Shape-Selective Recognition and Self-Assembly of mm-Scale Components

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Molecular recognition requires the mating of two different molecular surfaces, complementary in shape and surface properties (hydrophobicity, hydrogen-bonding capability, electrical potential). Molecular recognition is ubiquitous in molecular science, with examples from protein−ligand interactions to asymmetric catalysis.[1−6] This paper describes the export of ideas taken from molecular recognition to the recognition of macro-scale (∼1 mm) objects. The demonstration system examined here used "receptors" and "ligands", fabricated as complementary shapes by joining small hexagonal plates and suspended at a perfluorodecalin/water interface. The interactions between the surfaces of these objects were controlled by manipulating the capillary forces between them. Receptors showed excellent selectivity for ligands based on complementarity of shape and juxtaposed hydrophobic surfaces. This system points to a new way of fabricating and assembling small, nonmolecular components using shape- and surface-selective recognition and self-assembly, extends a strategy demonstrated previously for self-assembly of extended arrays of objects[7] to the directed assembly of different objects, and provides a macroscopic experimental model for molecular recognition that matches some aspects of the abstract lattice models used in statistical mechanical treatments of molecular phenomena.[8,9]

We fabricated the required shapes by gluing together small hexagonal poly(dimethylsiloxane) (PDMS) plates having dimensions f (the width of a face) = 2.7 mm, and h (the height) = 1 mm. In all of the experiments described here, the bottom face of the plates was hydrophobic, and the top was hydrophilic. The relative disposition of the hydrophobic sides is indicated by [*x*,*y*,...]; thus, a *[1,4] hexagon* is a hexagon with two opposite sides (and the bottom) hydrophobic, and all other sides (and the top) hydrophilic. The resulting objects were suspended at the interface between perfluorodecalin and water in a Petri dish, and swirled at a frequency $\omega = 1.5-1.8$ s^{-1} on an orbital shaker. Recognition and assembly of complementary shapes occurred spontaneously when the distance between them was within the distance (∼3h) required for interaction through capillarity.[10,11]

We have developed a number of systems in which recognition is both size- and shape-selective. We will call the object presenting a *concave* surface a "receptor" and that presenting a *convex* surface a "ligand", by loose analogy with biological systems: for example, the *receptor* **1** recognized two [1,3] hexagons as *ligands* and formed a stable aggregate (Figure 1a).

The overall process of recognition and assembly can be represented by eqs 1 and 2. A representative experiment involved

$$R + L \rightarrow R||L$$

Encounter (R: receptor, L: ligand, R||L: encounter pair) (1)

$$R||L \rightarrow [R{\cdot}L] \rightarrow A$$

Recognition and assembly (A: aggregate) (2)

two receptors **1** and 10 ligands (2.5 equiv of [1,3] hexagons) at the liquid−liquid interface. In these conditions—a rotation frequency of the orbital shaker of $\omega = 1.8$ s^{-1} and interfacial densities of 10^3 objects/m^2—the encounter frequency between the receptor and ligands was about 1 s^{-1}, and the first combination of encounter, recognition, and assembly to form the aggregate **1**·2[1,3] required about 10 min (in the order of 10^2-10^3 encounters) to take place; thus, the rate of assembly was $10^{-2}-10^{-3}$ sec^{-1}. Formation of this aggregate in these conditions was an irreversible process, but the aggregate dissociated when the agitation was made more vigorous by increasing the frequency of rotation of the shaker.

The receptor **1** recognized and bound two [1,3] hexagons selectively in the presence of added [1,4] or [1,2,3] hexagons. To demonstrate that **1**·2[1,3] was not simply a kinetically formed, metastable aggregate, but was more stable than the corresponding aggregate with [1,4] hexagons, we assembled **1**·2[1,4] by hand and agitated the system at $\omega = 1.8$ s^{-1} in the presence of [1,3] hexagons.[12] The [1,4] hexagons spontaneously dissociated from the receptor, and were replaced by [1,3] hexagons. In this system, the rate of assembly of **1**·2[1,3] was lower than that in the system with only [1,3] hexagons, as a result of the reversible aggregation between **1** and [1,4] hexagons. The dissociation of bound [1,4] hexagons from **1** occurred at approximately the same rate as the association of [1,4] hexagons to **1**.

