

# Study of nano-sized micelles formation with surfactant critical packing parameter and its applications

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**Abstract** -In this manuscript, formation of the nanosized micelles is studied in relation to critical packing parameter and the formations of various aggregates are also emphasized. The theory for the aggregate structure is based upon the area occupied by the hydrophilic and hydrophobic groups of surfactant. The polar head groups in water, if ionic, will repel each other because of same charge repulsion. The larger the charge, the greater the repulsion and lower the tendency to form aggregates. Spherical micelles are formed where the value of surfactant packing parameter is less than 1/3 (single chain surfactants with large head group areas such as anionic surfactants). The spherical aggregates are extremely small and their radius is approximately equal to the maximum stretched out length of the surfactant molecule. Any change in solution properties which causes a reduction in the effective size of hydrophilic head groups will change the aggregate size and shape from spherical to cylindrical form. Conceptual framework that relates molecular parameter (head group area, chain length and hydrophobic tail volume) and intensive variables (temperature, ionic strength etc.) to surfactant are given as:

Critical Packing Parameter / Packing parameter = CPP or  $P = v / l \cdot a_0$

$v$  = volume of hydrocarbon core

$l$  = hydrocarbon chain length

$a_0$  = effective head group area

The applications of nanomicelles have been found to be very effective and efficient in solving various therapeutical, clinical, and bioengineering problems. Nanomicelles, because of their low toxic nature, can be bioengineered as smart, efficient and excellent drug delivery systems as it has the ability to minimize drug degradation, high ability to permeate tissues easily for drug bioavailability, and lowering adverse drug side effects thereby can act as highly useful and smart drug vehicles too.

**Keywords:** Aggregates, Spherical micelles, Surfactant number, Micellar growth, Critical packing parameter, Bioengineering, Drug vehicle, etc.

## I. INTRODUCTION

Surfactants (or 'surface active agents') are organic compounds with at least one lyophilic ('solvent - loving') group and one lyophobic ('solvent-fearing') group in the molecule. When amphiphilic molecules are dissolved into solvents, such as water, the hydrophobic nature of the hydrocarbon chains drives these molecules to self-assemble into a variety of structures where the hydrophilic heads form a surface which shields the hydrophobic tails from water. Surfactants at low concentration in aqueous solution exist as monomers (free or unassociated surfactant molecules). These monomers pack together at the interface, form monolayer and contribute to surface and lowering of interfacial tension. Although, this phenomenon is highly dynamic (surfactant molecules arrive and leave the

interface on a very rapid timescale), molecules at the interface interact with the neighboring molecules very strongly which enables the measurement of the rheological properties of the monolayer. The properties of surfactant at low concentration in water are similar to those of simple electrolytes except that the surface tension decreases sharply with increase in concentration [1-7].

## II. CRITICAL MICELLE CONCENTRATION

In surfactant solutions, the micelle formation (also called self-association or self-assembly) is an unique phenomenon. All properties in surfactant solutions are related to the micelle formation of these molecules. At fairly well defined concentrations, several physical properties e.g. osmotic pressure, electrical conductivity, surface tension, etc, abruptly change their values in aqueous

surfactant solutions. McBain and Swain (1936) suggested that this anomalous behaviour could be explained in terms of the formation of organized aggregates of the surfactant molecules, the micelles. The concentration above which micelle formation becomes appreciable is termed “critical micelle concentration (CMC)”. However, the CMC is a narrow concentration range, not a fixed value. When the hydrophobic part of the surfactant is a hydrocarbon chain, the micelle will consist of a hydrocarbon core, with hydrophilic groups at the surface serving to maintain solubility in water. In such micelles, the hydrophobic core is, in effect, a small volume of liquid hydrocarbon because the hydrocarbon chains are generally regarded as disordered (Tanford, 1980) [ 8-11 ].

