Supporting Information for

Fragmentation and coagulation in supramolecular (co)polymerization kinetics
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S1 Modeling supramolecular (co)polymerization

A general model for the supramolecular polymerization of a single monomer type $X_1$ that proceeds completely via monomer associations and dissociations is given by:

$$
\begin{align*}
X_1 + X_1 & \leftrightarrow \quad K_1 = \frac{k_1^+}{k_1^-} = \frac{[X_2]\text{eq}}{[X_1]\text{eq}^2} \\
X_2 + X_1 & \leftrightarrow \quad K_2 = \frac{k_2^+}{k_2^-} = \frac{[X_3]\text{eq}}{[X_2]\text{eq}[X_1]\text{eq}} \\
& \quad \vdots \\
X_i + X_1 & \leftrightarrow \quad K_i = \frac{k_i^+}{k_i^-} = \frac{[X_{i+1}]\text{eq}}{[X_i]\text{eq}[X_1]\text{eq}} \\
& \quad \vdots
\end{align*}
$$

(S1)

Here $k_i^+$ ($M^{-1} s^{-1}$) and $k_i^-$ ($s^{-1}$) are the rate constants of the forward and backward reactions, i.e., for the association and dissociation of a monomer unit, $K_i$ is the corresponding equilibrium constant for this reaction, and $[X_i]\text{eq}$ is the concentration of polymers of length $i$, $X_i$, in equilibrium. From the changes in the standard Gibbs free energies, rate constants are calculated under conditions of detailed balance when

$$
K_i = \frac{k_i^+}{k_i^-} = \exp(-\frac{\Delta G_i^\circ}{RT}) = \exp(-\frac{\Delta G_{i-1}^\circ}{RT})
$$

(S2)

Here $\Delta G_i^\circ$ is the standard Gibbs free energy increment for the reaction of $i$ monomers to a polymeric chain of length $i$, $R$ is the gas constant and $T$ the temperature.

To include also fragmentations and coagulations, the following reactions should be added for all $i \geq 2$ and $j \geq 2$:

$$
\begin{align*}
X_i + X_j & \leftrightarrow \quad K_{ij} = \frac{k_{ij}^+}{k_{ij}^-} = \frac{[X_{i+j}]\text{eq}}{[X_i]\text{eq}[X_j]\text{eq}}
\end{align*}
$$

(S3)

As we will see later, in order to obey detailed balance and microscopic reversibility, in this latter equation not all rate constants $k_{ij}^+$ and $k_{ij}^-$ can be chosen independently.

In general, the rate constants depend continuously on the aggregate length $i$. In a model where we want to keep the number of parameters limited, a number of interesting cases are (i) isodesmic polymerization, where $K_1 = K_2 = K_3 = K_4 = \cdots = K_{\text{iso}}$; (ii) cooperative aggregation, where $K_1 = K_2 = \cdots = K_{n-1} = K_{\text{nuc}} < K_n = K_{n+1} = \cdots = K_{\text{elo}}$; and (iii) anti-cooperative aggregation $K_1 = K_2 = \cdots = K_{n-1} = K_{\text{nuc}} > K_n = K_{n+1} = \cdots = K_{\text{elo}}$. In the next two subsections we will zoom into isodesmic self-assembly, while in the third subsection we will focus on cooperative nucleation-elongation models with nucleus size $n = 2$. In the fourth and fifth subsection, this analysis is extended to supramolecular polymerization into two aggregate types and supramolecular copolymerization of two monomer types, respectively.
S1.1 Isodesmic supramolecular polymerization via monomer associations and dissociations

Model
First we consider the case where aggregation proceeds only via monomer associations and dissociations and where we assume all bonds in the system equal. As a dimer only has one bond between its two constituting monomers and longer polymers have two bonds that could break for a monomer dissociation to occur, \( k_1^- \) will in this case be twice as small as all other \( k_i^- \). Moreover, with \( n_i \) copies of species \( X_i \), the number of possible reaction pairs between two \( X_1 \)'s equals \( n_1(n_1 - 1)/2 \), while the number of possible reaction pairs between an \( X_1 \) and an \( X_i \) equals \( n_1n_i \). Therefore also the forward rate constant \( k_1^+ \) should in this case be twice as small as all other \( k_i^+ \). With \( k_1^+ = a \) and \( k_i^- = b \) for \( i \geq 2 \), Eq. (S1) thus becomes for a supramolecular polymerization where all bonds are assumed equal:

\[
\begin{align*}
X_1 + X_1 & \xrightleftharpoons[a/2]{b/2} X_2, & K_a = \frac{a}{b} = \frac{[X_2]_{eq}}{[X_1]_{eq}^2} \\
X_2 + X_1 & \xrightleftharpoons[a]{b} X_3, & K_a = \frac{a}{b} = \frac{[X_3]_{eq}}{[X_1]_{eq}[X_2]_{eq}} \\
& \quad \vdots \\
X_i + X_1 & \xrightleftharpoons[a]{b} X_{i+1}, & K_a = \frac{a}{b} = \frac{[X_{i+1}]_{eq}}{[X_1]_{eq}[X_i]_{eq}}
\end{align*}
\]

In this case all equilibrium constants are identical, i.e., \( K_1 = K_2 = K_3 = K_4 = \cdots = K_i = \cdots = \frac{a}{b} = K_a \), and the equilibrium concentrations of all aggregate lengths can be expressed in terms of the equilibrium monomer concentration as

\[
[X_i]_{eq} = \left( \frac{1}{K_a} [X_1]_{eq} \right)^i
\]

ODE approach
One way to obtain the kinetics of such a supramolecular polymerization is by truncating at a maximum polymer length \( N \) and then integrating the reaction rate equations corresponding to Eq. (S4), i.e.,

\[
\begin{align*}
\frac{dx_1}{dt} &= -ax_1 \sum_{i=1}^{N-1} x_i + b \sum_{i=2}^{N} x_i \\
\frac{dx_2}{dt} &= \frac{a}{2} x_1^2 - ax_1 x_2 - \frac{b}{2} x_2 + bx_3 \\
\frac{dx_3}{dt} &= ax_1 (x_{k-1} - x_k) + b (x_{k+1} - x_k) \\
\frac{dx_N}{dt} &= ax_N x_{N-1} - bx_N
\end{align*}
\]

where \( x_k = [X_k] \) is the concentration of supramolecular polymers of length \( i \) and \( 3 \leq k < N \).
Stochastic simulation approach

A second way to obtain the kinetics of this supramolecular polymerization is to perform kinetic Monte Carlo simulations. Following Gillespie’s direct simulation approach, such a simulation proceeds as follows. Given the current composition of the system (i.e., its volume \( V \), the number of monomers \( n_1 \) and the number of supramolecular polymers and their lengths) the propensities for all possible reactions in Eq. (S4) are calculated. For a unimolecular reactions \( A \rightarrow B \) with rate constant \( k_A \), the propensity is given by \( k_A n_A \), where \( n_A \) is the number of molecules of type \( A \). For bimolecular reactions \( A + B \rightarrow C \) with rate constant \( k_{AB} \), the propensity is given by \( k_{AB} n_A n_B / (N_A V) \), where \( n_A \) and \( n_B \) are the numbers of molecules of type \( A \) and \( B \), respectively, \( N_A \) is Avogadro’s number and \( V \) is the simulated volume. Once the propensities of all possible reactions are calculated, one reaction is randomly selected proportional to these propensities. The selected reaction is performed, resulting in the new composition of the system. The time is increased by drawing a random number from an exponential distribution with the total propensity as parameter. The propensities for all possible reactions in the new configuration are calculated, etc. This process is repeated for a fixed number of times \( \langle N_{\text{react}} \rangle \) or until a certain time point \( (t_{\text{end}}) \) has been reached.

In order to simulate the supramolecular polymerization kinetics we start with a system of \( N_{\text{mol}} \) monomers and set the volume \( V \) such that the concentration \( N_{\text{mol}} / V \) corresponds to the concentration at which we want to follow the supramolecular polymerization. Starting from only monomers, the only possible reaction is dimerization, so the first reaction will be a dimerization event. The system then consists of \( N_{\text{mol}} - 2 \) monomers and one dimer. The propensities of the three different possible reactions (new dimerization, monomer association to the dimer, and collapse of the dimer) are calculated and one reaction is selected randomly proportional to these propensities, etc. A visualization of a small simulation, containing only 60 molecules, is shown at the left hand side in Movie 1. In this movie the supramolecular polymerization is followed reaction by reaction. At the left hand side of Movie 2 a larger simulation is shown where 1000 molecules are followed and 9 reactions occurred between consecutive frames.