Receptor **1** formed a complex with [1,3] hexagons selectively in a mixture of [1,3] and [1,2,3] hexagons. We believe that there are two reasons for this selectivity. First, [1,2,3] hexagons tended to form stable, self-assembled structures (hexamers, trimers, and dimers) themselves. Second, [1,2,3] hexagons did not form stable aggregates with **1** under the conditions used: surface tension pulled the hydrophobic sides of [1,2,3] hexagons into the perfluorodecalin/water interface, and in this orientation, the menisci at the hydrophobic surface of [1,2,3] hexagons and the receptor did not match well. When we made aggregates of the receptors with [1,2,3] hexagons by hand (i.e., **1**·2[1,2,3]), and mixed them with [1,3] hexagons with agitation, there was no dissociation or exchange; this observation indicates that recognition and assembly of **1**·2[1,3] in this system occurred under kinetic control. The yields were 83, 73, and 73%, respectively.[13]

A second system of receptors and ligands showed selectivity in recognition based on chirality. The pairs of receptors (**2a**/**2b** and **3a**/**3b**) and ligands (**4a**/**4b** and **5a**/**5b**) were enantiomeric (Figure 1b, c). The enantiomers of **2** (**2a** and **2b**) and **3** (**3a** and **3b**) recognized and aggregated with only one enantiomer from

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(12) The objects were large enough to be manipulated easily with tweezers. We manually assembled aggregates at the interface and tested their stabilities by agitating the system at $\omega = 1.8$ s^{-1}.

(13) We addressed the statistics of these assembly processes in this system by repeating representative assemblies 20 times. The assemblies were allowed to aggregate in 20 trials, each for 1 h; at the end of the hour, we counted the receptors and ligands that had bound correctly as a success, and all other assemblies as failures. Each experiment contained two receptors for a total of 40 possible receptor−ligand pairs.

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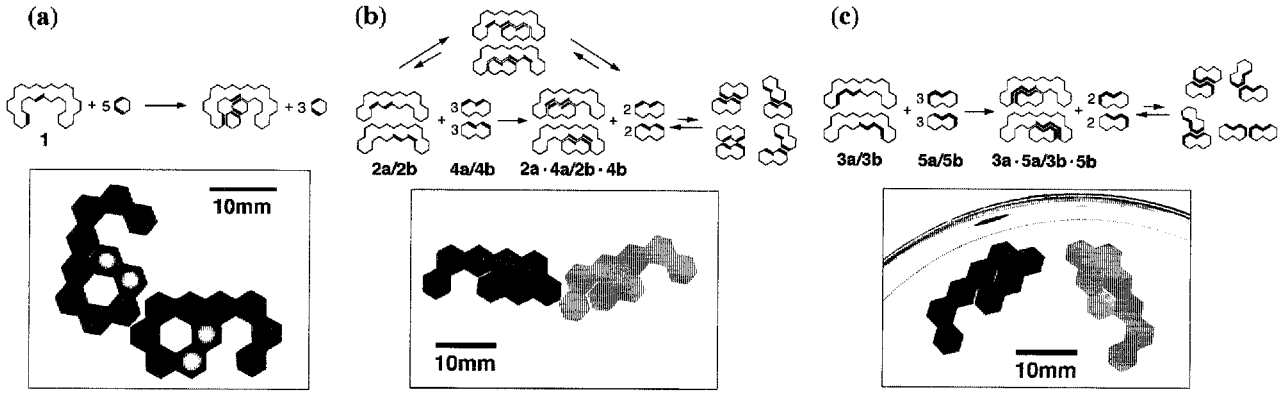

Figure 1. (a) Size- and shape-selective recognition and assembly. The receptors are dyed a solid color; the [1,3] hexagons are dyed only on the periphery, and are distinguishable by their light centers. The hydrophobic edges are indicated by thick lines; hydrophilic edges by thin lines. Two receptors, **1**, and 10 [1,3] hexagons were agitated at a frequency sufficiently high ($\omega = 1.8\ s^{-1}$) to break up the lattice formed by the [1,3] hexagons. The [1,3] hexagons added to the receptor individually or in sets of two, and the array of hexagons bound to the receptor was stable to dissociation. (b and c) Chiral recognition and assembly. In each case, receptors and ligands having correct chirality to join are indicated with the same shade of gray. One receptor **2a**, one receptor **2b**, three ligands **4a**, and three ligands **4b** were placed at the perfluorodecalin/water interface. The agitation was adjusted to $\omega = 1.5\ s^{-1}$ to break up all arrays except the ones shown (b). One receptor **3a**, one receptor **3b**, three ligands **5a**, and three ligands **5b** were placed at the perfluorodecalin/water interface. The system was agitated at $\omega = 1.8\ s^{-1}$ to form the array shown (c).