### A geometrical consideration of chain packing

One of the most popular ways of dealing with surfactant geometry is to use the packing parameter concept. Critical packing parameter CPP is a reflection of the balance of the interaction between the hydrophobic moieties and the polar part. Surfactants in aqueous solution are normally used at conditions where the critical packing parameter is small. The geometric or packing properties of surfactants depend on their optimal head group area ‘a’ as well as on the hydrocarbon volume ‘v’ and the extended length of the surfactant hydrophobic chain,  $l_{max}$ . The value of ‘a’ is governed by repulsive forces acting between the head groups and attractive hydrophobic forces between the hydrocarbon chains (Figure.1). The value of the dimensionless critical packing parameter CPP,  $v/l_{max}a$  can be used to determine what type of aggregate will be spontaneously formed in solution.

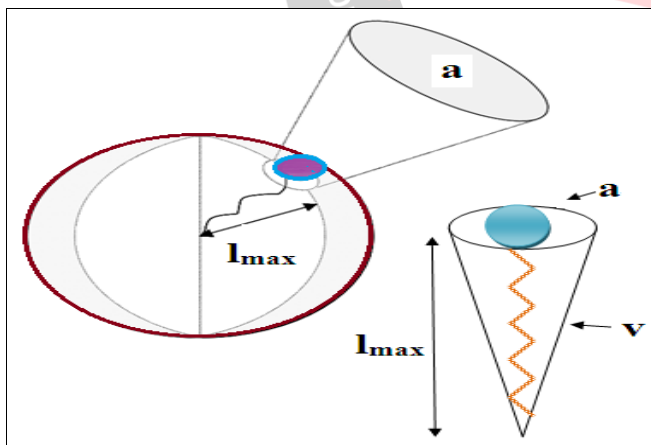


Figure. 1 Critical packing parameter

The critical packing parameter (CPP) relates the head group area, the extended length and the volume of the hydrophobic part of a surfactant molecule into a dimensionless number

$$CPP = v/a \cdot l_{max}$$

Since the cross section area per chain decreases radially towards the centre, only one chain can be fully extended while the others are more or less folded. The aggregation

number N, can be expressed as the ratio between the micellar core volume,  $V_{mic}$ , and the volume, v, of one chain:

$$N = V_{mic}/v = 4/3 \pi R_{mic}^3/v$$

The aggregation number as the ratio between the micellar area,  $A_{mic}$ , and the cross sectional area, a, of one surfactant molecule:

$$N = A_{mic}/a = 4 \pi R_{mic}^2/a$$

On putting aggregation numbers equal,

$$v/R_{mic} a = 1/3$$

Since  $R_{mic}$  can't exceed the extended length of the surfactant alkyl chain:

$$l_{max} = 1.5 + 1.265 n_c$$

It is found, that,

$$v/l_{max} a \leq 1/3 \text{ for a spherical micelle}$$

The ratio  $v/l_{max}a$  which gives geometric characterization of a surfactant molecule will be seen to be very useful when discussing the type of structure formed by a given amphiphile (Table 1). It is denoted as a ‘critical packing parameter’ CPP or the ‘surfactant number’ [12-16].

$P_c$	General Surfactant Type	Expected Aggregate Structure
<0.33	Single-chain surfactants with large head groups	Spherical or ellipsoidal micelles
0.33 – 0.5	Single-chain surfactants with small head groups, or ionics in the presence of large amounts of electrolyte	Large cylindrical or rod-shaped micelles
0.5 – 1.0	Double-chain surfactants with large head groups and flexible chains	Vesicles and flexible bilayers structures
1.0	Double-chain surfactants with small head groups or rigid, immobile chains	Planar extended bilayers
>1.0	Double-chain surfactants with small head groups, very large and bulky hydrophobic groups	Reversed or inverted micelles

Table.1 The packing parameter of a surfactant molecule and the various structures they form in aqueous solutions.

### III. FACTORS EFFECTING THE CPP

Various conditions with causes the changes in the CPP values can be analyzed as below.

