1 One dimensional aggregates: Cylindrical micelles

In the case of a one-dimensional growth process, as is the case of cylindrical micelles, one can associate to molecules in the body of the cylinder a free-energy f_{bulk} and an extra free-energy penalty to the particles at the end Δf_{endcup} Then we can express the free energy per particle as

$$\beta f_b(n) = \frac{n\beta f_{bulk} + 2\beta \Delta f_{endcup}}{n} = \beta f_{bulk} + \frac{2}{n} \beta \Delta f_{endcup}$$

Calling $\alpha = 2\beta\Delta f_{endcup}$, this functional form gives, since $\beta f_b(n) - \beta f_b(1) = \frac{\alpha}{n} - \alpha$

From the general expression we have previously derived

$$\rho_n = \left(\rho_1 e^{-\beta f_b(n)} e^{+\beta f_b(1)}\right)^n$$

we obtain for the cylindrical case

$$\rho_n = \left(\rho_1 e^{-\frac{\alpha}{n}+\alpha}\right)^n = e^{-\alpha}\left(\rho_1 e^{+\alpha}\right)^n$$

confirming the exponential decay of N_n at equilibrium and the decay proportional to $\rho_1 e^{\alpha}$.

We can find ρ_1 for each ρ by evaluating

$$\rho = \sum_n n\rho_n = \frac{N}{V} = e^{-\alpha}\sum_n n\left(\rho_1 e^{\alpha}\right)^n$$

which by now we know using the identity $\sum nx^n = x/(1-x)^2$

$$\rho = e^{-\alpha}\frac{\rho_1 e^{\alpha}}{1-(\rho_1 e^{\alpha})^2}$$

When $\rho_1 e^{\alpha}$ approaches 1 the solution of cylindrical surfactants can be thought of as a solution of living polymers. Micelles are continuously brewing and reforming; the drive to merge comes from the reduction in end-cap energies that occurs when two micelles merge, while the driving force for long micelles to break into two arises from the extra entropy the system gains by having more micelles.

8.2 Two-dimensional aggregates (disks, sheets and vesicles....)

Let us assume we are considering now particles (atoms, molecules) which self assemble into disk-like two-dimensional structure. We can try to write a very rough partition function by considering that the number of particles in the bulk of the disk will be proportional to the surface area (or to the total number of particles (n) while the number of partially bonded particles will be proportional to the circumference ($n^{1/2}$). These boundary particles are described by a free energy $f_{bulk}n + \Delta f_{surface}n^{1/2}$.

$$\beta F_b(n) = f_{bulk}n + \Delta f_{surface}n^{1/2}$$

or

$$\beta f_b(n) = f_{bulk} + \Delta f_{surface}n^{-1/2}$$

where f_{bulk} and $\Delta.f_{surface}$ are the free energy of a particle in the bulk and the additional cost of being located on the surface of the disk.

Then

$$\beta f_b(n) - \beta f_b(1) = \beta f_{surface}n^{-1/2} - \beta f_{surface} = \alpha n^{-1/2} - \alpha$$

The thermodynamic equilibrium condition results in

$$\rho_n = \left(\rho_1 e^{-\beta f_b(n)} e^{+\beta f_b(1)}\right)^n = \left(\rho_1 e^{\alpha - \alpha n^{-1/2}}\right)^n = (\rho_1 e^{\alpha})^n \, e^{-\alpha n^{1/2}}$$

Comparing this with the equation for cylinders, we find the factor e^{α} is replaced by. $e^{-\alpha n^{1/2}}$. The factor of $n^{1/2}$ leads to a qualitatively different situation. Rather than there being a distribution of sizes of micelles, as there is for cylinders, in the case of disks we see that the number of large but finite disk aggregates is exponentially small.

Above the CMC, any extra amphiphile we add to the system must join an infinite, two-dimensional, sheet-like aggregate. There is one possibility that we have not considered that could alter this conclusion. If the edges of the sheet can join up on one another, to give a closed surface of bilayer, then the extra energy of the edge may be eliminated. Such a structure is known as a vesicle. However, there is an energy cost in forming a vesicle, which arises from the curvature that it is necessary to impart to the bilayer. This energy cost needs to be set against the energy gain from eliminating the edge, together with a gain in translational entropy that arises because the vesicles are of finite size. It turns out that, for a system containing only one type of amphiphile, vesicles are stable only at extremely low concentrations. In practice, vesicles can be obtained reasonably easily, for example by breaking up the bilayers in a lamellar phase using ultrasound; these are metastable but reasonably long-lived on experimental timescales. Vesicles can also be formed at equilibrium from mixtures of surfactants. Vesicles are potentially of great importance as a means of encapsulating particular molecules. For example, if drug molecules are encapsulated in vesicles they can be delivered to a target part of the body without unwanted interactions; if the vesicle can be made to break up in a controlled way at the target then this provides a very efficient way of delivering the drug. Vesicles can also be considered to be a simple model of a biological cell, whose contents are separated from the outside world by a bilayer membrane of this kind.

