

Linear Self-Assemblies: Equilibria, Entropy and Convergence Rates

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Abstract Self-assembly is a ubiquitous process by which objects autonomously assemble into complexes. In the context of computation, self-assembly is important to both DNA computing and amorphous computing. Thus a well developed mathematical theory of self-assembly will be useful in these and other domains. As a first problem in self-assembly, we will explore the creation of linear polymers. Polymers are chains of molecular units. For examples, a molecule of DNA is a polymer made from the bases adenine, guanine, cytosine and thymine; and proteins are polymers formed from the twenty amino acids. In our model the dynamics of a linear polymerization system is determined by difference and differential equations with initial conditions, and we investigate the equilibrium behavior of such a system. A good characterization of the equilibria of these systems will allow us to predict which computations can be carried out with adequate yields and what quantities of initial substrates these computations require. The rates at which such systems approach equilibria

¹Research supported by grants from NASA/JPL, NSF, ONR, and DARPA.

²Research supported by NSF Grant CCR-9820778.

³Research supported by NSF Grant CCR-9820778.

are equally important since convergence rates are an obvious measure of the time complexity of computation through self-assembly.

Keywords Self-assembly, Linear polymerization, Difference equations, Differential equations

AMS Subject Classification 39A11, 68Q05, 92B05

1 Introduction

Self-assembly is a ubiquitous process by which objects autonomously assemble into complexes. Atoms react to form molecules; molecules react to form crystals; cells coalesce to form organisms. In the context of computation, self-assembly is important to both DNA computing [1, 7, 8, 10, 11] and amorphous computing [3]. Thus we believe that a well developed mathematical theory of self-assembly will be useful in a variety of domains.

In this paper we study reversible tile systems and ask the following basic questions: Do reversible self-assembling systems achieve equilibria? Do there exist good characterizations of these equilibria? What is the number of steps required for these self-assemblies to converge to equilibria? These questions were first asked by Adleman [2] and partially answered in the context of what he called the irreversible n -linear polymerization problem.

Our motivations for studying the equilibria and convergence rates of reversible systems are manifold. Since self-assembly is universal, a good characterization of the equilibria of these systems will allow us to predict which computations can be carried out with adequate yields and what quantities of initial substrates these computations require. Convergence rates are an obvious measure of the time complexity of computation through self-assembly.

As a first problem in self-assembly, we will explore the creation of linear polymers. We model linear polymerization systems as linear tile systems, in which the tiles are assumed to lie on a line. In our model the dynamics of a linear polymerization system is determined by difference and differential equations with initial conditions, and we investigate the equilibrium behavior of such a system. Motivated by thermodynamics and physical chemistry [5], we define the *profit* of the system as the sum of a term related to information-theoretic entropy and a term related to bond stability. The latter term is motivated by the definition of free energy in chemical reactions. We show that profit is maximized at equilibrium, and prove a weak equivalent of the second law of thermodynamics. We conclude with a study of an important class of linear self-assembling systems: the reversible and irreversible cases of n -linear polymerization. For these systems, we give tight bounds on the number of steps required to reach distance ε from equilibrium, showing in most cases that the distance from equilibrium decays exponentially over time.

2 Linear self-assemblies

We assume that there are n types of tiles T_1, \dots, T_n , arranged on the doubly infinite line, with α_i being the relative fraction of tiles of type i , $\alpha_i > 0$, $\sum_i \alpha_i = 1$. Some of these tiles may be bonded to their neighbors. By a slight abuse of notation, we will use T_i as well as i to refer to the type of a tile. We are also given (sticking, breaking) probabilities (σ_{ij}, τ_{ij}) , $1 \leq i \leq n$, $1 \leq j \leq n$, $0 \leq \sigma_{ij} < 1$, $0 < \tau_{ij} \leq 1$.

Let r_{ij} denote the fraction of T_i tiles that are bonded to a T_j tile on the right. Let l_{ij} be the fraction of T_j tiles that are bonded to a T_i tile on the left. Thus, r_{ij}, l_{ij} change with time and are initially 0. Define r_i to be the fraction of tiles of type T_i that are unbonded on the right, and similarly define l_j to be the fraction of tiles of type T_j that are unbonded on the left. Clearly⁴, $r_i + \sum_j r_{ij} = 1$, and $l_j + \sum_i l_{ij} = 1$.