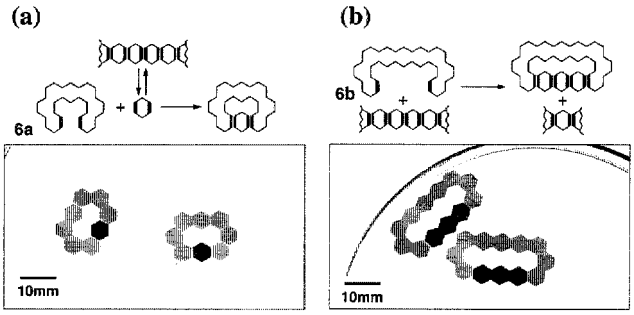

Figure 2. Size-selective recognition and assembly. In each of a and b, two receptors and 1.5−2 times the number of [1,4] hexagons needed to complete the assembly were used. The conditions are those summarized in Figure 1, with $\omega = 1.5\ s^{-1}$. (a) Agitation of two receptors **6a** and five [1,4] hexagons resulted in aggregation of a free [1,4] hexagon with the receptor. (b) Two receptors **6b** and 11 [1,4] hexagons were used.

the racemic pairs comprising **4a**/**4b** and **5a**/**5b**. The receptors **3a**/**3b** had higher probability of aggregation per encounter than did the receptors **2a**/**2b**; in the system comprising **3** and **5**, no mismatched complexes were observed. In contrast, the system based on **2** and **4** gave mismatched complexes with only one hydrophobic side in contact (Figure 1b).[14] The yields for assemblies were determined from twenty runs lasting 1 h each; the yields for the assemblies in Figure 1b and c were 85 and 93% respectively.

In a third system, two different receptors, **6a** and **6b**, were fabricated with recognition sites designed to bind one and three [1,4] hexagons, respectively (Figure 2). Although the receptors recognized the expected number of [1,4] hexagons, they also bound [1,2] or [1,3] hexagons (although less strongly than [1,4] hexagons). The receptors were therefore size-selective, but not highly shape-selective. The mechanism of assembly that we observed for **6b** differed from that which we observed for **6a**. Assembly of **6a**·[1,4] required collision with a free [1,4] hexagon in the correct orientation; by contrast, **6b** would abstract the required number of [1,4] hexagons from a self-assembled line of these species. The rate of assembly was about three times lower for **6a**·[1,4] than for **6b**·3[1,4]. The assemblies were each allowed to proceed 20 times for 1-h intervals to collect statistical information about assembly; the yields were 95 and 93% for Figure 2a and b, respectively.

The processes illustrated here form structured, macroscopic (mm- to cm-scale) aggregates incorporating multiple, different components. We believe that these processes have the potential to contribute to at least two areas of science and technology. First, by providing a new strategy for assembling small objects, they will be useful in materials science and in device fabrication. The utility of this strategy for directing the self-assembly of different components will depend on the range of the sizes of objects that can be manipulated, on the development of flexible methods for fabricating components having appropriate shapes and surfaces, and on the invention of procedures for connecting objects functionally once they have been assembled. Second, because these processes resemble those occurring among molecules, they suggest experimental realizations of the lattice models of molecular processes commonly used in statistical mechanics. Although considering possible analogies between macro- and molecular-scale processes will be stimulating, we emphasize that there are three substantial differences between them. First, the encounter frequencies in these systems are substantially lower than those occurring among molecules. In these macroscopic systems, the receptor encounters ligands at a rate of approximately 10^{-2}−10^{-3} sec^{-1}; a protein receptor encounters a ligand present at micromolar concentration at a rate of 10^{2}−10^{3} sec^{-1}. Differences in collision frequencies within an encounter complex are even greater for macro- and molecular-scale systems. Second, the distribution of energies in these macroscopic systems, in which agitation is achieved by stirring and shear, is not described by a Boltzmann distribution. Third, the potential functions that determine the interactions in the macroscopic and molecular systems are different.

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Supporting Information Available: Procedures for fabrication of ligands and receptors, and experimental procedures (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) Ligands themselves formed unstable heterodimers depicted in Figure 1b and c. We also observed the formation of homodimers of **4a** and **4b**, **4a**·**4a** and **4b**·**4b**. After they formed, the homodimers were stable and did not dissociate under the conditions used.