8.3 Three-dimensional aggregates (spheres)

A similar calculation for a spherical aggregate suggests to write

$$\beta f_b(n) = f_{bulk} + f_{surface} n^{-1/3}$$

where f_{bulk} and $f_{surface}$ are the free energy of a particle in the bulk and on the surface of the sphere. The surface free energy can also be expressed as interfacial free energy γ

$$f_{surface} n^{2/3} = 4\pi R^2 \gamma = \frac{3}{R}\frac{4}{3}\pi R^3 \gamma = \frac{3}{R} n v \gamma$$

and per particle

$$\frac{f_{surface} n^{2/3}}{n} \sim \frac{3}{n^{1/3}} v\gamma$$

9 Competing interactions

10 Reasonable classification of the shape of the aggregates

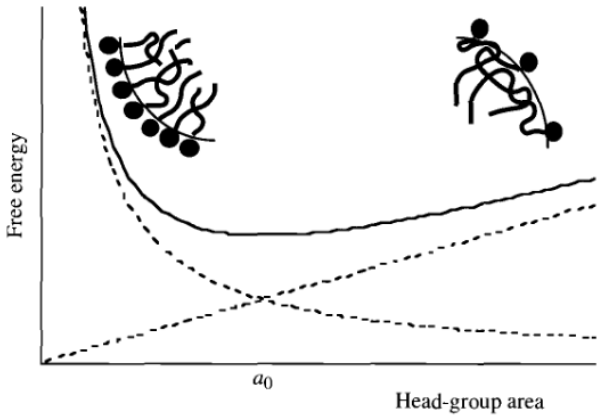

Fig. 9.2 The optimum head-group area for an amphiphile in a micelle. If the headgroups are too tightly packed, they repel each other by electrostatic and other forces, leading to an increase in free energy. If they are too far apart, hydrophobic chains are forced to come into contact with the water. The optimum head-group area a_0 is set by a balance between these two factors.

Some insight into the factors which determine what kind of micelle is formed by a given amphiphile is obtained from a simple geometrical argument due to Israelachvili. In this approach, we characterise an amphiphile by three parameters:

- the optimum head-group area a_0,
- the critical chain length l_c,
- the hydrocarbon volume v_0.

The hydrocarbon volume is simply the volume of the hydrocarbon chain, while the critical chain length is related to the length of the hydrocarbon chain if it is in a fully extended, straight configuration. The optimum head-group area needs more consideration. The idea of an optimum head-group area for an amphiphile in a micelle is illustrated in Fig. 9.2. If the head-groups are forced too closely together they will repel each other by electrostatic and other interactions. On the other hand, if the head-groups are too far apart, this forces the hydrophobic tails to come into contact with the water, with a resulting increase in interfacial energy. A balance between these two factors gives rise to the optimum head-group area a0. Note that this is not solely a geometric factor; because it arises from a balance between attractive and repulsive forces, if the range of the forces is modified (e.g. by changing the salt concentration to screen out electrostatic forces) then the optimum

head-group area can be altered. The condition for various shapes of micelle to be adopted can now be derived.

- Sphere:

  For a sphere of radius r, the volume is $V_{sphere} = 4\pi r^3/3$. If there are M molecules in the micelle, then $V_{sphere} = Mv_0$. The surface are is $S_{sphere} = 4\pi r^2$. Each of the M molecules contributes with a_0 and thus $S_{sphere} = Ma_0$. Taking the ratio

  $$\frac{V_{sphere}}{S_{sphere}} = \frac{Mv_0}{Ma_0} = \frac{4\pi r^3/3}{4\pi r^2} = \frac{r}{3}$$

  This means that the radius is $3v/a_0$. In order to be able to form a spherical micelle this radius must be less than the fully stretched chain length l_c (i.e. $l_c > r$), giving the condition for spherical micelles as

  $$\frac{v}{l_c a_0} < \frac{1}{3} \quad \text{(spheres)}$$

- Cylinders:

  For cylinders of radius r and length L, the same reasoning gives

  $$\frac{V_{cylinder}}{S_{cylinder}} = \frac{Mv_0}{Ma_0} = \frac{\pi r^2 L}{2\pi r L} = \frac{r}{2}$$

  Thus the radius is $2v/a_o$, and then the stretched polymer length $l_c > 2v/a_o$. The resulting condition for cylindrical micelles is

  $$\frac{1}{3} < \frac{v}{l_c a_0} < \frac{1}{2} \quad \text{(cylinders)}$$

- Bilayers

  When the combination $v/(l_c a_o)$ becomes larger than $1/2$, then the favoured shape of the aggregate will be a bilayer.

11 Cooperative polymerization: Slaved equilibrium polymerization

A relevant case of self-assembly is provided by the "explosive" formation of very long one dimensional aggregates (fibers, fibrils and so on). In this cases, a very small change in the external control parameters determines the formation of extremely long chains. This fast growth of fibers originates from the presence of two distinct aggregation mechanisms.

A very slow preliminary aggregation process, with a very small reaction constant and a subsequent fast aggregation process with a large reaction constant. A typical example is provided by the coil to helix transition, where first four monomers need to arrange in an proto-helix configuration and then the helix polymerization is rather fast.

In chemical language cooperative polymerization is described (in its simplest form) by the expressions

$$\frac{[N_2]}{[N_1]^2} = K_2$$

$$\frac{[N_3]}{[N_1][N_2]} = K_3$$

while all successive K_n terms are equal to K_3. In other words, we assume that first one need to nucleate a dimer and then the dimer can grow with an isodesmic process. In this case

$$\frac{[N_n]}{[N_{n-1}][N_1]} = K_3, \qquad n \geq 3$$

In terms of concentrations

$$\frac{[N_2]}{[N_1]^2} = K_2$$

and

$$\frac{[N_n]}{[N_1]^n} = K_2 K_3^{n-2}, \qquad n \geq 3$$

The total monomer concentration can thus be written as

$$\rho = \sum_1^\infty n N_n = N_1 + K_2 N_1^2 + \sum_3^\infty K_2 K_3^{n-2} [N_1]^n$$

$$\rho = \sum_1^\infty n N_n = [N_1] + 2K_2[N_1]^2 + \sum_3^\infty n K_2 K_3^{n-2} [N_1]^n = [N_1] + \sum_2^\infty n K_2 K_3^{n-2} [N_1]^n$$

and using

$$\sum_2^\infty n x^n = \frac{(2-x)x^2}{1-x)^2}$$

$$\rho = [N_1] + \frac{K_2}{K_3} \frac{(2 - K_3[N_1])K_3[N_1]^2}{(1 - K_3[N_1])^2}$$

By multiplying for K_3 one obtains a a-dimensional expression

$$K_3\rho = K_3[N_1] + \frac{K_2}{K_3} \frac{(2 - K_3[N_1])K_3^2[N_1]^2}{(1 - K_3[N_1])^2}$$

A plot shows that for small $\frac{K_2}{K_3}$ the total density coincides with the monomer density till $\rho = K_3^{-1}$ and then it abruptly decay to zero.

