

## Clustering in Complex Fluids

The tendency of molecules to associate with other molecules of the same species and to shun dissimilar molecules by bulk separation is well established. There is another kind of association, however, that is less understood in science: how do molecules or particles spontaneously form clusters that contain many particles or molecules and yet have a finite size? In the past decade, research on colloids and on solutions of proteins or polyelectrolytes has uncovered many cases of equilibrium clusters that have a finite and steady-state size that is substantially larger than the constituent particles. The equilibrium nature of this mesoscopic size is the defining characteristic of what we here refer to as “clustering.” Equilibrium clustering is distinct, for example, from diffusion-limited processes, in which finite-size aggregates appear for an interval of time before the system reaches steady state. For the materials scientist, clustering offers the potential to create mesoscopic order in a system by harnessing equilibrium self-assembly; such an approach should be more readily controlled than nonequilibrium, quench-based approaches. For scientists studying proteins, clustering in solution may be relevant for the rate of crystallization *in vitro* (an important topic that is notoriously perplexing)<sup>1,2</sup> and might be relevant *in vivo*.

Why would clusters have finite size in equilibrium? Surfactants and other amphiphilic molecules accomplish this by forming micelles; in these cases the clustering arises from anisotropic interactions. Even with isotropic interactions, however, equilibrium clusters can form in a manner described by Groenewold and Kegel<sup>3,4</sup> in a body of work that stimulated substantial investigations in this area. They proposed that a combination of short-range attraction and longer-range repulsion (SALR) could lead to a minimum of the free energy at a finite, mesoscopic cluster size. In this model, when a particle attempts to join an equilibrium cluster, the favorable energy of attraction from nearby surface particles is counterbalanced by the repulsive interactions from the more distant yet more numerous particles in the cluster volume. In general terms, SALR is the opposite of the typical interactions among atoms and molecules, which have a short-range repulsion and longer-range attraction. It turns out, however, that SALR is found, and may indeed be common, in macromolecular and colloidal systems that have electric charge. In these cases, the SA might arise from polarization of one particle by the other particle's charge and the LR can arise from a screened-Coulomb interaction. Computer simulations,<sup>5</sup> theoretical calculations,<sup>3,4,6</sup> and experiments<sup>7,8</sup> show that, even at low density, SALR yields clusters. There are, however, many open questions remaining: Is the repulsive part of the potential necessary to form stable mesoscopic clusters?<sup>9,10</sup> What are the microscopic origins of SALR interactions? What sets the size of the clusters? Do the clusters form a fluid or a superlattice? Are clusters compact or can they be stringy, and can they form lamellar or other liquid-crystalline phases? In short, what is the overall phase diagram and how does it depend on the macromolecule- or particle-scale interactions?

Surprisingly, there is an alternative route to clustering that involves purely repulsive interaction potentials.<sup>11,12</sup> Even in cases

where the interaction is purely repulsive, the precise shape of interparticle potential curve has critical, nonintuitive consequences. A hard-core repulsion with a softer repulsive shoulder (HCSS), for instance, forms a canonical sequence of phases with increasing particle density or pressure: a superlattice of spherical clusters, a 2D array of columnar clusters, multilamellar stacks, and the corresponding “inverse” phases of columnar and spherical voids.<sup>13–18</sup> In contrast to the clusters formed by SALR, theory and simulation find clustering in HCSS particles only above a threshold particle density; the stability of clusters in purely repulsive systems, in a sense, requires the presence of intercluster repulsions encountered at high density. Though recent density-functional studies of SALR systems suggest that mesocluster thermodynamics of SALR is essentially identical to that of HCSS systems, it is quite clear that in SALR equilibrium may be stabilized by intracluster interactions alone, even in the limit of extremely dilute systems.<sup>3</sup> Hence, understanding to what extent and under what conditions the clustering phenomena exhibited by these two fundamentally different types of interactions are really a manifestation of the same, underlying thermodynamic mechanism remains an outstanding and perplexing challenge.

This special issue assembles 15 articles that deal with experiments, simulations, and theory of clustering. The reader will quickly find that the materials are as diverse as the kinds of interactions. Clusters can form spontaneously from isotropic interactions (as described above) or from particles that are fabricated with anisotropic shapes, for example by the method described here by Kraft et al.;<sup>19</sup> Saric et al. show that asymmetrically shaped particles can form mesophases.<sup>20</sup> Clusters can also appear among proteins exhibiting attractive and repulsive interactions in two-dimensional membranes, as discussed by Meilhac and Destainville.<sup>21</sup> Theoretical papers by Zihl and Kamien<sup>22</sup> and by Košmrlj et al.<sup>23</sup> describe the formation of cluster phases in two dimensions (2D) and three dimensions (3D) in the presence of HCSS-like repulsive potentials, and Lenz et al. describe 3D computer simulations of a model dendrimer system with soft repulsive interactions.<sup>24</sup> Experimental studies of aggregation in protein solutions by small-angle X-ray scattering, small-angle neutron scattering, and neutron spin echo are described by Cardinaux et al. (without added salt)<sup>25</sup> and by Liu et al. (with salt-containing buffer), who additionally comment on the need for both dynamic and static scattering measurements.<sup>26</sup> Articles by Cametti and Truzzolillo<sup>27</sup> and by Kizilay et al.<sup>28</sup> report experimental studies of mesoscopic-cluster formation in mixtures of charged polymers and oppositely charged particles, which may be examples of SALR. Groenewold et al. describe a theoretical model of the electrophoretic mobility of clusters in charged suspensions, which might serve as a useful guide to future experimental efforts to study the intermonomer and intercluster interactions.<sup>29</sup> Hadgivanova et al. describe a theory for the kinetics of cluster

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formation (micelles) in surfactant solutions.<sup>30</sup> Finite-size structures can be formed out of equilibrium and trapped by structural arrest, which prevents equilibration in observable time scales; though this possibility is already known, a new set of questions is addressed here by Fierro et al., who describe simulations of aggregation in colloids,<sup>31</sup> and by Royall and Williams, who describe simulations of C<sub>60</sub> buckeyballs and the possibility of an amorphous gel composed of a single molecular species with no solvent.<sup>32</sup> Hydrodynamic interactions caused by solvent flow during aggregation can also alter cluster structure, as reported by Whitmer and Luijten.<sup>33</sup> Together, these articles will introduce the reader to the current understanding of cluster formation in solutions and suspensions.

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