Comparison of ODE and stochastic results

In Figure S1 results of the ODE approach and the stochastic approach are compared for the case \( Kc_\text{tot} = 10 \). Parameters used are \( a = 10^6 \text{M}^{-1}s^{-1} \), \( b = 1 \text{s}^{-1} \) and \( x_i(0) = c_\text{tot} = 10 \mu M \). Fig. S1a shows the degree of polymerization \( \varphi \) as a function of time, while Fig. S1b shows the mean polymer length. This mean aggregate length is defined as \( l(t) = \sum_{i=2}^{\infty} i[X_i](t) / \sum_{i=2}^{\infty} (X_i)(t) \). At time zero the degree of polymerization \( \varphi \) is zero and the mean polymer length is, in the absence of any aggregates, not defined (and thus also not plotted) as we start from all monomers. The ODE solution is obtained by integrating the ODEs in Eq. (S6) using Matlab® for a maximum aggregation length \( N = 2000 \) and using \( \varphi = \sum_{i=2}^{\infty} iX_i / c_\text{tot} \). Apart from the ODE solution, the figures also show the results of three stochastic simulations, each with a different total number of molecules present, where \( \varphi \) is again calculated as the fraction of molecules not present as monomers. Comparison of the ODE and the stochastic solutions shows that the stochastic results fluctuate around the deterministic ODE result, but also that with an increasing number of molecules the kinetics of the stochastic simulations nicely converge to the deterministic solution.
Figure S1: Comparison of the kinetics for the isodesmic monomer association/dissociation model obtained from the deterministic ODE approach with that from the stochastic simulations. a) The degree of aggregation \( \phi \), i.e., the fraction of molecules not present as monomers, as a function of time when aggregation is initiated from monomers. b) The mean length of all aggregates as a function of time. In all cases \( a = 10^6 \ M^{-1}s^{-1} \), \( b = 1 \ s^{-1} \) and \( x_1(0) = c_{\text{tot}} = 10 \ \mu M \). The stochastic solutions oscillate around the deterministic solution of the ODEs and the amplitude of these oscillations decreases with the number of molecules (\( N_{\text{mol}} \)) considered in the simulations.

S1.2 Isodesmic supramolecular polymerization via coagulation and fragmentation

Model
To include also fragmentations and coagulations in an isodesmic supramolecular polymerization mechanism, the reactions of Eq. (S3) are added to the reactions in Eq. (S4). The rate constants \( k_{ij}^+ \) and \( k_{ij}^- \) in Eq. (S3) cannot both be chosen freely without violating detailed balance. Namely, for such an isodesmic supramolecular polymerization, the equilibrium constants for the coagulation steps (i.e., \( k_{ij}^+/k_{ij}^- \)) should equal those of the monomer addition steps. This can be reasoned in a number of ways.
The first is by considering a specific reaction cycle such as the two different pathways to form a tetramer from a dimer and two monomers, as illustrated in Fig. S2. The product of the rate constants when going in one direction should equal the product of the rate constants when going in the opposite direction. For this to hold, \( a^2 a / b^2 = a / c b^2 \), i.e. \( a/b = c/d \).

\[
\begin{align*}
X_2 + 2X_1 & \underset{b}{\overset{a}{\rightleftharpoons}} X_3 + X_1 \\
2X_2 & \underset{d}{\overset{c}{\rightleftharpoons}} X_4
\end{align*}
\]

**Figure S2:** Reaction cycle consisting of two different pathways to form a tetramer from a dimer and two monomers in an isodesmic supramolecular polymerization. This shows that \( c/d = a/b \) and thus that the equilibrium constant of a coagulation step should equal the equilibrium constant of a monomer addition step.

The second way of reasoning that for an isodesmic supramolecular polymerization the rate constant for a coagulation step should equal that of a monomer addition step considers the free energy landscape. This is illustrated in Fig. S3 using two different pathways to form a tetramer out of four monomers. The system containing 4 monomers will have a certain free energy that we denote as zero. If aggregation proceeds via a dimerization followed by 2 consecutive monomer associations, the tetramer will have a free energy \( 3\Delta G^\circ_a \), as both the energy gain on a dimerization and each monomer association is \( \Delta G^\circ_a \). The tetramer could however also be formed via a different pathway, i.e., via two dimerizations followed by a coalescence of these two dimers. With \( \Delta G^\circ_c \) again the energy gain on a dimerization and \( \Delta G^\circ_c \) that on the coalescence the tetramer will have a free energy \( 2\Delta G^\circ_a + \Delta G^\circ_c \). A tetramer being a tetramer, its free energy should be independent on the way it was formed. Thus should hold that \( \Delta G^\circ_c = \Delta G^\circ_a \). Via Eq. (S2) this implies that the equilibrium constants for a monomer association and a coagulation should be equal as well.

**Figure S3:** Schematic illustration of the free energy landscape for the formation of a tetramer in an isodesmic polymerization. This shows that for an isodesmic polymerization the change in free energy for a coagulation step equals that of a monomer association step.
That $K_{ij} = K_a$ should hold for all coagulation steps, and not only for formation of tetramers, follows from substituting the equilibrium concentration of the monomer association and dissociation model, Eq. (S5), into $K_{ij}$ in Eq. (S3). This yields, for any combination of $i$ and $j$,

$$K_{ij} = \frac{k^+_{ij}}{k^-_{ij}} = \left(\frac{K_a[X_1]_{eq}}{K_a[X_1]_{eq}}\right)^{i+j} = K_a = \frac{a}{b} \tag{S7}$$

For any $i$ and $j$ the ratio of the two rate constants $k^+_{ij}$ and $k^-_{ij}$ is thus fixed by the choice of $a$ and $b$. This implies that only $k^+_{ij}$ or $k^-_{ij}$ can be chosen freely after which the other one is fixed.

Again considering all bonds equal, we set $k^-_{ij}$ equal to $b$ for all $i \neq j$. To obey detailed balance all $k^+_{ij}$ then need to be equal to $a$. Moreover, because fragmentation into two equal aggregates can only occur via breakage of a single bond (as opposed to two bonds for unequal fragments) $k^+_{ii}$ then equals $b/2$, and because the number of possible reaction pairs between two $X_i$'s equals $n_i(n_i - 1)/2$ while the number of possible reaction pairs between an $X_i$ and an $X_j$ equals $n_in_j$, $k^+_{ii} = a/2$. The whole isodesmic supramolecular polymerization is thus described by

$$X_i + X_i \xrightleftharpoons[\frac{a/2}{b/2}]{[\frac{b}{a}]} X_{2i} \tag{S8}$$

$$X_i + X_j \xrightleftharpoons[\frac{a}{b}]{[\frac{b}{a}]} X_{i+j}$$

with $i, j \geq 1$ and $j \neq i$.

**ODE approach**

The corresponding set of differential equations for an aggregation model without an upper bound to the polymer lengths is

$$\frac{dx_i}{dt} = -ax \sum_{i=1}^{\infty} x_i + b \sum_{i=2}^{\infty} x_i \tag{S9}$$

$$\frac{dx_k}{dt} = -\left(a \sum_{i=1}^{\infty} x_i + b \frac{k-1}{2} \right) x_k + a \frac{k-1}{2} \sum_{i=k}^{\infty} x_i x_{k-i} + b \sum_{i=k+1}^{\infty} x_i$$

When truncated at a maximum polymer length $N$ the differential equations are given by

$$\frac{dx_i}{dt} = -ax \sum_{i=1}^{N-1} x_i + b \sum_{i=2}^{N} x_i \tag{S10}$$

$$\frac{dx_k}{dt} = -\left(a \sum_{i=1}^{N-1} x_i + b \frac{k-1}{2} \right) x_k + a \frac{k-1}{2} \sum_{i=k}^{N} x_i x_{k-i} + b \sum_{i=k+1}^{N} x_i$$

**Stochastic simulation approach**

Addition of the coagulation and fragmentation reactions in the stochastic simulations means that, if there are aggregates present, also the propensities for all possible coagulation and fragmentation reactions should be calculated, and that if selected these should be performed. The procedure furthermore remains the same as described for the model with only monomer associations and dissociations. Visualizations of simulations containing again 60 and 1000 molecules are shown at the right hand side of Movies 1 and 2, respectively.
Figure S4: Comparison of the kinetics for the isodesmic coagulation/fragmentation model as obtained from the deterministic ODE approach with that from the stochastic simulations. a) The degree of aggregation $\varphi$, i.e., the fraction of molecules not present as monomers, as a function of time when polymerization is initiated from monomers. b) The mean length of all aggregates as a function of time. c) The rates of the different types of reactions as a function of time. In all cases $a = 10^6 \text{M}^{-1}\text{s}^{-1}$, $b = 1 \text{s}^{-1}$ and $x_1(0) = c_{\text{tot}} = 10 \mu\text{M}$. The stochastic solutions oscillate around the deterministic solution of the ODEs and the amplitude of these oscillations decreases with the numbers molecules ($N_{\text{mol}}$) considered in the simulations.
**Comparison of ODE and stochastic results**