Recently, a simple model for patchy particles interacting with pair-wise additive interactions has been shown to undergoes cooperative polymerisation, forming abruptly extremely long tubes.

12 Simplified thermodynamic model for DNA hybridation

Let's consider a reactions, to which is associated a (standard) free energy variation, that is the free energy needed for single strands α and β to hybridize into a double strand $\gamma = \alpha\beta$:

$$A + B <=> AB$$

The approach is similar of course to what we have studied before for a generic reaction.

Assuming the simplifying initial condition that number of A and B strands originally placed in solution were equal, and let that value be (for each strand) N_0, then

$$N_0 = N_A + N_{AB} \tag{21a}$$

$$N_A = N_B \tag{21b}$$

where N_α is the number of α strands when equilibrium has been reached. In terms of probability of observing two paired DNA strands (an AB double helix) , we can write

$$p_b = \frac{N_{AB}}{N_0} = 1 - \frac{N_A}{N_0}$$

Note that when half of the strands are in double helix, $N_{AB} = N_0/2$ and $p_b = 1/2$.

In the ideal gas of clusters approximation, the equilibrium conditions read

$$\frac{N_{AB}}{N_A N_B} = \frac{Q_{AB}}{Q_A Q_B} \tag{22a}$$

where Q_α is the partition function of species α; they can be written as follows

$$Q_A = \frac{V}{\lambda_A^3} e^{-\beta f_A} \qquad Q_B = \frac{V}{\lambda_B^3} e^{-\beta f_B}$$

$$Q_{AB} = \frac{V^2}{\lambda_A^3 \lambda_B^3} \frac{V_b}{V} e^{\beta\epsilon} e^{-\beta f_{AB}^{solvation}}$$

$$\frac{N_{AB}}{N_A N_B} = \frac{Q_{AB}}{Q_A Q_B} = e^{-\beta(f_{AB} - f_A - f_B)} = e^{-\beta \Delta G} \tag{24}$$

Note that inside ΔG it is included the information of the volume of the system.

Going to bond probability, since $p_b = \frac{N_{AB}}{N_0} = 1 - \frac{N_A}{N_0}$ we can write

$$\frac{N_{AB}}{N_A N_B} = \frac{N_{AB} N_0^2}{N_A N_B N_0^2} = \frac{p_b}{(1-p_b)^2} \frac{1}{N_0} \tag{25}$$

and hence

$$\frac{p_b}{(1-p_b)^2} = \frac{N_0 V_b}{V} e^{\beta\epsilon} e^{-\beta(f_{AB}^{solvation} - f_A - f_B)} = e^{\ln \frac{N_0 V_b}{V} + \beta\epsilon} e^{-\beta(f_{AB}^{solvation} - f_A - f_B)}$$

All these terms on the right describe the change in free energy on going from undissociated to associated strands, at strand-A concentration N_0/V. When this concentration is 1 molar, one writes

$$\frac{p_b}{(1-p_b)^2} = e^{-\beta \Delta G_{1M}}$$

For other concentrations C_0, always expressed in molarity

$$\Delta G_{C_0} = \Delta G_{1M} - k_B T \ln(C_0)$$

The values of ΔG_{1M} can be experimentally evaluated by measuring, in a 1 Molar solution, the fraction of paired strands via circular dicroism, extracting in this way (from a best fit of the temperature dependence) the term ΔH and ΔS.

Theoretically, the hybridization free energies can be estimated using the nearest-neighbor method proposed by SantaLucia. These values are estimated at a specific molar concentration of 1M/liter

To evaluate the free-energy difference between the strand

$$3' - ATGGAC - 5'$$

and its complementary strand

$$3' - GTCCAT - 5'$$

one needs to write the "helix" complex

$$5' - TACCTG - 3' \tag{26}$$
$$3' - ATGGAC - 5' \tag{27}$$

and then consider all possible blocks of four bases. In the selected sequence we have the following blocks (one plus the length of the sequence)

$$TA \quad AC \quad CC \quad CT \quad TG \tag{28}$$
$$AT \quad TG \quad GG \quad GA \quad AC \tag{29}$$

TABLE 1 Nearest-neighbor thermodynamic parameters for DNA Watson-Crick pairs in 1 M NaCl[a]

Propagation sequence	ΔH° (kcal mol^{-1})	ΔS° (e.u.)	ΔG°_{37} (kcal mol^{-1})
AA/TT	−7.6	−21.3	−1.00
AT/TA	−7.2	−20.4	−0.88
TA/AT	−7.2	−21.3	−0.58
CA/GT	−8.5	−22.7	−1.45
GT/CA	−8.4	−22.4	−1.44
CT/GA	−7.8	−21.0	−1.28
GA/CT	−8.2	−22.2	−1.30
CG/GC	−10.6	−27.2	−2.17
GC/CG	−9.8	−24.4	−2.24
GG/CC	−8.0	−19.9	−1.84
Initiation	+0.2	−5.7	+1.96
Terminal AT penalty	+2.2	+6.9	+0.05
Symmetry correction	0.0	−1.4	+0.43

[a]The slash indicates the sequences are given in antiparallel orientation. (e.g., AC/TG means 5′-AC-3′ is Watson-Crick base paired with 3′-TG-5′). The symmetry correction applies to only self-complementary duplexes. The terminal AT penalty is applied for each end of a duplex that has a terminal AT (a duplex with both end closed by AT pairs would have a penalty of +0.1 kcal/mol for ΔG°_{37}).