Define $R_{ij} = \alpha_i r_{ij}$, $R_i = \alpha_i r_i$, $L_{ij} = \alpha_j l_{ij}$, and $L_j = \alpha_j l_j$. Clearly, $\sum_j R_{ij} + R_i = \alpha_i$, and $\sum_i L_{ij} + L_j = \alpha_j$. R_{ij} can be interpreted as the fraction of neighboring pairs of tiles such that the left tile is of type T_i , the right tile is of type T_j , and there is a bond between the two. R_i is then the fraction of tiles that are free to the right and are of type T_i . It follows that $R_{ij} = L_{ij}$ and that $\sum_i R_i = \sum_j L_j$. We define $F = \sum_i R_i$; F denotes the fraction of tiles that are unbonded to their right (or equivalently, unbonded to their left).

As a result of a toss, an existing bond between tile T_x and T_y breaks with probability τ_{xy} . Thus a fraction τ_{xy} of bonds of type $T_x T_y$ break as a result of a toss.

Now consider the formation of new bonds. Concentrate on a specific tile of type T_x that is unbonded to its right before the toss. After the toss, the right surface of such a tile comes in contact with a previously unbonded left surface of a tile of type T_y with probability L_y/F ; these two surfaces then form a bond with probability σ_{xy} . Thus, a fraction $(L_y/F) \cdot \sigma_{xy}$ of free right surfaces of tiles of type T_x form a bond with a tile of type T_y as a result of a toss.

Therefore the update rule is,

$$\Delta R_{xy} = -R_{xy} \cdot \tau_{xy} + R_x \cdot (L_y/F) \cdot \sigma_{xy}.$$

If we assume continuous-time model, then

$$\dot{R}_{xy} = -R_{xy} \cdot \tau_{xy} + R_x \cdot (L_y/F) \cdot \sigma_{xy}. \quad (1)$$

In either case, at (bond) equilibrium, $R_{xy} \cdot \tau_{xy} = R_x \cdot (L_y/F) \cdot \sigma_{xy}$, for all x, y .

Note that F , R_x , and L_y all are (linear) functions in R_{xy} . Hence the set of equilibrium conditions is a set of polynomial conditions on R_{xy} . The set

⁴All summation indices range from 1 to n , unless stated to the contrary.

of R_{xy} which satisfies all the equilibrium conditions, where $0 \leq R_{xy} \leq 1$, is called the *equilibrium set*.

In the continuous model, the set of differential equations in (1) defines a dynamical system on the convex region defined by $0 \leq R_{xy} \leq 1$ for all x, y , and $0 \leq \sum_y R_{xy} \leq \alpha_x$ for all x .

Note also that in formulating the update rule, we implicitly assume that what happens to the right of a tile is independent of what happens to its left. We refer to this as the *independence assumption*.

A supertile is a maximal contiguous set of tiles that are bonded together. For a supertile Γ , $\{\Gamma\}$ denotes the fraction of supertiles of type Γ . Consider a supertile $\Gamma = T_{i_1} T_{i_2} T_{i_3} \dots T_{i_k}$. Given independence, $\{\Gamma\} = (L_{i_1}/F) \cdot r_{i_1, i_2} \cdot r_{i_2, i_3} \dots r_{i_{k-1}, i_k} \cdot r_k$. Let T_i denote the last tile in Γ_1 and T_j denote the first tile in Γ_2 . Given independence and assuming bond equilibrium, we have

$$\frac{\{\Gamma_1 \Gamma_2\}}{\{\Gamma_1\}\{\Gamma_2\}} = \frac{r_{ij} F}{r_i L_j} = \frac{R_{ij} F}{R_i L_j} = \frac{\sigma_{ij}}{\tau_{ij}}.$$

We say that the system is at *strong equilibrium* if for all supertiles Γ_1 and Γ_2 , $\frac{\{\Gamma_1 \Gamma_2\}}{\{\Gamma_1\}\{\Gamma_2\}} = \frac{\sigma_{ij}}{\tau_{ij}}$, where T_i is the last tile in Γ_1 and T_j is the first tile in Γ_2 . Therefore