In Fig. S4 results of both methods are compared, again for the case \( K_{c_{\text{tot}}} = 10 \). Parameters used are the same as for the monomer association model in Fig. S1, i.e., \( a = 10^6 \, M^{-1}s^{-1}, b = 1 \, s^{-1} \) and \( x_i(0) = c_{\text{tot}} = 10 \, \mu M \). Fig. S4a shows again the degree of aggregation \( \varphi \) as a function of time, where for the ODE solution again a maximum polymer length \( N = 2000 \) is used and also the numbers of molecules for three stochastic simulations are equal to those in Fig. S1. Comparison of the ODE and the stochastic solutions shows that the stochastic results once more fluctuate around the deterministic ODE result and that with increasing number of molecules the kinetics of the stochastic simulations converge to the deterministic solution. Figs. S4b and S4c show that the same holds for the mean aggregate length and the rates of the different reactions. The rates in Fig. S4c are the summed rates of all monomer addition reactions, etc. That is, for rate for the monomer additions is given by

\[
    r_{\text{mono}}(t) = a [X_1](t) \sum_{i=2}^{\infty} [X_i](t),
\]

the rate for dimerizations by

\[
    r_{\text{dimer}}(t) = \frac{a}{2} [X_1]^2(t),
\]

and the rate for coagulations by

\[
    r_{\text{coag}}(t) = \frac{a}{2} \left( \sum_{i=2}^{\infty} [X_i](t) \right)^2.
\]

**S1.3 Cooperative supramolecular polymerization**

**Model**

The analysis performed so far for isodesmic supramolecular polymerizations can be extended to cooperative supramolecular polymerizations as well. For this we focus on cooperative nucleation-elongation models with a nucleus of size two in which aggregate growth only occurs via monomer associations and dissociations. This means that the equilibrium constants \( K_i \) in Eq. (S1) are equal for all \( i \geq 2 \) and only \( K_1 \) differs. We will denote the equilibrium constant for all \( i \geq 2 \) the elongation equilibrium constant \( K_e \) and \( K_1 \) the nucleation equilibrium constant \( K_n \). The cooperativity is given by \( \sigma = K_n/K_e \). Considering the cooperativity related to the stability of the dimer, we keep all reaction constants equal to the isodesmic supramolecular polymerization in the previous section, except for the rate constant \( k_1^{-} \) for the dimer collapse which is multiplied by a factor \( \sigma^{-1} \). For such a cooperative supramolecular polymerization via monomer associations and dissociations Eq. (S1) thus becomes:
\[ X_1 + X_1 \xrightleftharpoons{a/2}{b/(2\sigma)} X_2 \]
\[ K_n = \sigma \frac{a}{b} = \frac{[X_2]_{eq}}{[X_1]_{eq}^2} \]
\[ X_2 + X_1 \xrightleftharpoons{a}{b} X_3 \]
\[ K_e = \frac{a}{b} = \frac{[X_3]_{eq}}{[X_1]_{eq}[X_2]_{eq}} \]
\[ X_i + X_1 \xrightleftharpoons{a}{b} X_{i+1} \]
\[ K_e = \frac{a}{b} = \frac{[X_{i+1}]_{eq}}{[X_1]_{eq}[X_i]_{eq}} \]

The equilibrium concentrations of all aggregate lengths \( i \geq 2 \) can again be expressed in terms of the equilibrium monomer concentration, now as
\[
[X_i]_{eq} = \frac{\sigma}{K_e} (K_e [X_1]_{eq})^i 
\] (S12)

Also in such a cooperative supramolecular polymerization, reactions of Eq. (S3) can be included by adding the reactions of Eq. (S3). Also now the rate constants \( k_{ij}^+ \) and \( k_{ij}^- \) cannot both be chosen freely without violating detailed balance. This can again be seen from the reaction cycle formed by the two different pathways to form a tetramer out of a dimer and two monomers. This is illustrated in Fig. S5. Because the product of the rate constants when going in one direction should still equal the product of the rate constants when going in the opposite direction, here it should hold that \( a^2 d \frac{b}{2\sigma} = \frac{a}{2} cb^2 \), i.e. \( c/d = a/(\sigma b) \).

**Figure S5:** Reaction cycle formed by the two different pathways to form a tetramer from a dimer and two monomers in a cooperative supramolecular polymerization. This shows that \( c/d \) should equal \( a/(\sigma b) \) and thus that the equilibrium constant of a coagulation step should equal the equilibrium constant of a monomer association step divided by \( \sigma \).

One could also look again at the free energy landscape, as is illustrated in Fig. S6 using two different pathways to form a tetramer out of four monomers. If the free energy change for a monomer association step \( \Delta G^+_e \) corresponds to \( K_e \), then the equilibrium constant \( K_n = \sigma K_e \) corresponds to a free energy change \( \Delta G^+_e - NP \), where \( NP \) denotes the nucleation penalty and is related to \( \sigma \) as \( \sigma = \exp(NP/RT) \). The first pathway, via one dimerization followed by two consecutive monomer associations, thus results in a free energy change \( 3\Delta G^+_e - NP \). The two dimerizations in the second pathway result in a free energy change \( 2\Delta G^+_e - 2NP \). As the two pathways in which the tetramer can be
formed should again result in the same change in free energy, the free energy change for the coalescence of the two dimers \( \Delta G^*_c \) should equal \( \Delta G^*_e + NP \).

Figure S6: Schematic illustration of the free energy landscape for formation of a tetramer in a cooperative polymerization. This shows that for a cooperative polymerization the change in free energy for a coagulation step equals the sum of change in free energy for a monomer addition step and the nucleation penalty.

Another way to see this is that a bond yields a gain in free energy of \( \Delta G^*_e \), while each supramolecular polymer costs \( NP \). In a dimer formation both a new polymer and a new bond are formed, thus \( \Delta G^*_e - NP \). In an elongation step only a new bond is formed, thus \( \Delta G^*_e \). And in a coagulation step a new bond is formed and a polymer is lost, thus \( \Delta G^*_e + NP \).

To see that the relation between the coagulation and monomer association steps holds again for all possible coagulations, we substitute once more the equilibrium concentration of the monomer association and dissociation model, Eq. (S12), into \( K_{ij} \) in Eq. (S3). This yields, for any combinations of \( i \) and \( j \),

\[
K_{ij} = \frac{k^+_{ij}}{k^-_{ij}} = \frac{\sigma}{K_e} \left( \frac{K_e[X_i]_{eq}^{i+j}}{K_e[X_i]_{eq}^i \sigma (K_e[X_i]_{eq})^j} \right) = \frac{K_e}{\sigma} = \frac{a}{\sigma b} \tag{S13}
\]

This means that the ratio of the two rate constants \( k^+_{ij} \) and \( k^-_{ij} \) is fixed by the choice of \( a, b \) and \( \sigma \). Thus only \( k^+_{ij} \) or \( k^-_{ij} \) can be freely chosen after which the other one is fixed. If we keep the forward rate constants equal to what they were in the isodesmic case, i.e., \( k^+_{ij} = a \) for \( i \neq j \) and \( k^+_{ii} = a/2 \), that implies that \( k^-_{ij} = \sigma b \) and \( k^-_{ii} = \sigma b/2 \). The whole cooperative supramolecular polymerization is thus described by

\[
\begin{align*}
X_i + X_i &\overset{a/2}{\underset{b/(2 \sigma)}{\leftrightarrow}} X_2 \\
X_i + X_i &\overset{a}{\underset{b}{\leftrightarrow}} X_{i+1} \\
X_i + X_i &\overset{a/2}{\underset{\sigma b/2}{\leftrightarrow}} X_{2i} \\
X_i + X_j &\overset{a}{\underset{\sigma b}{\leftrightarrow}} X_{i+j}
\end{align*} \tag{S14}
\]

with \( i, j \geq 2 \) and \( j \neq i \).
**Thermodynamic equilibrium**

The thermodynamic equilibrium can be obtained using a mass balance approach. The sum of the concentration of monomers plus the concentrations of monomers present in the supramolecular polymers of all different length should equal the overall concentration $c_{\text{tot}}$ the polymerization started with, i.e.,

$$[X_1]_{\text{eq}} + \sum_{i=2}^{\infty} i[X_i]_{\text{eq}} = c_{\text{tot}} \quad (S15)$$

Substituting Eq. (S12) in the second term on the left hand side yields

$$\sum_{i=2}^{\infty} i[X_i]_{\text{eq}} = \sum_{i=2}^{\infty} i \frac{\sigma}{K_e} \left( K_e[X_1]_{\text{eq}} \right)^i = \frac{\sigma}{K_e} \left( \frac{K_e[X_1]_{\text{eq}}}{1-K_e[X_1]_{\text{eq}}} \right)^2 \quad (S16)$$

The mass balance equation Eq. (S15) thus becomes

$$[X_1]_{\text{eq}} + \frac{\sigma}{K_e} \left( K_e[X_1]_{\text{eq}} \right)^2 \frac{(2-K_e[X_1]_{\text{eq}})}{(1-K_e[X_1]_{\text{eq}})^2} = c_{\text{tot}} \quad (S17)$$

This is a polynomial of degree three in the monomer concentration $[X_1]_{\text{eq}}$ that can readily be solved numerically.

