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Control of self-assembly in micro- and nano-scale systems

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ABSTRACT

Control of self-assembling systems at the micro- and nano-scale provides new opportunities for the engineering of novel materials in a bottom-up fashion. These systems have several challenges associated with control including high-dimensional and stochastic nonlinear dynamics, limited sensors for real-time measurements, limited actuation for control, and kinetic trapping of the system in undesirable configurations. Three main strategies for addressing these challenges are described, which include particle design (active self-assembly), open-loop control, and closed-loop (feedback) control. The strategies are illustrated using a variety of examples such as the design of patchy and Janus particles, the toggling of magnetic fields to induce the crystallization of paramagnetic colloids, and high-throughput crystallization of organic compounds in nanoliter droplets. An outlook of the future research directions and the necessary technological advancements for control of micro- and nano-scale self-assembly is provided.

1. Introduction

Self-assembly is a process in which particles spontaneously arrange into complex patterns or organized superstructures [1]. Systems with self-organizing characteristics are commonly encountered in nature and engineered technologies, where particles can be of all scales ranging from molecules in a crystal to cells in a tissue to planets in a galaxy [2]. Bottom-up engineering of self-assembly systems enables manufacturing materials and devices with novel optical, mechanical, and electronic properties. The innovative applications of self-assembly at the micro- and nano-scales have sparked interest in understanding the physics, dynamics, and implementation of self-organizing systems. Control of self-assembly processes is key to the manufacture of materials with unique properties.

This paper aims to provide an overview on the recent progress of controlling self-assembly of micro- and nano-scale systems. Controlled self-assembly implies promoting or accelerating the organization of particles towards desired structures. Intervention is expected in a self-organizing process, for example, by changing the particle interactions [3,4] or by manipulating the environment (i.e., global system variables) in which self-assembly takes place [5–7]. This idea is often called "directed self-assembly" [8,9]. The concept should be distinguished from "directed assembly", which refers to the precise manipulation of particles one-by-one during the construction of the structure (like a mason building a brick wall) [5]. Directed assembly at the microscale is now considered standard manufacturing technology such as in three-dimensional printing (see e.g., [10–12] and the citations therein). In addition, directed assembly was recently demonstrated at the nanoscale by moving particles using the tip of an atomic force microscope [13,14]. Directed assembly has a very strong bottleneck from a manufacturing point of view due to the limiting speeds at which you can manipulate the building blocks of the system. For example, a reasonable estimate for the printing speed of a three-dimensional printer with resolutions on the micro- to macro-scale is $\sim$1 cm/s [15]. Assuming nanometer resolution is attainable with this printing speed, it would take $\sim 10^{14}$ s to print a device of 1 cm^3 volume with nanometer precision. Although directed assembly is a very active area of research, the topic is beyond the scope of this paper.

In the attempt to control self-assembly systems, many practical difficulties arise that are associated with the small-scale characteristics of the systems, which limit current technology and practice. This article outlines the major challenges in the control of self-assembly systems. Promising research directions in the areas of active self-assembly, open-loop control, and closed-loop control are motivated using examples from the literature. The paper concludes with perspectives on the research outlook of control of self-assembly systems.

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2. Challenges

2.1. High-dimensional stochastic nonlinear dynamics

In macroscopic systems, measured variables (i.e., outputs) typically are stochastic due to sensor noise and unknown disturbances arising from environmental fluctuations in variables (e.g., temperature) acting on the system. Isolated stochastic terms can be included in deterministic models to account for this behavior on the macroscale [16]. In other words, the measured outputs of macroscale systems are most often deterministic in the absence of noise and unknown disturbances.

Micro- and nano-scale systems are different in that their underlying phenomena are *inherently stochastic* so that repeated experiments can produce different results even if the system has no noise or unknown disturbances [17]. This inherent stochasticity can greatly impact the self-assembly of particles at these scales. For example, self-assembly of colloidal particles (at fixed conditions) can require excessively long periods of waiting time before initiation of the first step of the process (e.g., nucleation) needed to make a product, due to the first step having a high-energy activation barrier [5]. Another example is a microfluidic platform that uses evaporation to induce crystal nucleation of organic compounds such as amino acids and proteins [18,19]. The measured output for a single droplet is the *induction time* (i.e., the time at which the first crystal nucleates) and is best represented as an induction time *distribution* due to the stochastic nature of the system.