Figure 2: Table of SantaLucia values from Annu. Rev. Biophys. Biomol. Struct. 2004. 33:415-40

Then one has to find the contribution of each block from the Santalucia table for both ΔS (in J/mol/K) and ΔH (kJ/mol)

$$\Delta H = -30.1 - 35.1 - 33.5 - 32.6 - 35.6 = -166.9$$

$$\Delta S = -89.1 - 93.7 - 83.3 - 87.9 - 95.0 = -449$$

To these values one need to add the contribution of the two terminals, one AT and one GC, giving

$$\Delta H = -166.9 + 9.6 + 0.4 = -156.9$$

$$\Delta S = -449 + 17.2 - 11.7 = -443.5$$

This provides the ΔG at 1 Molar NaCl concentration and 1 molar concentration of each strand. To find the ΔG at the desired concentration and salt molarity one need to add two entropic terms: a salt contribution (which depends linearly in the number of bases N

$$\Delta S_{salt} = 0.368 N \ln[\mathrm{N}a^+]$$

As we have discussed, in the entropy one has also to account for a term which depends on the strand concentration (C), expressed in mole/liter. If C is not equal to 1 Molar, one need to add

$$\Delta S_c = -R \ln[C]$$

The melting temperatures (defined as $p_b = 0.5$) are then given by

$$\ln 2 = -(\Delta H^{SL}_{AB} - T_m \Delta S^{SL} - R T_m \ln[C_0])/R T_m$$

$$\ln 2 - \Delta S^{SL}/R - \ln[C_0] = -\Delta H^{SL}_{AB}/R T_m$$

or

$$T_m = \frac{\Delta H^{SL}_{AB}}{\Delta S^{SL} + R \ln[C_0] - R \ln 2}$$

Often one express C_0 in term of total DNA concentration, $C_{DNA} = 2C_0$, and in this case

$$T_m = \frac{\Delta H^{SL}_{AB}}{\Delta S^{SL} + R \ln[C_{DNA}/4]}$$

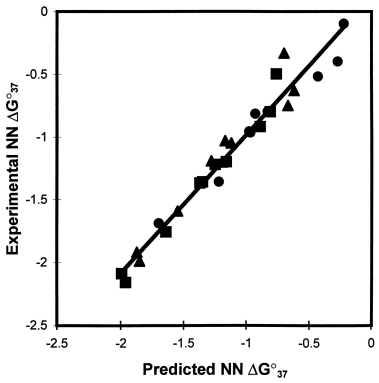

Figure 3: Comparison between the experimentally measured (via the melting temperature and the SantaLucia predictions.

13 Colloidal Gels: Depletion interactions

Gels are ubiquitous in nature. At atomic and molecular level, network liquids form extended open transient networks of bonds of quantum-mechanics origin (tetrahedral in water and silica). In the amorphous state, the bonding pattern is frozen in a permanent network. At polymer level, gels arise from multiple chemical or physical connections between distinct chains.At colloidal level, gels occur when the inter-particle interaction strength becomes considerably larger than the thermal energy k_BT and particles stick together forming a disordered highly porous material.

The origin of the colloidal gel state is one of the fascinating questions in soft matter: why particles prefer to form an arrested state of matter (a disordered solid), despite the very limited amount of occupied volume, i.e. in the absence of excluded volume caging effects? Does colloidal gelation always require an underlying phase-separation? When and how the gel state is a real equilibrium state of matter, that does not age or coarsen with time? Some of these questions are discussed here.

We specifically focus on particle colloidal gels, e.g. on systems in which the monomeric unit is a particle, although some of the concepts we will develop are also relevant to molecular and polymeric gels. While we deliberately discuss only one-component gels, the same ideas can be generalized to multicomponent systems. We thus focus on systems in which gelation arises from the onset of a network of long-lived interparticle bonds between identical particles. The solvent, when present, and its quality enter only in the definition of the effective interaction potential between particles. Under these simplifying assumptions, the phase behavior of the system can be represented on a two-dimensional plane. In colloids, it is conventional to indicate the state of the system as a point in the attraction strength-density or temperature-density plane. The plane is commonly partitioned in different regions: fluid, gas (colloid-poor phase), liquid (colloid-rich phase), crystal (ordered) and

their coexistence regions.

The most common colloidal gels (depletion gels) are formed by a quench into a thermodynamic unstable region, followed by spinodal decomposition and kinetic arrest, which finally prevent a complete phase-separation.This process creates dynamically arrested structures encoding information of the underlying decomposition process in the resulting material.Such gels are in a non-equilibrium state and display restructuring processes aiming at slowly completing phase-separation. Colloidal particles interacting via competing long-range electrostatic repulsion and short-range attraction also give rise to slowly aging filamentous gels.

One of the most common arrest mechanisms derives from a phase separation interrupted by the formation of a glass. In all interacting particle systems with potentials characterized, in addition to the ubiquitous repulsive part determined by the excluded volume, by an attractive spherical interaction, when the interaction energy u_0 becomes comparable with the heat energy k_BT, minimization of the free energy determine a separation in two phases characterized by a significantly different density (the order parameter). Also in colloidal systems, when u_0/k_BT exceeds a critical value, it triggers a phase separation, which determines the formation of regions with large and small concentration of particles respectively, in full analogy with the liquid-gas separation observed in atomic and molecular systems. The thermodynamics *driving force* at the basis of phase separation can therefore be exploited to generate regions that locally have a concentration of particles significantly higher than average.

The concentration of the particles in the dense phase increases with the depth of the quench (i.e. with u_0/k_BT), and under appropriate conditions can determine a sufficiently high density to make the excluded volume interactions relevant, giving rise to the local (non-homogeneous) formation of an arrested glassy state. The formation of the glass contributes to the sudden decrease of the mobility of the particles, with consequent arrest on the experimentally observable time scales of the phase separation process. The competition between phase separation and glass formation determines the final structure of the system. In fact, the spatial modulation of density — and as far as gel formation is concerned, the interconnectivity of dense zones — is controlled by the process of phase separation, and more precisely by the depth of the *quench*. The interruption of the coarsening process freezes the system in a two-continuous structure formed by an arrested phase and another one with low particle concentration. Since the glassy phase extends from one end of the sample to another end (percolation) the sample assumes properties typical of a solid, although the volume occupied, on average, is quite small.