The total concentration of polymers in equilibrium is given by

$$\sum_{i=2}^{\infty} [X_i]_{\text{eq}} = \sum_{i=2}^{\infty} \frac{\sigma}{K_e} \left( K_e[X_1]_{\text{eq}} \right)^i \approx \frac{\sigma}{K_e} \left( K_e[X_1]_{\text{eq}} \right)^2 \sum_{i=0}^{\infty} \left( K_e[X_1]_{\text{eq}} \right)^i \quad (S18)$$

The average aggregate length is given by the total number of molecules in the polymers divided by the number of aggregates. Dividing Eq. (S16) by Eq. (S18) yields for this average aggregate length

$$l = \frac{2-K_e[X_1]_{\text{eq}}}{1-K_e[X_1]_{\text{eq}}} \quad (S19)$$

For a cooperative supramolecular polymerization with $\sigma \ll 1$ at sufficiently high concentration $K_e c_{\text{tot}} > 1$ it holds that $K_e[X_1]_{\text{eq}} \approx 1$. Substituting this in mass balance Eq. (S17) yields

$$K_e c_{\text{tot}} - 1 \approx \frac{\sigma}{(1-K_e[X_1]_{\text{eq}})^2} \quad (S20)$$

This yields the following approximation for the average aggregate length

$$l \approx \frac{1}{1-K_e[X_1]_{\text{eq}}} \approx \sqrt{\frac{K_e c_{\text{tot}} - 1}{\sigma}} \quad (S21)$$

For the degree of polymerization then holds

$$\phi \approx 1 - \frac{1}{K_e c_{\text{tot}}}$$

**ODE approach**

The set of differential equations corresponding to the reaction in Eq. (S14) truncated at a maximum polymer length $N$ is given by
\[ \frac{dx_i}{dt} = -ax_i \sum_{j=1}^{N-1} x_j + \frac{b}{\sigma} x_2 + b \sum_{j=3}^{N} x_j \]
\[ \frac{dx_2}{dt} = \frac{a}{2} x_1^2 - ax_2 \sum_{i=1}^{N-2} x_j - \frac{b}{2\sigma} x_2 + bx_3 + b \sigma \sum_{j=4}^{N} x_j \]
\[ \frac{dx_k}{dt} = - \left( a \sum_{i=1}^{N-k} x_i + b + \frac{\sigma b}{2} (k-3) \right) x_2 + \frac{a}{2} \sum_{i=1}^{k-1} x_i x_{k-i} + bx_{k+1} + \sigma b \sum_{i=k+2}^{N} x_i \]

where \( 3 \leq k \leq N \).

**Stochastic simulation approach**

Addition of cooperativity in the stochastic simulations means that the cooperativity factor \( \sigma \) should be taken into account when calculating the propensities for dimer collapse and fragmentation reactions. The procedure furthermore remains the same as described for the isodesmic model. A movie of two small simulations, the first with only monomer associations and dissociations and the second with also fragmentations and coagulations, with again the same number of monomers as in the previous movies, is given as Movie 3. This illustrates the effect of cooperativity and the influence of fragmentations and coagulations on cooperative aggregate growth.
Figure S7: Comparison of the kinetics for the cooperative coagulation/fragmentation model as obtained from the deterministic ODE approach with that from the stochastic simulations. a) The degree of aggregation $\varphi$, i.e., the fraction of molecules not present as monomers, as a function of time. b) The mean length of all polymers as a function of time. c) The rates of different reactions. In all cases $a = 10^6 \text{ M}^{-1}\text{s}^{-1}$, $b = 1 \text{ s}^{-1}$, $\sigma = 10^{-4}$ and $x_1(0) = c_{\text{tot}} = 10 \mu\text{M}$. The stochastic solutions oscillate around the deterministic solution of the ODEs and the amplitude of these oscillations decreases with the numbers molecules ($N_{\text{mol}}$) considered in the simulations.

Comparison of ODE and stochastic results
Comparison between stochastic simulations and the deterministic ODE solution is given in Fig. S7 for an example where $\sigma = 10^{-4}$ and $K_e c_{\text{tot}} = 10$. Because in such a cooperative supramolecular
polymerization the mean aggregate length is much larger than for an isodesmic polymerization at the same concentration, more molecules are needed for the simulations to start following the deterministic solution, but for sufficiently many molecules the solutions again converge to the ODE solution.

For this case with $\sigma = 10^{-4}$ and $K_e c_{\text{tot}} = 10$ the average polymer length according to Eq. (S21) equals 300. Truncating the ODEs at $N=2000$ then still suffices. However, Fig. S8 illustrates that for higher concentrations such a truncation results in errors. The red line in Fig. S8a shows the equilibrium polymer concentrations as a function of the aggregate length as calculated from Eqs. (S12) and (S17) for $K_e c_{\text{tot}} = 100$. The figure also shows that truncating at $N=500$ yields aggregate concentrations that increase with increasing aggregate length rather than the expected decrease. Truncating at $N=5000$ does give the expected result, whereas truncating at $N=2000$ still yields a small deviation.

**Figure S8: Truncating the ODEs at a maximum aggregate length N may introduce errors for cooperative polymerizations.** a) Equilibrium concentrations of monomers and aggregates up to length 500 for $K_e c_{\text{tot}} = 100$. Results are given for ODEs with three different cutoff lengths N as well as for an infinite cut-off length via solution of Eqs. (S12) and (S17). b) Equilibrium rates for the different reactions as a function of reduced concentration start to deviate from the analytically derived expressions with increasing concentration. Even a cut-off of 5000 does not suffice to describe growth of cooperative aggregates at reduced concentrations above 100. In all cases with $a = 10^6 \, M^{-1} \, s^{-1}$, $b = 1 \, s^{-1}$, $\sigma = 10^{-4}$.

The lines Fig. S8b show analytical expressions for the rates of the different types of reactions in equilibrium as a function of the reduced concentration. These analytical expressions are derived in
Section S2 in this Supporting Information. The figure also shows the rates for these different reactions as obtained from the steady state solution of the ODEs when truncating at either $N=500$ or $N=5000$. This shows that the solution of the ODEs starts to deviate from the analytically derived expressions with increasing concentration when the reduced concentration becomes too high. Even a cut-off of 5000 does not suffice to describe growth of cooperative aggregates at reduced concentrations above 100. This may not be surprising as for $\sigma = 10^{-4}$ and $K_c c_{\text{tot}} = 10^6$ Eq. (S21) predicts an average polymer length of $10^5$. Figure 2f in the main text shows that the stochastic simulations do follow the analytical expressions. This provides a first example of the benefit of using the stochastic simulation approach to study supramolecular polymerization kinetics.

From the simulations we can also extract the time it takes for the average aggregate size to reach the value half of its value in equilibrium. Figs. S9a and S9b show this time both as a function of the reduced concentration as well as a function of the cooperativity.