Stochastic dynamics with continuous states are typically described by Langevin equations [20–22], which describe the time evolution of a group of variables that change slowly relative to other variables in the system. The original Langevin equation was derived as a modification to Newton's equations of motion to include Brownian motion and frictional drag due to collisions of particles (slow variables) with the solvent (fast variables). This system can be formulated as a stochastic differential equation (SDE) of the form [23]

$$d\mathbf{X}_t = \boldsymbol{\mu}(\mathbf{X}_t, t)dt + \boldsymbol{\sigma}(\mathbf{X}_t, t)d\mathbf{W}_t, \tag{1}$$

where $\mathbf{X}_t \in \mathbb{R}^n$ denotes an n-dimensional stochastic process, $\boldsymbol{\mu} = (\mu_1, \ldots, \mu_n)$ denotes the drift vector, $\mathbf{W}_t$ denotes an m-dimensional Weiner process (i.e., Brownian motion), and $\boldsymbol{\sigma} = [\sigma_{ij}]$ is directly related to the diffusion tensor $\mathbf{D} = [D_{ij}]$ with elements

$$D_{ij}(\mathbf{X}_t, t) = \frac{1}{2}\sum_{k=1}^{m}\sigma_{ik}(\mathbf{X}_t, t)\sigma_{jk}(\mathbf{X}_t, t). \tag{2}$$

This SDE is nonlinear and difficult to solve directly. Methods such as Monte Carlo simulation or Molecular Dynamics (MD) are available for obtaining time-averaged quantities of interest while avoiding direct simulation of (1). However, these methods are very computationally expensive and are only able to simulate complex systems for a very short period of time.

The dynamics of self-assembling systems involve the evolution of hierarchical components at different time scales due to their architecture (e.g., atoms make up proteins, proteins make up capsomers, and capsomers make up viral capsids [24]). Eq. (1) alone cannot describe this behavior; instead, a multiscale approach is required (e.g., see [25]). However, multi-scale modeling approaches are very computationally expensive, taking on the order of days to simulate a relatively small self-assembly system (a system consisting of ~50 particles) using standard personal computers.

For systems with a discrete number of possible states, the stochastic dynamics are described by the Master equation [26,27]

$$\frac{dP_\sigma}{dt} = \sum_{\sigma'} w_{\sigma'\to\sigma}(t)P_{\sigma'}(t) - \sum_{\sigma'} w_{\sigma\to\sigma'}(t)P_\sigma(t), \tag{3}$$

where $P_\sigma(t)$ denotes the probability that the system is in configuration σ at time t and $w_{\sigma'\to\sigma}(t)$ denotes the rate of transition from configuration σ' to configuration σ at t. The overall system is described by writing (3) (i.e., conservation equation for probability of configuration σ) for every possible configuration of the system. The probabilities can be stacked into a state vector $x(t)$ and the transition rates collected into a matrix $A(t, u(t); p)$ so that (3) can be written in the state-space form

$$\frac{dx}{dt} = A(t, u(t); p)x(t), \tag{4}$$

where $A(t, u(t); p)$ depends on time-varying variables (e.g., temperature), system inputs (i.e., manipulated variables) $u(t)$, and model parameters p such as chemical kinetic rate constants, diffusion coefficients, and thermodynamic properties of the system.

The main challenge in implementing control systems for processes modeled by (4) is that the number of states is usually very large (usually much greater than 10^{10}) for processes of practical importance [17]. Kinetic Monte Carlo (KMC) simulations are commonly used to approximate the solution of (4) by computing specific realizations of the Master equation. This approach uses calls from a random number generator to select a specific event to occur from a queue of all possible events, along with its corresponding time step, so that the time simulated in the KMC algorithm corresponds to real time [26]. Although this approach is usually much faster than solving (4) directly, KMC simulations can still take in the order of days for realistic systems. If state or output distributions are required for control, then a large number of KMC simulations are needed, which makes real-time control infeasible even for relatively simple systems. If the control objective depends only on coarse statistics of the distribution, then one approach is to develop low-order "equation free" models (e.g., [28,29]) by fitting the KMC simulation results; however, the relationship between the manipulated variables and the system states in these models will no longer be transparent, making control less intuitive and more black box in nature [17].

2.2. Limited sensors for real-time measurements

Controlling self-assembly systems at the micro- and nano-scale requires the acquisition of real-time information about the system status. This requirement leads to the needs of advanced real-time sensing techniques, while traditional self-assembly systems often rely on imaging or other characterization techniques performed after the assembly process to measure the local properties (e.g., using transmission electron micrographs to inspect the morphology in a self-assembling block copolymer system [30]).

Several factors result in real-time sensing in self-assembly systems being a challenge, including the small length scales, the slow and invasive nature of most observation techniques, and the limited variables that can be used to quantify the system status. For crystallization in a nanoliter droplet implemented in a microfluidic platform [18,19,31], the small scale of the system inhibits implementing conventional methods of probing the solute concentration. While visual observation of the dynamics in self-assembled systems could be accessible through advanced microscopes (such as the fluorescent imaging technique used to track the real-time movement and clustering of Janus particles [32]), such information has to be translated into a variable that can represent the assembly status for control.

2.3. Limited actuation for control

Another challenge that naturally arises in controlling self-assembly systems is the limited availability of actuators. For a micro- or nano-scale self-assembly system, localized manipulation