This scenario is schematically illustrated for a generic system in Fig. 4. For our purposes it is interesting to observe the position of the point where the glass transition curve (experimentally defined as the set of points where the characteristic time of structural relaxation of the system reaches hundreds of seconds) meets the thermodynamic instability curve. Bringing the system abruptly inside the unstable zone, with values of k_BT/u_0 lower than the point of intersection, the dense phase of equilibrium will dynamically arrest and

the system will form a gel.

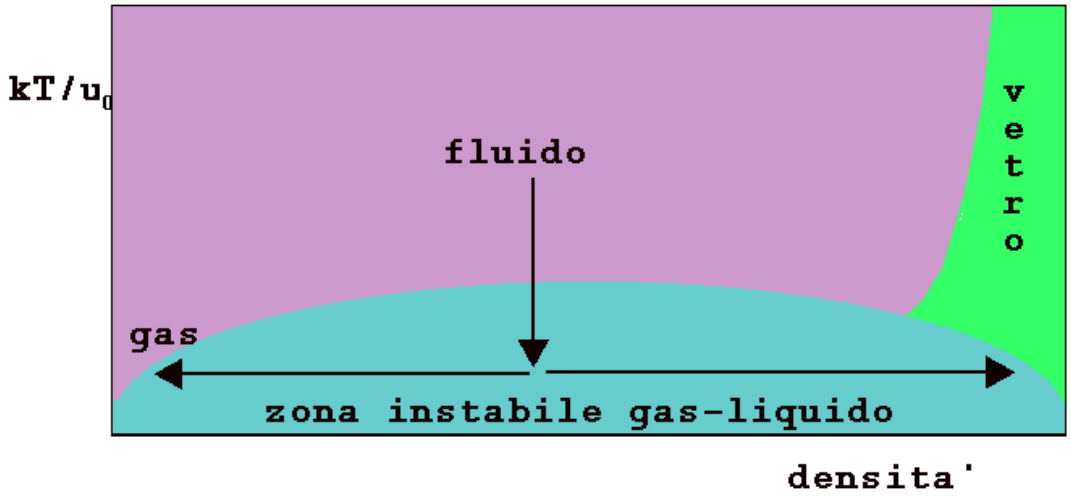

Figure 4: Schematic representation of the phase diagram of a colloidal particle system interacting with an attractive potential (in addition to excluded volume interaction) of depth u_0. The areas of thermodynamic instability and non-ergodicity (glass) are represented. If the system is brought inside the unstable zone, but under the yellow dotted curve, the density of the denser zones during the spinodal separation process increases over time until it reaches a value for which the vitrification system and the resulting reduction in mobility interrupts the separation process. Phases arrested at very small volume fractions can be generated with this mechanism.

The arrest following a spinodal decomposition is a widespread phenomenon, which characterizes all physical systems for sufficiently low values of u_0/k_BT and in principle observable also in atomic and molecular systems. Several reasons make this observation difficult in those systems: (i) the propensity to crystallize at low temperature (which in colloids is disadvantaged by the intrinsic polydispersity in colloidal particle size) (ii) the density of atomic and molecular liquids at ambient pressure and temperature, a value typically comparable with the density of the liquid phase, greater than the density of the point of intersection. In this case, a cooled and non-crystallizing system creates a dense homogeneous glass. Finally (iii) the difficulty to generate significant variations of k_BT/u_0, so that often the quench is shallow and the phase separation process is completed.

In the case of colloidal systems it is not difficult to work at low particle concentrations and, even more important, it is possible, by modifying the chemical-physical properties of the solution, to generate interactions between colloidal particles significantly more intense

than thermal energy. Finally, as we have mentioned, it is possible to control the range of the interaction, and in particular to generate very narrow ranges of interactions through the mechanism of depletion. The interaction of depletion, attraction, arises when you add in solution a co-solute much smaller than the size of the colloidal particle. For geometric reasons, the co-solute has a larger accessible volume when the colloidal particles are close together. The intensity of this entropic interaction is controlled by the concentration of cosolute and is characterized by a range of interaction in the order of size of the cosolute itself. For attractive interactions with very narrow range, prerogative of colloidal systems, the region of instability is very large in concentration and the glassy curve intersects the instability curve at values of kT/u_0 not very different from those of the critical point.

It is just a model system of spherical colloidal particles in solution, to which a polymer (not *adsorbing*) has been added — whose radius of rotation is one tenth of that of colloidal particles — that has been recently used to study in detail the phenomenon of colloidal gel formation. This work of confocal microscopy, preceded and stimulated by several theoretical, numerical and experimental work, has recently demonstrated that for particles where the excluded volume interactions are complemented by an attractive (spherical symmetry) interaction, the formation of a gel always requires phase separation as a prerogative, regardless of the value of the interaction range. Fig. 5 shows a confocal image of the system structure for two very similar values of kT/u_0, corresponding to a state in which the fluid is stable and a state in which the system separates phase and forms a gel.

Many colloidal gels are produced in the limit of *quench* infinitely deep, i.e. in conditions where the attraction between the particles is much bigger than k_BT. In these cases the phase separation is entirely controlled by the (local) energy minimization kinetics and we prefer to talk about irreversible aggregation (limited by diffusion) rather than interrupted phase separation, even if conceptually the irreversible aggregation between the particles is to all intents and purposes the way in which the system tends to minimize, as far as possible and compatible with kinetics, its free energy. The aggregation is present for all concentration values of colloidal particles, even for extremely small values. In this limit the system forms fractal aggregates that grow by aggregation with other clusters and the process, studied in great detail in the 80s, takes the name DLCA *diffusion limited cluster-cluster aggregation*. Since the aggregates have a fractal dimension smaller than the spatial dimension, the *clusters* progressively fill all the space, decreasing the process of diffusion of the aggregates that is in fact dictated by excluded volume conditions.