**Figure S9: The time for polymers to reach half their equilibrium lengths.**

**a)** Dependence on the reduced concentration for $\sigma = 10^{-4}$ **b)** Dependence on the cooperativity for $c_{\text{tot}} = 10 \mu M$. The symbols represent simulation results with $a = 10^6 \, M^{-1}s^{-1}$, $b = 1 \, s^{-1}$ and starting from monomers. For a supramolecular polymerization via monomer associations the dependence on the reduced concentration and $1/\sigma$ is both linear. With coagulation and fragmentation reactions the time decreases with the square root of both the reduced concentration as well as $\sigma$. 
S1.4 Supramolecular polymerization into two polymer types

Model
The analysis performed so far can be extended to supramolecular polymerizations where monomers can aggregate into two different polymer types as well. These two different aggregate types may for instance resemble a meta-stable (kinetic) assembly and a thermodynamic product, or helical supramolecular polymers with opposite helicity. We will denote polymers of the first type of length $i$ as $X_i$ and those of the second type as $Y_i$. If we assume that the two polymer types cannot coalesce to form a mixed polymer, we can use for the first polymer type again the rate constants as obtained in the previous section. Because isodesmic supramolecular polymerization is a special case of the cooperative aggregation, i.e., with $\sigma = 1$, we will just consider the cooperative case. For the second aggregate type we also use the same forward rate constants and the same relations between nucleation, elongation and coagulation steps, but as the aggregates may have a different stability and cooperativity with different parameters $b'$ and $\sigma'$. The dimer formation, though, is affected by the presence of a second aggregate type. When two monomers meet, they now either form a dimer $X_2$ or a dimer $Y_2$. If the total rate of dimer formation remains the same (for instance because the dimer formation is diffusion limited) the sum of the two dimer formation rate constants should thus add up to the single dimer formation rate constant in the previous section. Keeping the dimer formation symmetric, the whole cooperative supramolecular polymerization with two aggregate types is thus described by

\[
\begin{align*}
X_1 + X_1 & \xrightleftharpoons[\sigma b/(2\sigma)]{a/(2\sigma)} X_2 \\
X_i + X_1 & \xrightarrow{a/b} X_{i+1} \\
X_i + X_i & \xrightarrow[\sigma b/(2\sigma)]{a/(2\sigma)} X_{2i} \\
X_i + X_j & \xrightarrow[\sigma b/(2\sigma)]{a/b} X_{i+j}
\end{align*}
\]

\[
\begin{align*}
X_1 + X_1 & \xrightleftharpoons[\sigma b/(2\sigma)]{a/(2\sigma)} Y_2 \\
Y_i + X_1 & \xrightarrow{a/b} Y_{i+1} \\
Y_i + Y_i & \xrightarrow[\sigma b/(2\sigma)]{a/(2\sigma)} Y_{2i} \\
Y_i + Y_j & \xrightarrow[\sigma b/(2\sigma)]{a/(2\sigma)} Y_{i+j}
\end{align*}
\]

with $i, j \geq 2$ and $j \neq i$.

The equilibrium concentrations of all aggregate lengths ($i \geq 2$) can again be expressed in terms of the equilibrium monomer concentration, now as

\[
[X_i]_{eq} = \frac{\sigma}{2K_e} (K_e[X_1]_{eq})^i
\]

and

\[
[Y_i]_{eq} = \frac{\sigma'}{2K'_e} (K'_e[X_1]_{eq})^i
\]

where $K'_e = \frac{a}{b'}$. 

S17
**ODE approach**

The set of differential equations truncated at a maximum aggregate length $N$ corresponding to the reactions in Eq. (S23) is given by

$$
\begin{align*}
\frac{dx_1}{dt} &= -ax_1^2 - ax_1 \sum_{i=2}^{N-1} (x_i + y_i) + \frac{b}{\sigma} x_2 + b' \sum_{i=3}^{N} x_i + \frac{b'}{\sigma} y_2 + b' \sum_{i=3}^{N} y_i \\
\frac{dx_2}{dt} &= \frac{a}{4} x_1^2 - ax_2 x_1 - ax_2 \sum_{i=2}^{N-2} x_i - \frac{b}{2\sigma} x_2 + bx_3 + \sigma b \sum_{i=3}^{N} x_i \\
\frac{dx_k}{dt} &= -\left(ax_k + a \sum_{i=2}^{N-4} x_i + b + \frac{\sigma b}{2} (k-3)\right) x_k + ax_1 x_{k-1} + \frac{a}{2} \sum_{i=2}^{k-2} x_i x_{k-i} + b x_{k+1} + \sigma b \sum_{i=k+2}^{N} x_i \\
\frac{dy_2}{dt} &= \frac{a}{4} x_2^2 - ay_2 x_1 - ay_2 \sum_{i=2}^{N-2} y_i - \frac{b'}{2\sigma} y_2 + b' y_3 + \sigma' b' \sum_{i=4}^{N} y_i \\
\frac{dy_k}{dt} &= -\left(ax_k + a \sum_{i=2}^{N-4} y_i + b' + \frac{\sigma' b'}{2} (k-3)\right) y_k + ax_1 y_{k-1} + \frac{a}{2} \sum_{i=2}^{k-2} y_i y_{k-i} + b' y_{k+1} + \sigma' b' \sum_{i=k+2}^{N} y_i
\end{align*}
$$

where $3 \leq k \leq N$.

**Stochastic simulation approach**

Addition of the second aggregate type in the stochastic simulations means that each assembly should be labeled with its type and that for calculation of the propensities of reactions involving these species these types should be taken into account. Furthermore the procedure remains the same as described before. As an example a movie of two small simulations (again one without and one with coagulation and fragmentation reactions) of a cooperative supramolecular polymerization of a single monomer type into thermodynamically favored aggregates $X$ in the presence of a kinetically-controlled, parallel operating pathway $Y$ is given as Movies 5.

**Comparison of ODE and stochastic results**

Comparison between stochastic simulations and the deterministic ODE solution is given in Fig. S10 for an example where $a = 10^6 M^{-1} s^{-1}$, $b = b' = 1 s^{-1}$, $\sigma = \sigma' = 10^{-4}$ and $x_1(0) = c_{tot} = 10 \mu M$. This would resemble a case where an achiral molecule forms two aggregates with opposite helicity (denoted as $P$ and $M$) with no preference for any one of the two. The stochastic solutions again nicely oscillate around the deterministic solution of the ODEs.
Figure S10: Comparison of the kinetics for the cooperative coagulation/fragmentation model with two polymer types as obtained from the deterministic ODE approach with that from the stochastic simulations. 

(a) The degree of aggregation \( \phi \), i.e., the fraction of molecules not present as monomers, as a function of time. 

(b) The mean length of all polymers as a function of time. In all cases \( a = 10^6 \, M^{-1} s^{-1}, b = b' = 1 \, s^{-1}, \sigma = \sigma' = 10^{-4} \) and \( x_1(0) = c_{tot} = 10 \, \mu M \). The stochastic solutions, with \( 10^6 \) monomers, once more oscillate around the deterministic solution of the ODEs.
S1.5  Supramolecular copolymerization of two monomer types into two polymer types

Model

The analysis performed so far can be further extended to supramolecular copolymerizations of two types of monomers that we denote as \( R \) and \( S \) into two types of aggregates \( P \) and \( M \). This increases the number of reactions that can take place. Assuming that one can discern the two ends of a polymer, say the bottom and the top, now 4 different \( P \) dimers as well as 4 different \( M \) dimers can be formed:

\[
\begin{align*}
R + R &\xrightleftharpoons[k_{\text{RR}^P}^\text{a}]{k_{\text{RR}^M}^\text{a}} RR^P \quad R + R \xrightleftharpoons[k_{\text{RR}^M}^\text{a}]{k_{\text{RR}^P}^\text{a}} RR^M \\
R + S &\xrightleftharpoons[k_{\text{RS}^P}^\text{a}]{k_{\text{RS}^M}^\text{a}} RS^P \quad R + S \xrightleftharpoons[k_{\text{RS}^M}^\text{a}]{k_{\text{RS}^P}^\text{a}} RS^M \\
S + R &\xrightleftharpoons[k_{\text{SR}^P}^\text{a}]{k_{\text{SR}^M}^\text{a}} SR^P \quad S + R \xrightleftharpoons[k_{\text{SR}^M}^\text{a}]{k_{\text{SR}^P}^\text{a}} SR^M \\
S + S &\xrightleftharpoons[k_{\text{SS}^P}^\text{a}]{k_{\text{SS}^M}^\text{a}} SS^P \quad S + S \xrightleftharpoons[k_{\text{SS}^M}^\text{a}]{k_{\text{SS}^P}^\text{a}} SS^M
\end{align*}
\]  

(S25)

Each of these 8 different dimers could grow to a trimer by association of either an \( R \) or an \( S \) monomer, giving rise to 8 different \( P \)-type as well as 8 different \( M \)-type trimers. More generally, there will be \( 2^i \) different \( P \)-type aggregates of length \( i \) as well as \( 2^i \) different \( P \)-type aggregates of length \( i \). If monomers can associate to both ends of the assemblies, these reactions alone already introduce cycles. For instance, association of an \( S \) monomer to the end of an \( RR \) dimer would result in the same trimer as association of an \( R \) monomer to the front of an \( RS \) dimer. As this implies a lot of constraints on the reaction rate constants, we will not consider this completely general case.