Theorem 2.1 *Independence and bond equilibrium imply the system is at strong equilibrium.*

2.1 Total entropy density

Let $\Gamma(t)$ be the tile-type that occupies position t on the line. Let $B(t) = 1$ if tiles at positions $t - 1$ and t are bonded together. The information-theoretic entropy of a discrete random variable X that draws its values from a countable universe U is given by

$$\mathbf{H}[X] = - \sum_{x \in U} \mathbf{Pr}[X = x] \ln \mathbf{Pr}[X = x].$$

We define the internal entropy density S_I of a linear self-assembly as the information-theoretic entropy of the tuple $\langle \Gamma(t), B(t) \rangle$ given the values of $\langle \Gamma(t'), B(t') \rangle$ for all $t' < t$. Intuitively, this is the additional amount of information stored in a tile-position, given a description of all the tile-positions to its left. Given the independence assumption,

$$S_I = \mathbf{H}[\langle \Gamma(t), B(t) \rangle | \Gamma(t-1)] = \sum_i \alpha_i \mathbf{H}[\langle \Gamma(t), B(t) \rangle | \Gamma(t-1) = T_i].$$

If the tile at position $t - 1$ is T_i then the probability of the tile at position t being of type T_j with a bond between the two tiles is r_{ij} , and the probability

of the tile at position t being of type T_j without a bond between the two tiles is $r_i \cdot (L_j/F)$. Consequently,

$$\mathbf{H}[\langle \Gamma(t), B(t) | \Gamma(t-1) = T_i] = - \sum_j r_{ij} \ln r_{ij} - \sum_j \frac{r_i L_j}{F} \ln \frac{r_i L_j}{F}$$

and therefore,

$$S_I = \sum_i \alpha_i \sum_j \left(r_{ij} \ln \frac{1}{r_{ij}} + \frac{r_i L_j}{F} \ln \frac{F}{r_i L_j} \right).$$

With some algebraic manipulation one can show that

$$S_I = \sum_i \alpha_i \ln \alpha_i + \sum_i R_i \ln \frac{1}{R_i} + \sum_j L_j \ln \frac{1}{L_j} + F \ln F + \sum_{ij} R_{ij} \ln \frac{1}{R_{ij}}$$

Define the external entropy density S_X of the linear assembly as

$$S_X = \sum_{ij} R_{ij} \ln \frac{\sigma_{ij}}{\tau_{ij}}.$$

Define the total entropy density S of a linear self-assembly as the sum of its internal and external entropy densities.

Intuitively, the internal entropy density exactly captures the amount of information-per-tile-position stored in the linear assembly. The definition of external entropy density is motivated by a corresponding definition in physical chemistry. If r_f and r_r are the equilibrium forward and reverse reaction rates of a chemical process, then the process releases energy proportional to $\ln r_f/r_r$, and this energy is then available to increase the entropy of the external environment. As a consequence, the total entropy of the universe is maximized when the sum of the internal entropy of a system and the energy released by the system (appropriately normalized) is maximized.

As it turns out, $-S$ is a Lyapunov function for the dynamical system defined by the system of differential equations in Eq 1. More precisely, the following theorem can be proven.

Theorem 2.2 1. $\frac{\partial S}{\partial R_{xy}} = 0$ iff $\frac{R_{xy} \cdot F}{R_x \cdot L_y} = \frac{\sigma_{xy}}{\tau_{xy}}$. Thus, the bond equilibrium conditions derived from the update rules for R_{xy} are exactly the same as those that characterize the set of stationary points of S , as a function in R_{xy} in the unit hypercube $0 \leq R_{xy} \leq 1$.

2. S is a concave function; that is,

$$\sum_{v_{ij}, v_{xy}} \frac{\partial^2 S}{\partial R_{ij} \partial R_{xy}} v_{ij} v_{xy} \leq 0$$

for any vector $(v_{11}, v_{12}, \dots, v_{nn})$ and the equality holds only when $(v_{11}, v_{12}, \dots, v_{nn})$ is zero vector. Thus, every point in the equilibrium set, which is also stationary point of S , is a local maximum for S .

