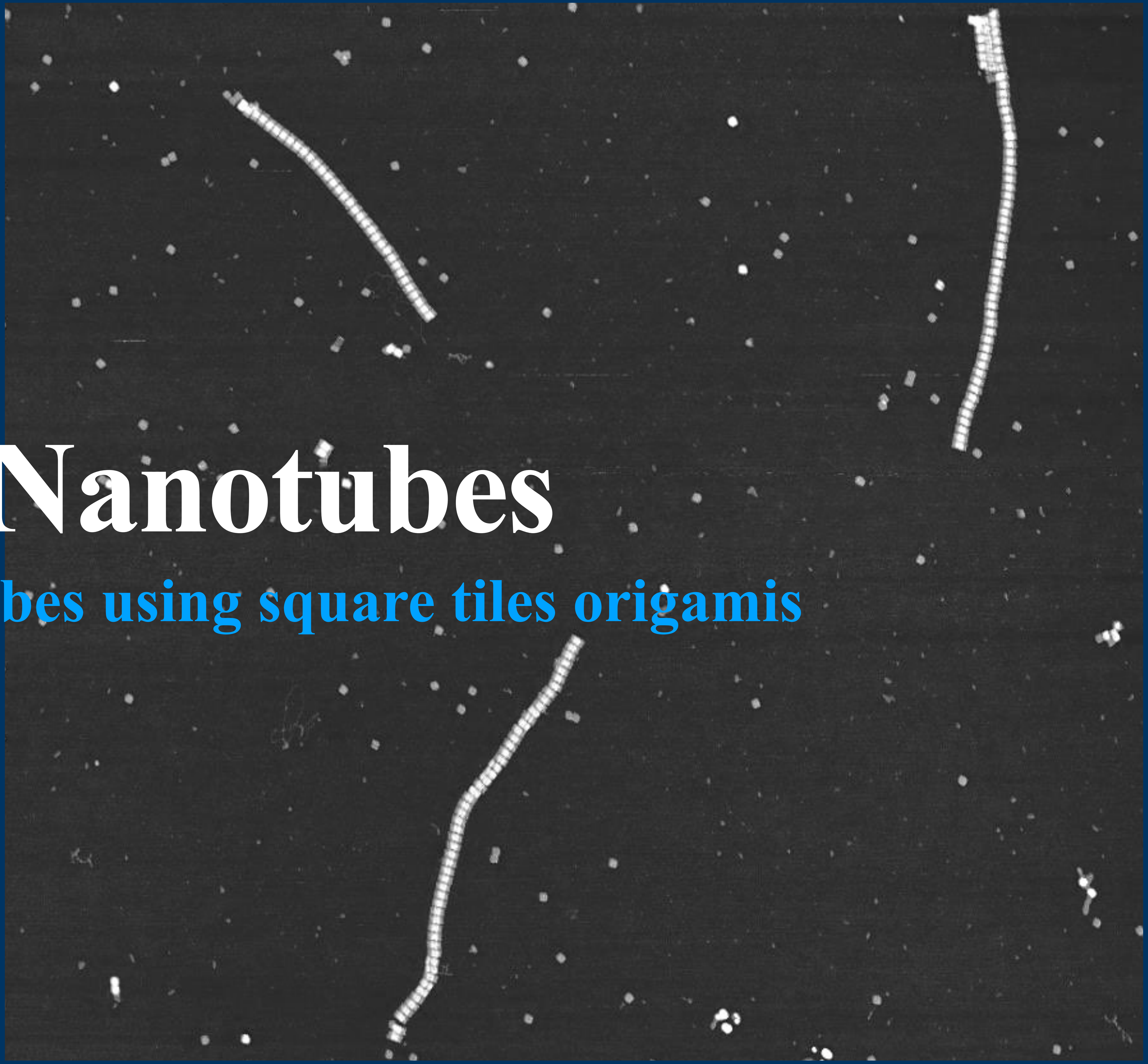
DNA Origami Nanotubes

The formation of DNA