Building upon the cooperative polymerization model from Section S1.3 which assumed that (i) each non-covalent bond provides a free energy gain \( \Delta G_e \), (ii) each aggregate bears a free energy penalty \(-RT\ln(\sigma)\) and (iii) all forward rate constants are equal, the kinetic copolymerization model is thus constructed by assuming additionally, and in line with our previous approach, that (iv) the helicity of an aggregate is fixed upon dimer formation and remains unaltered throughout its growth and (v) a second free energy penalty accounts for the helical preference. Point (v) is implemented by subtracting a penalty \( \text{MMP} \) from the free energy gain \( \Delta G_e \) upon formation of a bond when one of the two monomers involved in the bond is in a polymer of its unpreferred type. In terms of rate constants, this is described by a factor \( \nu \) increase in the backward rate constant, where \( \nu = \exp(-\text{MMP}/RT) \). Taking \( P \) the preferred aggregate type for \( R \) and \( M \) the preferred aggregate type for \( S \), the dimer reactions become:

\[
\begin{align*}
R + R &\xrightleftharpoons[\nu a^P]{\nu a^P} RR^P \quad R + R \xrightleftharpoons[\nu a^M]{\nu a^M} RR^M \\
R + S &\xrightleftharpoons[\nu a^P]{\nu a^P} RS^P \quad R + S \xrightleftharpoons[\nu a^M]{\nu a^M} RS^M \\
S + R &\xrightleftharpoons[\nu a^P]{\nu a^P} SR^P \quad S + R \xrightleftharpoons[\nu a^M]{\nu a^M} SR^M \\
S + S &\xrightleftharpoons[\nu a^P]{\nu a^P} SS^P \quad S + S \xrightleftharpoons[\nu a^M]{\nu a^M} SS^M
\end{align*}
\]  

(S26)
For the monomer association reactions only the monomers involved in the bond that is formed or broken are relevant. Instead of writing all reactions for all different possible aggregate types individually, we describe the other $i$ monomers in the aggregate as $P_i$ or $M_i$ depending on the assembly type. For monomer associations to the end of the aggregate this yields (for all $i \geq 1$)

$$
P_i R + R \xrightleftharpoons{a/2}{b/2} P_i R R \quad M_i R + R \xrightleftharpoons{a/2}{a/2} M_i R R
$$

$$
P_i S + R \xrightleftharpoons{a/2}{v b/2} P_i S R \quad M_i S + R \xrightleftharpoons{a/2}{v b/2} M_i S R
$$

$$
P_i R + S \xrightleftharpoons{a/2}{v b/2} P_i R S \quad M_i R + S \xrightleftharpoons{a/2}{v b/2} M_i R S
$$

$$
P_i S + S \xrightleftharpoons{a/2}{v b/2} P_i S S \quad M_i S + S \xrightleftharpoons{a/2}{v b/2} M_i S S
$$

Similarly, for monomer associations to the front of the aggregate this yields

$$
R P_i + R \xrightleftharpoons{a/2}{b/2} R R P_i \quad R M_i + R \xrightleftharpoons{a/2}{a/2} R R M_i
$$

$$
S P_i + R \xrightleftharpoons{a/2}{v b/2} R S P_i \quad S M_i + R \xrightleftharpoons{a/2}{v b/2} S R M_i
$$

$$
R P_i + S \xrightleftharpoons{a/2}{v b/2} S R P_i \quad R M_i + S \xrightleftharpoons{a/2}{v b/2} S R M_i
$$

$$
S P_i + S \xrightleftharpoons{a/2}{v b/2} S S P_i \quad S M_i + S \xrightleftharpoons{a/2}{b/2} S S M_i
$$

Here the factor $\frac{1}{2}$ appears in all reactions because reactions at front and end are considered individually.

In order for the coagulation and fragmentation reactions to maintain detailed balance, it needs to be considered that upon a fragmentation (i) a new aggregate is formed which comes at the expense of a nucleation penalty and (ii) a bond disappeared which may result in the release of a mismatch penalty. The coagulation and fragmentation reactions are then fully described by

$$
P_i R + R_P j \xrightleftharpoons{a/2}{v b j/2} P_i R R_P j \quad M_i R + R_M j \xrightleftharpoons{a/2}{v b j/2} M_i R R_M j
$$

$$
P_i R + S_P j \xrightleftharpoons{a/2}{v b j/2} P_i R S_P j \quad M_i R + S_M j \xrightleftharpoons{a/2}{v b j/2} M_i R S_M j
$$

$$
P_i S + R_P j \xrightleftharpoons{a/2}{v b j/2} P_i S R_P j \quad M_i S + R_M j \xrightleftharpoons{a/2}{v b j/2} M_i S R_M j
$$

$$
P_i S + S_P j \xrightleftharpoons{a/2}{v b j/2} P_i S S_P j \quad M_i S + S_M j \xrightleftharpoons{a/2}{v b j/2} M_i S S_M j
$$

for all $i,j \geq 1$.

**Stochastic simulation approach**

Because the number of different aggregate types has become so large, describing the concentration of each with an ODE is unfeasible, and occurrences of especially specific longer assemblies may be so small (or even zero) that a description in terms of concentrations may be incorrect. Advantage of the simulation approach is that in the simulations we do not need to track all possible aggregates, but only those that have a finite concentration. And then we have to consider only those reactions that are possible on these actually present aggregates. By doing so, the simulation approach does remain feasible. As an example a movie of two small simulations (again one without and one with coagulation and fragmentation reactions) of a Majority Rules experiment is given as Movies 4.
In order to simulate the chiral amplification kinetics we first perform two simulations to obtain configurations representative for the equilibrium for the two components separately. This is followed by a single simulation of the combined system. For the simulation of a volume $V$ with a total concentration $c_{\text{tot}}$ and enantiomeric excess e.e. we thus first simulate $f_R N_{\text{mol}}$ molecules of type $R$ in a volume $f_R V$ as well as $(1 - f_R) N_{\text{mol}}$ molecules of type $S$ in a volume $(1 - f_R)V$. Here $f_R$ is the fraction of $R$ molecules which is related to the e.e. as $f_R = (\text{e.e.}+1)/2$. The final configurations of these simulations are combined as initial configuration for the simulation from which the chiral amplification is followed.

![Simulation Results](image)

**Figure S11:** Comparison of the kinetics for the cooperative coagulation/fragmentation copolymerization model with two aggregate types and two differently labeled but further identical monomer types as obtained from stochastic simulations with the solution from the deterministic ODE approach with a single monomer type.  

**a**) The degree of aggregation $\varphi$, i.e., the fraction of molecules not present as monomers, as a function of time. **b**) The mean length of all aggregates as a function of time. In the ODE model $a = 10^6 M^{-1}s^{-1}$, $b = b' = 1 s^{-1}$, $a = a' = 10^{-4}$ and $x_1(0) = c_{\text{tot}} = 10 \mu M$. In the stochastic solutions, with $10^6$ monomers, $r_1(0) = 0.6c_{\text{tot}} = 6 \mu M$, $s_1(0) = 0.4c_{\text{tot}} = 4 \mu M$, and $v = 1$.

**Simulation results**

Because we cannot obtain the deterministic solution via integration of the ODEs for this copolymerization, the comparison that we can do between stochastic simulations and ODE results is
limited. One comparison that we can do is for \( \nu = 1 \). In this case, corresponding to a MMP of zero, both monomers do not have a preference for either of the stack types. Both monomer types thus behave identically, and are only named differently. This should thus result in exactly the same kinetics as for one monomer type at a concentration that is the sum of the concentrations of \( R \) and \( S \), i.e., for which we obtained an ODE approach in the previous subsection. In Fig. S11 we therefore compare the solution of the ODEs in Eq. (S24) for \( a = 10^6 \, M^{-1} \, s^{-1}, b = b' = 1 \, s^{-1}, \sigma = \sigma' = 10^{-4} \), and \( x_1(0) = c_{tot} = 10 \, \mu M \) with stochastic simulations of this copolymerization model for \( r_1(0) = 0.6c_{tot} = 6 \, \mu M, s_1(0) = 0.4c_{tot} = 4 \, \mu M, \) the same \( a, b \) and \( \sigma \), and \( \nu = 1 \). This shows that the simulations indeed yield the expected results.