14 Colloidal Gels: Phase diagram of patchy colloids

We have learned that if a system forms clusters, then in the ideal gas approximation, the free energy can be expressed as

$$\beta F = N\beta\mu - \#_{clusters}$$

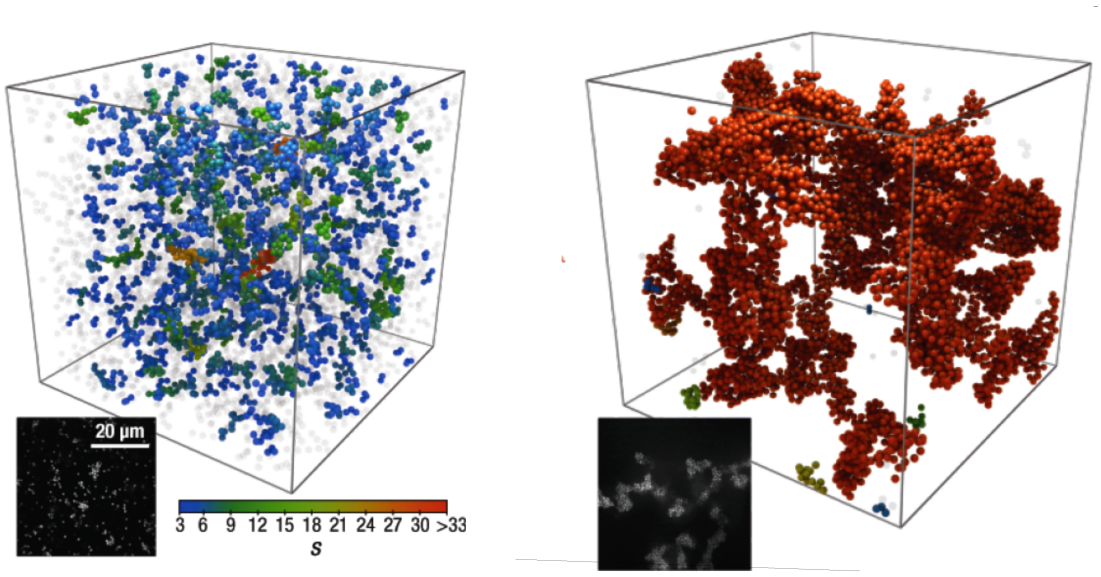

Figure 5: Confocal image (reconstructed with *rendering* programs) of the structure of a colloidal gel obtained by phase separation followed by kinetic stop. The image on the left shows the structure of the system in the homogeneous region. The image on the right shows the final arrested structure of a sample carried within the unstable region. The color of the particles indicates the size of the clusters. The black and white images show the data of the confocal measurement on a specific plane, before three-dimensional reconstruction and rendering.

In the case of a system of N particles with valence f (particles decorated with f identical attractive patches or with f reversibly reacting units), the ground state of the system corresponds to the state in which all bonds are formed. The maximum number of bonds is $Nf/2$. As usual, we can define a bond probability p_b (which will be dependent on T and ρ) as

$$p_b = \frac{\#_{bonds}}{Nf/2}$$

In terms of p_b, the number of monomers is

$$N_1 = N(1-p_b)^f$$

and thus the chemical potential

$$\beta\mu = \ln\frac{N_1}{V} = \ln\rho + f\ln(1-p_b).$$

In the mean field approximations when clusters do not contain loops,

$$\#_{clusters} = N - \#_{bonds} = N - p_b \frac{Nf}{2} = N\left(1 - \frac{fp_b}{2}\right)$$

We thus obtain an expression of the system free energy completely controlled by p_b,

$$\frac{\beta F}{N} = \beta\mu - \#_{clusters}/N = \ln\rho + f\ln(1-p_b) - \left(1 - \frac{fp_b}{2}\right)$$

and identifying $\ln\rho - 1$ with the reference ideal gas free-energy

$$\frac{\beta F}{N} = \frac{\beta F_{ideal\ gas}}{N} + f\ln(1-p_b) + \frac{fp_b}{2}$$

which clearly shows the effect of cluster formation on the free energy.

If the ideal gas free energy is substituted with the hard-sphere free energy, the previous expression coincides with the prediction of the graph-based theory of Wertheim:

$$\frac{\beta F}{N} = \frac{\beta F_{hard-sphere}}{N} + f\ln(1-p_b) + \frac{fp_b}{2}$$

The T and ρ dependence of p_b can be estimated assuming independent binding processes, estimating the probability that a bond exists between two particles. p_b can be estimated by looking at the chemical equilibrium between monomer and dimers. In this case we have seen that the equality of the chemical potential implies

$$\frac{N_2}{Q_2} = \left(\frac{N_1}{Q_1}\right)^2$$

Since $N_1 = N(1-p_b)$ and $N_2 = Np_b$

$$\frac{Np_b}{N^2(1-p_b)^2} = \frac{Q_2}{Q_1^2}$$

Since $Q_1 = V$ and $Q_2 = \frac{1}{2!}VV_bfe^{\beta\epsilon}$

$$\frac{p_b}{(1-p_b)^2} = \frac{Nf}{2V}V_be^{\beta\epsilon}$$

which provides the sought T and V dependence of the bond probability $p_b(T,V)$.

The equation of states can thus be calculated from

$$P = -\frac{\partial F}{\partial V} = P_{HS} + P_{bonding}$$

as a sum of the hard-sphere positive (repulsive) contribution and of the negative (attractive) bonding contribution.