3. Local maximum does not occur on the boundary.

4. $\dot{S} = \sum \frac{\partial S}{\partial R_{xy}} \dot{R}_{xy} > 0$ as long as $\dot{R}_{xy} \neq 0$ for some bond x, y , and $\dot{S} = 0$ when $\dot{R}_{xy} = 0$ for all x, y .

Note that 2 and 3 of the Theorem imply that there is a unique maximum and the maximum is an interior point, and 4 implies that the total entropy density of a linear self-assembly is increasing until (bond) equilibrium is reached, at which point, the total entropy density is maximized, and henceforth the system remains at equilibrium. But how fast does a linear self-assembly system approach this equilibrium? This question seems to be quite complicated in general. In what follows we will focus on an interesting subcase called the *n-linear polymerization* and analyze the convergence rates for such systems.

3 n-linear polymerization

In the cell, DNA and proteins are created by using highly specialized enzymes (polymerases) or enzyme complexes (ribosomes) to catalyze the addition of successive units to one end of a growing chain. In the case of some synthetic polymers and in DNA computation, the product is created by the recursive concatenation of smaller polymers. Here we wish to model the latter form of polymerization. This is our motivation for *n-linear polymerization*, which we define as follows:

Start with equal quantities of tiles T_1, \dots, T_n , where $n \geq 2$. The gluing rule is that the right side of each T_i , for $1 \leq i \leq n-1$, can glue to T_{i+1} only. Hence the allowable combinations are all subsequences of $T_1 T_2 \dots T_n$. Here we consider the *uniform* case, in which all allowable bonds have the same on-rate $\sigma \in [0, 1]$ and off-rate $\tau \in [0, 1]$.

Let time-dependent variables v_1, \dots, v_{n-1} be defined as follows: v_i is the portion of the T_i tiles which are currently free to the right. We assume below that $v_1 = v_2 = \dots = v_{n-1}$. This assumption is justified for several reasons. First, if it is ever true, then it is preserved over time. Hence it is justified if the initial state has this symmetry (for example, if we employ the natural initial state $v_1 = \dots = v_{n-1} = 1$). Second, we shall prove in Section 3.3 that, even if this symmetry does not initially hold, the system rapidly evolves toward it.

Hence let v denote the common value of v_1, \dots, v_{n-1} . How does v evolve over one time-step? Of the $1-v$ portion of T_i tiles currently bonded to the right, each will become free with probability τ . Meanwhile, of the v portion of

T_i tiles currently free to the right, each will become bonded with probability σ if the tile to its right is a T_{i+1} . What then is the probability that the tile to the right of a free T_i is a T_{i+1} ? Since all T_1 tiles are free to the left, while a v portion of T_2, \dots, T_n tiles are free to the left, this probability is $v/[v(n-1)+1]$. Hence the update rule for v (where v' denotes the new value) is given by:

$$v' - v = \frac{-v^2\sigma}{v(n-1)+1} + (1-v)\tau. \quad (2)$$

Now assume $\tau \neq 0$ and let $\rho := \sigma/\tau$. Then it is easily seen that, for v on legal domain $[0, 1]$, this transformation has a unique fixed point $v = \beta$, where β is defined as follows:

$$\beta = \frac{(n-2) + \sqrt{n^2 + 4\rho}}{2(\rho + n - 1)}. \quad (3)$$

Hence, when $v = \beta$, the system is at bond equilibrium. But then we can specify a strong equilibrium for the system, namely when each T_i (for $1 \leq i \leq n-1$) is free to the right with *independent* probability β . Indeed, since this state has bond equilibrium and independence, it follows from Theorem 2.1 that it is a strong equilibrium.

3.1 Dynamics of irreversible polymerization

Here we consider n -linear polymerization in the irreversible case ($\tau = 0, \sigma \neq 0$). For this case, the equilibrium is evidently for all tiles to form complete $T_1 T_2 \dots T_n$ strands. Equivalently, the v variable, representing the fraction of glueable surfaces free, goes to zero. We will next determine the rate at which v goes to this equilibrium.