System with a single straight chain ionic surfactant can be accomplished in the following way:-

- change of a surfactant to one with a longer hydrocarbon chain
- change of a surfactant to one with a branched hydrocarbon chain
- use of surfactant with two hydrocarbon chains
- addition of a long chain alcohol, amine or other hydrophobic amphiphilic molecule
- addition of a hydrophobic non-ionic surfactant
- addition of a small amount of surfactant with opposite charge
- addition of salt

System with a single straight chain non-ionic surfactant can be accomplished in the following ways:-

- change of a surfactant to one with a longer hydrocarbon chain
- change of a surfactant to one with a branched hydrocarbon chain
- use of surfactant with two hydrocarbon chains
- change of a surfactant to one with a shorter polyoxyethylene chain
- increase of temperature
- addition of salt

As the CPP increases, the surfactant at the air-water surface pack closer together and hence a higher co-hesion is attained. The CPP of non-ionic surfactant is easily altered by changing the length of the chain or by changing the temperature. In ionic surfactant systems, the CPP can be changed by altering the hydrocarbon chain length [17-23].

#### System dependant micellar growth

Micellar growth is a very common phenomenon and for ionic surfactants the following are the factors that influence the growth:

- The tendency to grow increases strongly with the alkyl chain length and there is no growth for shorter chain
- Micellar growth is strongly dependent upon the temperature and is strongly promoted by a decrease in temperature
- While CMC is only dependent on counter ion within a given class, micellar growth displays a strong variation. The dependence of growth on counter ions however is very different for different surfactant head groups.
- In the case of micellar growth, micellar size increases strongly with surfactant concentration
- Micelle size is very sensitive to co-solutes. Addition of salt promotes micelle growth. Solubilized molecules

can have very different effects depending on the surfactant systems. However, in general, non-polar solubilizates, like alkanes, which are located in the micellar core, tend to inhibit micellar growth, while alcohols or aromatic compounds, which are located in the outer part of the micelles, tend to strongly induce the growth.

For other classes of surfactants there are different characteristic of micellar growth. Non-ionic surfactants of the polyoxyethylene type enhance growth with increasing concentration. With four to six oxyethylene units there is a dramatic increase in growth, while with eight or more oxyethylene there is negligible growth under any condition. These surfactants show a micellar growth that is much more pronounced at a higher temperature, i.e. opposite to other class of surfactant [24-26].

#### Concentration effect on the micelle type and size

The spherical micelle cannot be formed at all for many amphiphiles and for others it occurs only in limited range of temperature and concentration. Surfactants or polar lipid shows three types of behaviour.

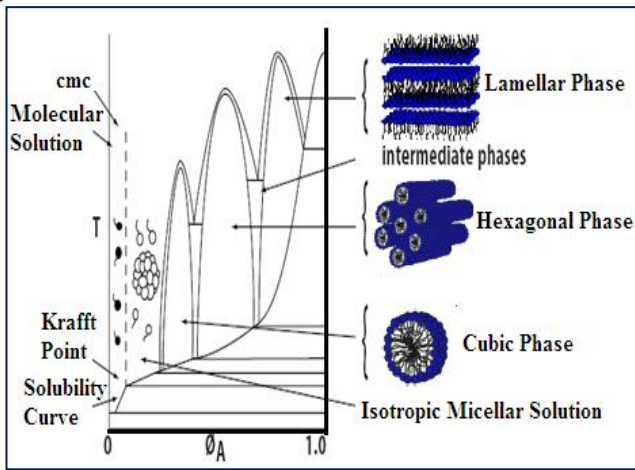
- The surfactant has a high solubility in water and physicochemical properties vary in a smooth way from the CMC region up to saturation. This suggests that there are no major changes in micelle structure, but the micelle remains small and don't depart much from a spherical shape.
- The surfactant has a high solubility in water but as the concentration increased there are quite dramatic changes in certain properties. This indicates that there are marked changes in self-assembly structure.
- The surfactant has a low solubility and there is a phase separation at low concentration.