Next, we will consider the supramolecular copolymerization of two enantiomers \( R \) and \( S \). The \( R \) enantiomer prefers helical aggregates with a right handed helicity \( P \) and the \( S \) enantiomer helical assemblies with a left handed helicity \( M \). By taking \( \nu = 1.1 \), monomers will more rapidly dissociate from aggregates of their unpreferred type than from assemblies of their preferred type. Figure S12 shows that if we perform such simulations for different ratios of \( R \) and \( S \), we obtain the expected Majority Rules curves.

![Figure S12: Majority Rules curve](image)

**Figure S12: Majority Rules curve.** The net helicity \( \varphi_P - \varphi_M \) in equilibrium versus the enantiomeric excess \( e.e. = (r_{tot} - s_{tot})/(r_{tot} + s_{tot}) \). Parameters used: \( r_{tot} + s_{tot} = 10 \, \mu M, a = 10^6 \, M^{-1} \, s^{-1}, b = 1 \, s^{-1}, \sigma = 10^{-4}, \) and \( \nu = 1.1 \).
S2. Derivation of analytical expressions for reaction rates

Dimer formation/collapse rates

The rate of dimer formation in thermodynamic equilibrium is given by

\[ r_{\text{dimer}} = \frac{a}{2}[X_1]_\text{eq}^2 \tag{S30} \]

For a cooperative supramolecular polymerization with \( \sigma \ll 1 \) and \( K_e c_{\text{tot}} > 1 \) holds for the monomer concentration in equilibrium that

\[ [X_1]_\text{eq} \approx \frac{1}{K_e} \tag{S31} \]

Substituting Eq. (S31) into Eq. (S30) yields for the rate of dimer formation

\[ r_{\text{dimer}} = \frac{a}{2}[X_1]_\text{eq}^2 \approx \frac{a}{2K_e^2} \tag{S32} \]

This expression for the rate of dimer formation (and equally the rate of dimer collapse) is used in Figure 2f of the manuscript.

Monomer association/dissociation rates

The rate of monomer association is given by

\[ r_{\text{mono}} = a[X_1] \sum_{i=2}^{\infty} [X_i] \tag{S33} \]

Using the fact that concentrations of aggregates in equilibrium can be expressed in terms of the monomer concentration by

\[ [X_i]_\text{eq} = \frac{\sigma}{K_e} (K_e[X_1]_\text{eq})^i \tag{S34} \]

and standard sums yields

\[ r_{\text{mono}} = a[X_1] \sum_{i=2}^{\infty} [X_i] = b[X_1] \sigma \frac{(K_e[X_1])^2}{1-K_e[X_1]} \tag{S35} \]

As \( 1 - K_e[X_1] = \sqrt{\sigma}/\sqrt{K_e c_{\text{tot}} - 1} + O(\sigma) \), the monomer association rate in thermodynamic equilibrium can be approximated by

\[ r_{\text{mono}} \approx \frac{b}{K_e} \sqrt{\sigma(K_e c_{\text{tot}} - 1)} \tag{S36} \]

This expression for the rate of monomer association (and equally the rate of monomer dissociation) is used in Figure 2f of the manuscript.
**Coagulation/fragmentation rates**

The rate of coagulation in thermodynamic equilibrium is given by

\[
r_{\text{coag}} = \frac{a}{2} \left( \sum_{i=2}^{\infty} [X_i] \right)^2
\]  
(S37)

Using again Eq. (S34) for the aggregate concentrations in combination with standard sums yields

\[
r_{\text{coag}} = \frac{a}{2} \left( \sum_{i=2}^{\infty} [X_i] \right)^2 = \frac{a}{2} \left( \frac{\sigma(K_e[X_1])^2}{K_e(1-K_e[X_1])} \right)^2
\]  
(S38)

Using again \( 1 - K_e[X_1] = \sqrt{\sigma}/\sqrt{K_e c_{\text{tot}}} - 1 + O(\sigma) \), this can be approximated by

\[
r_{\text{coag}} \approx \frac{a \sigma(K_e c_{\text{tot}}-1)}{2K_e^2}
\]  
(S39)

This expression for the rate of coagulation (and equally the rate of fragmentation) is used in Figure 2f of the manuscript.

**Coagulation/fragmentation versus monomer association/dissociation rates**

The concentration \( c_{\text{tot}} \) for which rates of coagulation and monomer association in equilibrium are equal, i.e., \( r_{\text{coag}} = r_{\text{mono}} \), can thus be solved from

\[
\frac{b}{K_e} \sqrt{\sigma(K_e c_{\text{tot}} - 1)} = \frac{a \sigma(K_e c_{\text{tot}}-1)}{2K_e^2}
\]  
(S40)

This yields

\[
K_e c_{\text{tot}} = 1 + \frac{4}{\sigma}
\]  
(S41)
Figure S13: Typical kinetic Majority Rules curves from which \( t_{50} \)'s in Figure 3d are obtained. a) Net helicity as a function of time for 4 different concentrations. b) Same curves as in part a) with time scaled by \( t_{50} \) and net helicity scaled by initial and final values. Parameters used are \( a = 10^6 \text{ M}^{-1}\text{s}^{-1} \), \( b = 1 \text{ s}^{-1} \), \( \sigma = 10^{-4} \), e.e. = 0.2, and \( v = 2 \). In all cases red curves are for aggregation via monomer associations and dissociations only, while blue curves are for case where also coagulation and fragmentation reactions are taken into account.
Figure S14: Typical kinetic Majority Rules curves from which $t_{50}$'s in Figure 3e are obtained. a) Net helicity as a function of time for 5 different values of the cooperativity $\sigma$. b) Same curves as in part a) with time scaled by $t_{50}$ and net helicity scaled by initial and final values. Parameters used are $a = 10^6 \, M^{-1}\, s^{-1}$, $b = 1 \, s^{-1}$, $c_{tot} = 100 \, \mu M$, e.e.= 0.2, and $v = 2$. In all cases red curves are for aggregation via monomer associations and dissociations only, while blue curves are for case where also coagulation and fragmentation reactions are taken into account.
Figure S15: Typical kinetic Majority Rules curves from which $t_{50}$'s as a function of the enantiomeric excess are obtained. 

a) Net helicity as a function of time for 5 different values of the enantiomeric excess e.e. b) Same curves as in part a) with time scaled by $t_{50}$, i.e. the time at which the scaled net helicity equals 0.5, and net helicity scaled by initial and final values. c) $t_{50}$'s as a function of the enantiomeric excess. Parameters used are $a = 10^6 \, M^{-1}s^{-1}$, $b = 1 \, s^{-1}$, $\sigma = 10^{-4}$, $c_{tot} = 100 \, \mu M$ and $\nu = 2$. In all cases red curves are for aggregation via monomer associations and dissociations only, while blue curves are for case where also coagulation and fragmentation reactions are taken into account.
Figure S16: Comparison of self-assembly kinetics of seeded supramolecular polymerizations in presence of a competing isodesmic pathway with or without fragmentation and coagulation reactions. a) Simulated time-evolution of the fraction of molecules in cooperative H-aggregates ($\varphi_H$) upon addition of H-aggregate seeds of length 250 to a system of kinetically trapped isodesmic J-aggregates consisting of $10^6$ monomers. The legend indicates the ratio between the numbers of monomers in the seeds and in the metastable isodesmic system. The line color indicates the growth mechanism, i.e., the red data correspond to the case where only monomer associations and dissociations are considered, while the purple data correspond to the case including also fragmentation and coagulation reactions for the J-aggregates. b) Log-log plot of the rate of increase in $\varphi_H$ during the initial 200 seconds as a function of seed concentration after mixing. The linear relationship (slope 1.00) indicates that the supramolecular polymerization is first order with respect to the seed concentration. Clearly, the presence of fragmentation and coagulation reactions for the J-aggregates hardly affects the growth rate of the cooperative H-aggregates.
Figure S17: Comparison of the self-assembly kinetics of cooperative supramolecular polymerizations in a single pathway with or without fragmentation and coagulation reactions. Simulated time-evolution of the fraction of molecules in aggregates of various length, where $X_i$ are aggregates consisting of $i$ monomers. The solid lines represent a cooperative supramolecular polymerization which proceeds via only monomer associations and dissociations, while the dashed lines represent a cooperative supramolecular polymerizations which proceeds also via additional fragmentation and coagulation events. In case only monomer association and dissociation reactions are possible, in the initial phase of the aggregation starting from monomers, lots of oligomers are formed. Once the monomers are (almost) depleted the growth of oligomers/polymers slows down since additional monomers to grow are only available after a dissociation step. In case also coagulation and fragmentation reactions are possible, the growth can continue immediately by coagulations of oligomers. This explains the intermediate plateau in the mean aggregate length in case of exclusively monomer associations/dissociations and its absence in case of additional coagulations/fragmentations, as observed in Figure 2d in the manuscript. Results are obtained from deterministic ODE simulations with $a = c = 10^6 \, \text{M}^{-1}\text{s}^{-1}$, $b = 1 \, \text{s}^{-1}$, $\sigma = 10^{-2}$ and $K_e c_{tot} = 10$. 
S4  Movie descriptions