Theorem 3.1 *For irreversible n -linear polymerization with on-rate σ , and for $\varepsilon > 0$, let t be the smallest time such that the v variable, starting from any initial value, is guaranteed to be at most ε if time elapsed is at least t . Then t is at least*

$$\frac{1}{2\sigma(e-1)}[1/(e\varepsilon) - 1] + \frac{n-1}{2\sigma}[\ln(1/\varepsilon)]$$

and at most

$$\frac{e}{\sigma(e-1)}[e/\varepsilon - 1] + \frac{n-1}{\sigma}[\ln(1/\varepsilon)].$$

The lower bound in the theorem is based on the observation from from (2) that v is multiplied at each step by a factor of

$$1 - \frac{v\sigma}{v(n-1)+1} = 1 - \frac{\sigma}{n-1} \left[1 - \frac{1}{v(n-1)+1} \right], \quad (4)$$

hence if the current value of v is v_0 , then v is multiplied at each step by a factor which is at least $1 - 1/Q$ where

$$Q = \left[\frac{\sigma}{n-1} \left[1 - \frac{1}{v_0(n-1)+1} \right] \right]^{-1} = \frac{n-1}{\sigma} + \frac{1}{\sigma v_0}.$$

The matching upper-bound can be proven based on the observation that as long as $v \geq v_0/e$, v is multiplied at each step by a factor which is at most

$$1 - \frac{\sigma}{n-1} \left[1 - \frac{1}{v_0(n-1)/e+1} \right].$$

Therefore the time to reduce v to ε is $\Theta((1/\varepsilon + n \log(1/\varepsilon))/\sigma)$. We can also show that the time for half of the tiles to form complete $T_1 T_2 \dots T_n$ strands is $\Theta((n \log n)/\sigma)$. It is perhaps surprising that the latter bound, as a function of n , is as large as $\Theta(n \log n)$. A priori, it is conceivable that a large volume of complete $T_1 T_2 \dots T_n$ strands could be assembled in just $\Theta(\log n)$ steps. This would be achieved if at step one many polymers of size 2 were created, at step two polymers of size 4, and so on. But the above bound shows that this is in fact not what occurs, and indeed that, roughly speaking, complete $T_1 T_2 \dots T_n$ strands are created by the addition of, on the average, just one tile every $\log n$ steps.

3.2 Dynamics of reversible polymerization

We now turn to reversible n -linear polymerization. Here we will prove that v in fact converges exponentially fast to equilibrium value β .

Theorem 3.2 *For reversible n -linear polymerization, the v variable, starting from any initial value, is guaranteed to be within distance ε from equilibrium value β if time elapsed is at least $\max\{3, 1/\tau\} \cdot \ln(1/\varepsilon)$.*

The theorem is proved by considering the current distance Δ from equilibrium, and showing that $|\Delta|$ is multiplied at each step by a factor which is at most $\max\{1 - \tau, 0.71\}$.

Observe that, for the irreversible case, the time for v to reach distance ε from equilibrium, expressed as a function of ε , is $\Theta(1/\varepsilon)$. For the reversible case, on the other hand, this time is $O(\log(1/\varepsilon))$. This may seem paradoxical but is in fact easily explained. At irreversible equilibrium, the quantities of tile strands which need to combine are brought down to zero, so that it becomes increasingly difficult for the remaining fragments to find each other.

3.3 Uniqueness of the n -linear equilibrium

Irreversible n -linear polymerization evidently goes to a unique equilibrium – i.e., a strong equilibrium corresponding to all tiles forming complete $T_1 T_2 \dots T_n$ strands. We now turn to the reversible case, for which, in Section 3, we specified a particular equilibrium—a strong equilibrium in which each glueable surface is free with independent probability β . The following theorem states that any system must in fact go to this unique equilibrium.

Theorem 3.3 *Starting from any initial state, a reversible n -linear polymerization system will go to a unique equilibrium, namely the state in which each glueable surface is free with independent probability β , where β is as given in (3).*

For $1 \leq i \leq n - 1$, let v_i denote the portion of the T_i tiles which are currently free to the right. The idea of the proof is to show that $|v_i - v_j|$ is multiplied at each time-step by a factor which is at most $\max\{1 - \tau, 2/3\}$. Hence all of v_1, \dots, v_{n-1} are rapidly squeezed together toward a common value.

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