The three cases are characterized by different ranges of existence of the isotropic solution phase. In either case the new phase formed above saturation may be:

- A liquid crystalline phase
- A solid phase of (hydrated) surfactant, or
- A second, more concentrated, surfactant solution.

Different phase structures give very different physicochemical properties, and therefore in any use of surfactants it is mandatory to have control over phase structure. The regions of existence of different phases and the equilibria between different phases are described by phase diagrams (Figure. 2). These are significant not only as the basis of applications but also for our general understanding of surfactant self-assembly [27-29].





$\phi_A$  = Surfactant Volume Fraction

**Figure 2. Schematic Phase diagram**

For a relatively short chain surfactant, like  $C_8$  or  $C_{10}$ , one usually observes a very slow and regular variation of relevant properties, and no phase separation upto high concentrations, say 10-40 wt%. The viscosity, which is an important property for uses of surfactants, varies smoothly and approximately as predicted for a dispersion of spherical particles upto high concentration. A frequently encountered behaviour for longer chain surfactants, say  $C_{14}$  or above, is that at low or intermediate concentration the viscosity starts to increase rapidly with concentration. Here the micelles grow with increasing concentration, at first to short prolates or cylinders and then to long cylindrical or thread like micelles.

At saturation micellar growth to rods can be considered to arise from two mechanisms:

- 1) In one there is an internal driving force to form large aggregates with another geometry and then micelle may grow also at low concentration.
- 2) In another micellar growth is induced by inter-micelle repulsions to allow a better packing of the micelle. This will occur at quite high concentrations, when the micelle comes in direct close contact.

The too strong crowding of micelles is observed by the structure transition into an ordered phase, which may be solid but is more frequently a liquid crystalline phase. Surfactant micelles and bilayers are the building blocks of most self-assembly structures. phase structure can be divided into two groups:

- I. Discrete self-assembly- characterized roughly as spherical, prolate, oblate or cylindrical (more or less flexible)
- II. Infinite or unlimited self-assembly - In this case the surfactant aggregate is connected over macroscopic distances in one, two or three dimensions.

The hexagonal phases are examples of one-dimensional continuity; the lamellar phases are two dimensional

continuity, while three dimensional continuity is found for the bicontinuous cubic phases, for the sponge phase and for many microemulsions. Phases built up of discrete aggregates include the normal and reversed micellar solutions, micellar type microemulsions and certain normal and reversed cubic phases [30-32].

Many experimentally observed features of surfactant self-assemblies are now well-understood qualitatively. The cooperativity of self-association is responsible for the formation of large aggregates instead of molecular clusters such as dimers, trimers, etc were studied and was also emphasized the important role played by anti-co-operativity which ensures that micelles remain finite rather than growing without limit. Subtle variations in the free energy of micellization control the transition between globular and rod like micelles using empirical expressions for the free energy were studied. Further, he derived for the first time an expression for the dependence of the average size of the rod like micelles on the surfactant concentration.

The physicochemical features of surfactant self-assembly were elucidated by the pioneering model of Tanford for the free energy change associated with micellization. It was demonstrated that the hydrophobic effect is responsible for the co-operative growth of micelles, while the interactions between the polar head groups of surfactants provide the anti-co-operativity that constrains the aggregates to remain of finite sizes. The critical micelle concentration which is usually defined only operationally in terms of the experimental method used for its determination was given a theoretical definition, independent of the experimental method employed. With recognition of the intimate connection between the measurable properties of micellar solutions and the size distribution of the micelles, the critical concentration was defined as the surfactant concentration at which the size distribution of micelles changes from a monotonically decreasing function to a function that exhibits extrema. This theoretically defined critical concentration was shown to be a close lower bound of the experimental critical micelle concentration. It was suggested on the basis of geometrical considerations how the micellar shape and its size are related together. This suggestion has received a clear treatment in the work of Israelachvili et al. It was studied that how the type of aggregate is formed and its size depends upon the length and the volume of the surfactant tail as well as on the aggregate surface area per molecule obtained from equilibrium free energy considerations.