**Movie 1: The simulation approach: Isodesmic supramolecular polymerization reaction by reaction**

An isodesmic supramolecular polymerization is followed reaction by reaction in a system initially containing just 60 monomers over 1000 reactions. At the left hand side the aggregation process proceeds only via monomer associations and dissociations, while at the right hand side also coagulations (recombinations of existing aggregates) and fragmentations (breakage of existing aggregates) occur. The cylinders indicate the numbers of molecules present as monomers and present in aggregates, respectively, while all aggregates are also visualized individually. Due to the small number of molecules and the fact that only a single reaction occurs between two consecutive frames of the movie, not only the difference in self-assembly kinetics of the two processes can be well observed, but also the simulation concept. That is, based on the current state of the system it is determined which reactions are possible and what the propensities of those reactions are. Then one reaction is selected randomly proportional to those propensities. The selected reaction is then performed by updating the state of the system accordingly. A process that is repeated in this case 1000 times. Parameters used are \( a = 10^6 \text{ M}^{-1} \text{s}^{-1}, \ b = 1 \text{ s}^{-1} \text{ and } x_i(0) = c_{\text{tot}} = 100 \ \mu M. \)

**Movie 2: The influence of coagulation and fragmentation on the self-assembly kinetics of an isodesmic supramolecular polymerization**

An isodesmic supramolecular polymerization is followed in a system initially containing 1000 monomers over 9000 reactions. At the left hand side the aggregation process proceeds only via monomer associations and dissociations, while at the right hand side also coagulations (recombinations of existing aggregates) and fragmentations (breakage of existing aggregates) occur. The cylinders indicate the numbers of molecules present as monomers and present in aggregates, respectively, while all aggregates are also visualized individually. Due to the larger number of molecules, as compared to Movie 1, a better distribution of the aggregate sizes is visible. The movie illustrates that in the presence of coagulations and fragmentations the supramolecular polymerization equilibrates much faster than with only monomer associations and dissociations, but also that the equilibrium aggregate size distribution with and without coagulation and fragmentation reactions are equal. Nine reactions took place between two consecutive frames. Parameters used are \( a = 10^6 \text{ M}^{-1} \text{s}^{-1}, \ b = 1 \text{ s}^{-1} \text{ and } x_i(0) = c_{\text{tot}} = 10 \ \mu M. \)

**Movie 3: The role of coagulation and fragmentation on the self-assembly kinetics of a cooperative supramolecular polymerization**

A cooperative supramolecular polymerization is followed in a system initially containing 1000 monomers over 99,900 reactions. A dimeric nucleus size is considered and the degree of cooperativity is given by the dimensionless cooperativity factor \( \sigma = 10^{-3}. \) At the left hand side the aggregation process proceeds only via monomer associations and dissociations, while at the right hand side also coagulations (recombinations of existing aggregates) and fragmentations (breakage of existing aggregates) occur. The cylinders indicate the numbers of molecules present as monomers and present in aggregates, respectively, while all aggregates are also visualized individually. Apart from the cooperativity factor \( \sigma \) all
parameters are equal to those in Movie 2 of the isodesmic supramolecular polymerization. The movie thus nicely illustrates that in a cooperative supramolecular polymerization much longer aggregates are being formed. Nine hundred ninety nine reactions took place between two consecutive frames. Parameters used are $a = 10^6 \text{M}^{-1} \text{s}^{-1}$, $b = 1 \text{s}^{-1}$, $\sigma = 10^{-3}$ and $x_i(0) = c_{\text{tot}} = 10 \mu M$.

**Movie 4: The influence of coagulation and fragmentation on the cooperative supramolecular copolymerization kinetics of Majority Rules**

The supramolecular copolymerization kinetics of a Majority Rules experiment is followed over 5,000,000 reactions. In such a supramolecular copolymerization two enantiomers (one here colored purple, the other green) can assemble into two types of helical aggregates, one here denoted as P-type, the other as M-type. Although the purple monomers prefer the P-type helical aggregates while the green monomers prefer the M-type helical aggregates, the monomers can assemble in either aggregate. The initial system for the Majority Rules experiment is made by combining two equilibrated smaller systems, i.e., the final states of two earlier simulations. Here an equilibrated system consisting of 6500 purple molecules (present as monomers and almost exclusively P-type aggregates) was combined with one containing 3500 green molecules (present as monomers and almost exclusively M-type aggregates). At the left hand side the mixing of the supramolecular polymers proceeds only via monomer associations and dissociations, while at the right hand side also coagulations (recombinations of existing aggregates) and fragmentations (breakage of existing aggregates) occur. The cylinders indicate the numbers of molecules present as monomers and present in the two types of aggregates, respectively, while all aggregates are also visualized individually, also depicting their helicity. The movie illustrates that the kinetics of a Majority Rules experiment (i.e. of the chiral amplification) is highly increased by the presence of coagulation and fragmentation reactions as with exclusively monomer associations and dissociations existing supramolecular polymers can only mix from the ends and to mix also the interiors those already mixed ends first need to be depolymerized again. Five thousand reactions took place between two consecutive frames. Parameters used are $a = 10^6 \text{M}^{-1} \text{s}^{-1}$, $b = 1 \text{s}^{-1}$, $\sigma = 10^{-3}$, $v = 2$ and $x_i(0) = c_{\text{tot}} = 10 \mu M$.

**Movie 5: The influence of fragmentation and coagulation on self-assembly kinetics in the presence of competing pathways**

A supramolecular polymerization is followed over 200,000 reactions in a system initially containing 2000 monomers of a single type that can assemble into two types of aggregates: one meta-stable (kinetically-controlled) product Y and a thermodynamically favored aggregate X. A dimeric nucleus size is considered for both aggregate types although the meta-stable aggregates are slightly less cooperative than the thermodynamically favored aggregates. At the left hand side the aggregation process proceeds only via monomer associations and dissociations, while at the right hand side also coagulations (recombinations of existing aggregates) and fragmentations (breakage of existing aggregates) occur. The cylinders indicate the numbers of molecules present as monomers and present in aggregates, respectively, while all aggregates are also visualized individually. The movie illustrates that the formation of the thermodynamically favored aggregates is highly slowed down by the presence of coagulation and fragmentation reactions as these reactions accelerate the formation of longer meta-stable aggregates.
Two hundred reactions took place between two consecutive frames. Parameters used are \( a = a' = 10^6 \, M^{-1}s^{-1}, b = 1 \, s^{-1}, \sigma = 2 \times 10^{-3}, b' = 1.25 \, s^{-1}, \sigma' = 10^{-2} \) and \( x_i(0) = c_{\text{tot}} = 50 \, \mu M \).

**Movie 6: Stochastic simulation of the self-assembly kinetics in seeded supramolecular polymerizations**

A supramolecular polymerization proceeding exclusively via monomer associations and dissociations is followed where repeatedly (twice in this movie) one equivalent of equilibrated isodesmic meta-stable \( J \)-aggregates is added to a solution initially containing 10 seeds of length 100 of highly cooperative \( H \)-aggregates. The cylinders indicate the numbers of molecules present as monomers and present in aggregates, respectively, while all aggregates are also visualized individually. Monomers are depicted at the left hand side, meta-stable \( J \)-aggregates in the middle and \( H \)-aggregates at the right hand side. First, the \( H \)-seeds are followed over 2000 seconds. Subsequently, another 1000 molecules are added as equilibrated \( J \)-aggregates. These added molecules are colored darker for visualization purposes, but interact equally to the original molecules. After another 2000 seconds, the volume is again doubled by adding another 2000 molecules as equilibrated \( J \)-aggregates. These molecules are colored equally to the molecules present in the initial seeds. The movie illustrates that the repeated addition of kinetically trapped \( J \)-aggregates to seeds of highly cooperative \( H \)-aggregates can give rise to supramolecular block copolymers. Parameters used are \( a = a' = 10^6 \, M^{-1}s^{-1}, b = 0.1 \, s^{-1}, \sigma = 10^{-9}, b' = 1 \, s^{-1}, \sigma' = 1 \) and \( x_i(0) = c_{\text{tot}} = 100 \, \mu M \). Fifty, a hundred and two hundred fifty reactions took place between two consecutive frames in the first, second and third part, respectively.