The HS equation of state is

$$\frac{\beta P_{HS}}{\rho} = \frac{1+\phi+\phi^2-\phi^3}{(1-\phi)^3}$$

In principle, we know already what the bonding contribution to pressure $P_{bonding}$ is, since $\beta PV = \#_{clusters} = N(1-\frac{f}{2}p_b)$ where the 1 is the ideal gas contribution and $-\frac{f}{2}p_b$ is the attractive bonding contribution. Let's derive this result again from the derivative of the free energy

$$\frac{\beta P_{bonding}}{N} = \left(\frac{f}{1-p_b} - \frac{f}{2}\right)\frac{\partial p_b}{\partial V} = f\frac{1+p_b}{2(1-p_b)}$$

$$\frac{(1-p_b)^2+2(1-p_b)p_b}{(1-p_b)^4}dp_b = -\frac{Nf}{2}V_b e^{\beta\epsilon}\frac{dV}{V^2} = -\frac{p_b}{(1-p_b)^2}\frac{dV}{V}$$

so that

$$\frac{\partial p_b}{\partial V} = -\frac{1}{V}\frac{(1-p_b)^2 p_b}{(1-p_b)^2+2(1-p_b)p_b} = -\frac{1}{V}\frac{p_b(1-p_b)}{1+p_b}$$

and

$$\frac{\beta P_{bonding}}{N} = -\frac{1}{V}f\frac{1+p_b}{2(1-p_b)}\frac{p_b(1-p_b)}{1+p_b} = -f\frac{p_b}{2V}$$

which confirm that the bonding contribution to pressure comes from the reduction of the number of clusters.

15 A trip to the kitchen (Nelson)

15.1 Milk, a solution of charged micelles

In addition to fat and water, milk contains two classes of proteins, the casein complex and whey (mainly α-lactalbumin and β-lactoglobulinlactoglobulins). In fresh milk the casein complexes self-assemble into micelles of radius around 50 nm. The micelles are kept apart in part by electrostatic repulsion and so the milk is fluid.

However, minor environmental changes can induce curdling, a coagulation (clumping) of the micelles into a gel. In the case of yogurt, the growth of bacteria such as Lactobacillus bulgaricus and Streptococcus thermophilus creates lactic acid as a waste product (alternatively you can add acid by hand, for example lemon juice). The ensuing increase in the concentration of $[H^+]$ ions reduces the effective charge on the casein micelles and hence also reduces the normal electrostatic repulsion between them. This change tips the balance toward aggregation; milk curdles when its pH is lowered from the natural value of 6.5 to below 5.3. The casein network in turn traps the fat globules.