#### IV. THERMODYNAMIC ENERGIES

A statistical thermodynamic model of surfactant aggregation was developed to study and analyse the physical origin of the attractive and repulsive contributions to the free energy of aggregation and explicit expressions for each of these free energy contributions were formulated. The essential role of steric repulsion between head groups

that governs the aggregational behavior of nonionic surfactants was identified. Research studies have been done to model the intra-aggregate conformations of the surfactant tail to obtain estimates of the extent of chain ordering inside the aggregates compared to analogous chains in liquid hydrocarbons. These studies also provide information about the extent to which the different parts of the surfactant tail come into contact with water, thus allowing a satisfactory interpretation of various probe-based studies. The problem of intermicellar interactions in concentrated solutions containing globular or rod like micelles and the phase behavior of such solutions has been reported. The consequences of intermicellar interactions for the growth of micelles have been examined and the aggregation behavior of mixed surfactant systems has been modeled from a molecular point. The non-ideal behavior exhibited by mixed surfactant systems has been traced to the fact that the interactions at the micellar surface depend nonlinearly on the composition of the mixed surfactant systems. The formation of spherocylindrical aggregates in mixed surfactant systems has been shown to be influenced by the asymmetric distribution of the surfactant components in the spherical endcaps and in the cylindrical middle. A unitary approach to micellization, solubilization, and microemulsions has been presented and emphasized more on the importance of the hydrophobic effect in the occurrence of critical concentrations in aqueous surfactant solutions and suggested a possible explanation for the critical micelle concentration also in non-polar solutions. Micelles that are sufficiently small in size pack into spherical aggregates or into somewhat distorted globular aggregates. Usually, such micelles are narrowly dispersed in sizes. A different realm of micellization behavior is, however, observed when micelles grow larger in size and rodlike micelles are generated. These aggregates can be visualized as having a cylindrical middle part with two spherical endcap [33-42].

## V. APPLICATIONS

Intensive research studies have revealed that nanomicelles could be extensively used in a variety of medicopharmacological procedures to catalyze drug effects or improve drug treatment. Studies also show that nanomicelles are very much helpful in facilitating therapeutic solutions that involve protein and peptide delivery. Depending on the type of nanomicelles, various applications include the use of drug polymer conjugates, reverse micelles, multilayer micelles prodrugs and novel polymers with low concentration. Recent studies have shown that anti-cancer drug nanomicelles that are formed by the self-assembly of the amphiphilic dendrimers are believed to alleviate drug resistance among the cancer cells. Studies also show that amphiphilic dendrimers have the ability to generate supramolecular nanomicelles with large void space in the core and can be highly applied for drug delivery systems [43-45]. Polymeric micelles can be

extensively applied in the field of drug and gene delivery because of the excellent biocompatibility, low toxic nature, enhanced blood circulation time, and ability to solubilize a large number of drugs within their micellar core thus resulting in enhanced bioavailability of these kinds of drugs.

## VI. CONCLUSION

The characteristics of surfactants have attracted huge attention from the scientific community. The amphiphilic nature of surfactant molecules results in many unique phenomenon when surfactants are dissolved in aqueous or non-aqueous solutions. The nanosized micelles have shown a new modern trend in wide range of applications in various fields. Although surfactants are often present in very small amounts in solution, they do affect the overall properties of the system greatly, such as surface tension, osmotic pressure, solubility, etc., because of their ability to adsorb at surfaces and to form micelles in the solutions. The characteristics of solutions containing surfactants, such as detergency, wetting, emulsification, dispersion and foaming, have been known for a long time and have many practical applications in daily life and industry. Many industrial products, like soap, shampoo, washing powders, etc. contain surfactants. The size and shape of the surfactant aggregates greatly affects the bottom-up approach of nanoparticles. Modern research studies show that nano micellar structures along with the surfactant engineered with the desired properties are widely used in the photodynamic therapies, drug loading systems, encapsulation and for the cancer drug delivery systems.

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