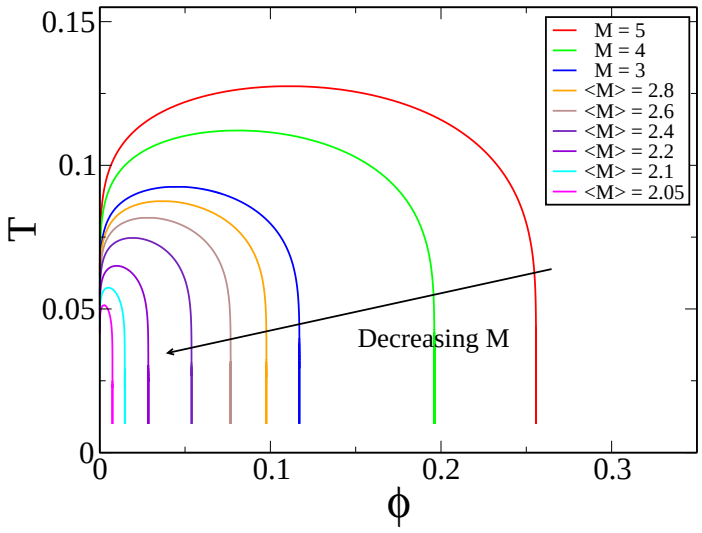

Figure 6: Phase diagram of patchy colloids for different values of the valence

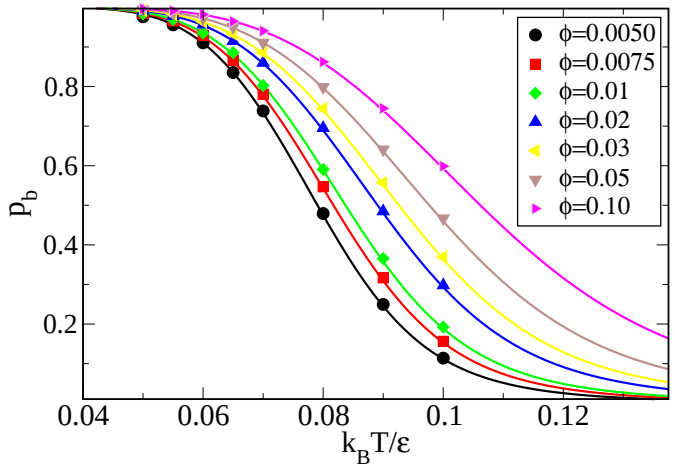

Figure 7: Typical T dependence of the bond probability

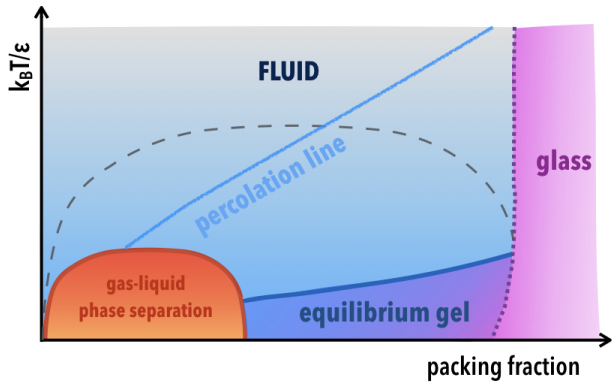

Figure 8: Schematic representation of the phase diagram of a low valence system

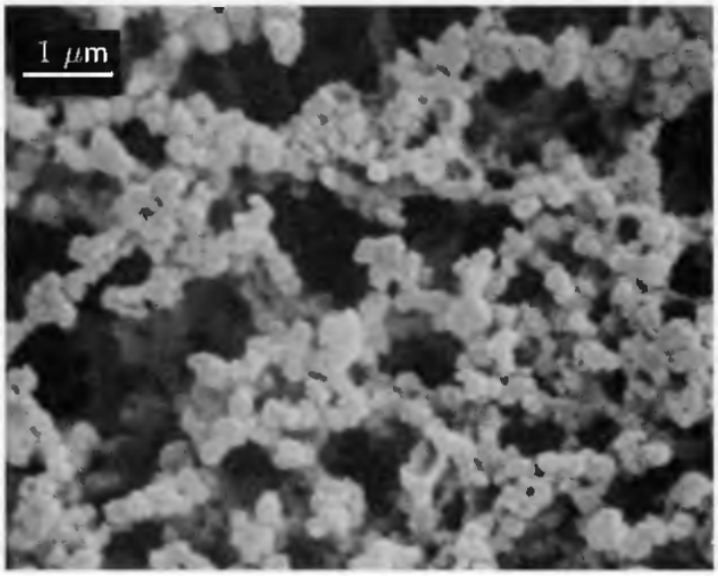

Figure 8.10: (Scanning electron micrograph.) Yogurt. Acid generated by bacteria triggers the aggregation of casein micelles (*spheres* of diameter 0.1 μm in the figure) into a network. The fat globules (*not shown*) are much bigger, with radius 1–3 μm in fresh milk. [Digital image kindly supplied by M. Kalab.]

15.2 Eggs, a solution of T-denaturable proteins

Eggs provide another example of a system of protein complexes. Each protein is a long, chemically bonded chain of amino acids. Most culinary operations do not disrupt the primary structure, or sequence, of this chain, since normal cooking temperatures don?t supply enough energy to break the peptide bonds. But each protein has been engineered to assume a useful native conformation under the assumption that it will live in an aqueous environment at temperatures below 37^o C. When the environment is changed (by introducing air or by cooking), the protein denatures. Raising the temperature can convert the precisely folded native structures into random chains. Once the chains open, the various charged and hydrophobic residues on one chain, previously interacting mainly with other residues elsewhere on the same chain, can now find and bind to those on other chains. In this way a crosslinked network of chains can form. The interstices of this network can hold water, and the result is a solid gel: the cooked egg.

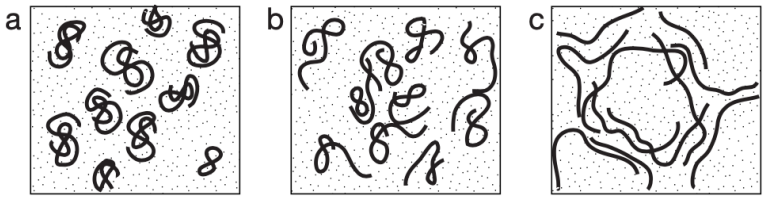

Figure 8.11: (Schematic.) The physics of omelettes. (a) Proteins in their native conformation (b) open up to form random coils upon heating. (c) Neighboring coils then begin to interact with each other, forming weak bonds previously used for stabilizing individual proteins. The resulting network can trap water.

15.3 Hydrophobic protein parts close to air: mousses

As with milk, one may expect that the addition of acid would enhance the coagulation of eggs once the proteins are denatured, and indeed it is so. Heating is not the only way to denature egg proteins and create a linked network. Merely whipping air into the eggs, to create a large surface area of contact with air, can totally disrupt the hydrophobic interactions. The ensuing surface denaturation of egg proteins like conalbumin is what gives chiffon pie or mousse their structural stability: A network of unfolded proteins arrange themselves with their hydrophobic residues facing the air bubbles, while their hydrophilic ones face the water. This network not only reduces the air-water tension like any amphiphile; it also stabilizes the arrangement of bubbles, since unlike simple amphiphiles the proteins are long chains. Other proteins, like ovomucin and globulins, play a supporting role by making the egg viscous enough that the initial foam drains slowly, giving

the conalbumin time to form its network. Still others, like ovalbumin, support air foams but require heat for their initial denaturation; these are key to supporting the stronger structures of meringue and souffle. All of these attributions of specific roles to specific proteins were established by isolating particular proteins and trying them alone or in various combinations.

15.4 La Bechamel: un gel polimerico di amilosio — Le scienze blog

Il responsabile della alta viscosità della besciamella e' l'amido idratato contenuto nella farina. Presente in forma di microscopici granuli, l' amido è formato da molecole di amilosio e amilopectina, a loro volta formate da moltissime molecole di glucosio legate tra loro.

L'amido non si scioglie in acqua ma i suoi granuli possono formare una sospensione. Quando l'acqua raggiunge una temperatura critica, dipendente dal tipo di amido ma solitamente tra i 50 e i 70 ^{o} C, i granuli si gonfiano, e cominciano ad assorbire acqua. Riducendo l?acqua disponibile e aumentando di volume i granuli riducono molto la loro possibilità di muoversi e questo causa un aumento della viscosità del liquido. Ad alte temperature l'amilosio viene espulso dai granuli e si scioglie in acqua. Le lunghe catene lineari di questa molecola cominciano a legarsi tra loro formando un reticolo tridimensionale che raffreddandosi intrappola ulteriore acqua al proprio interno: inizia il fenomeno della gelificazione.

É possibile addensare un liquido acquoso semplicemente disperdendo dell' amido in poco liquido freddo, formare una pastella e successivamente aggiungerla al resto scaldando. Tuttavia il metodo preferito per disperdere al meglio i granuli è ricoprirli di un grasso e successivamente di disperderli in un liquido.