nanotubes using square tiles origamis



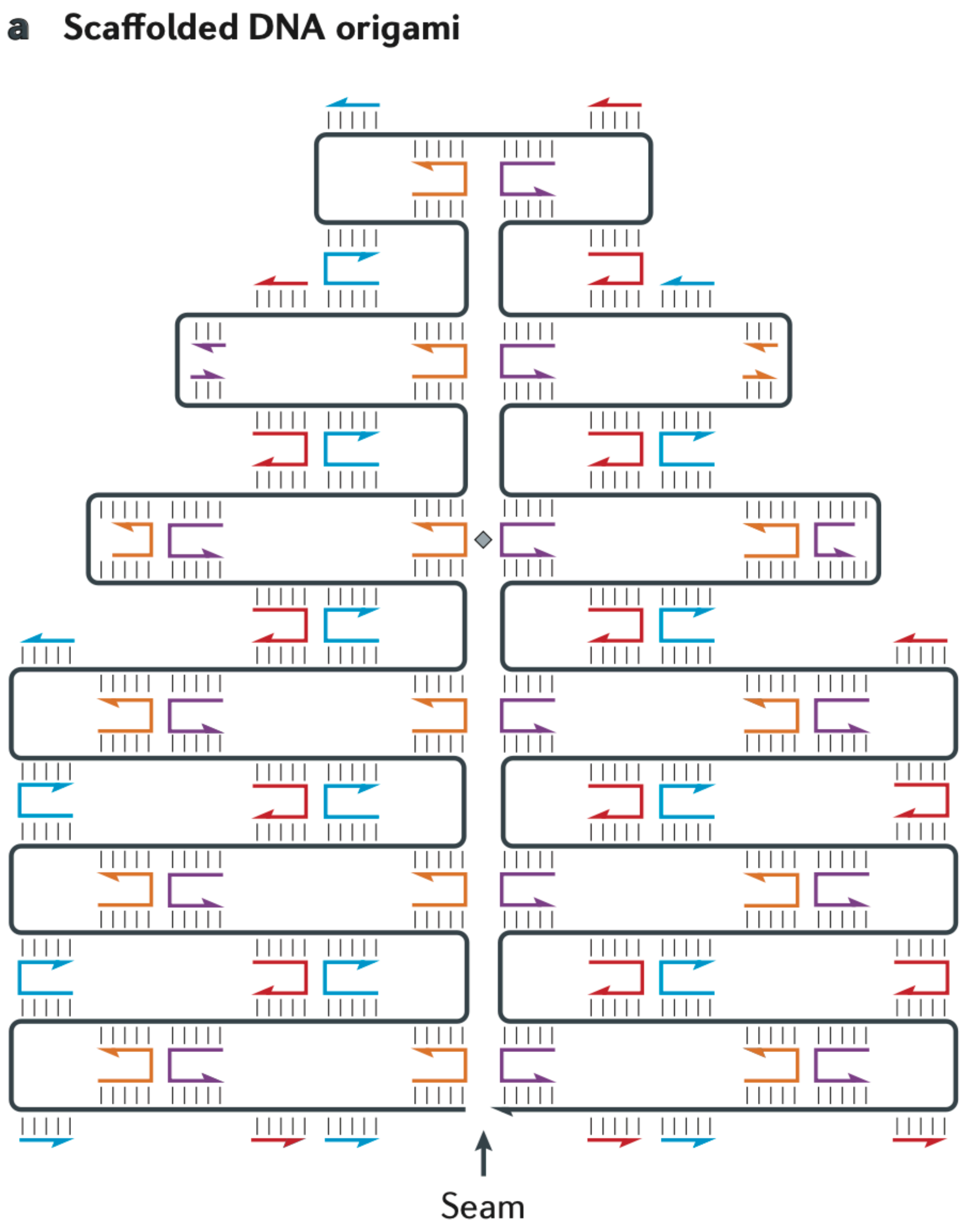
8.29.2023

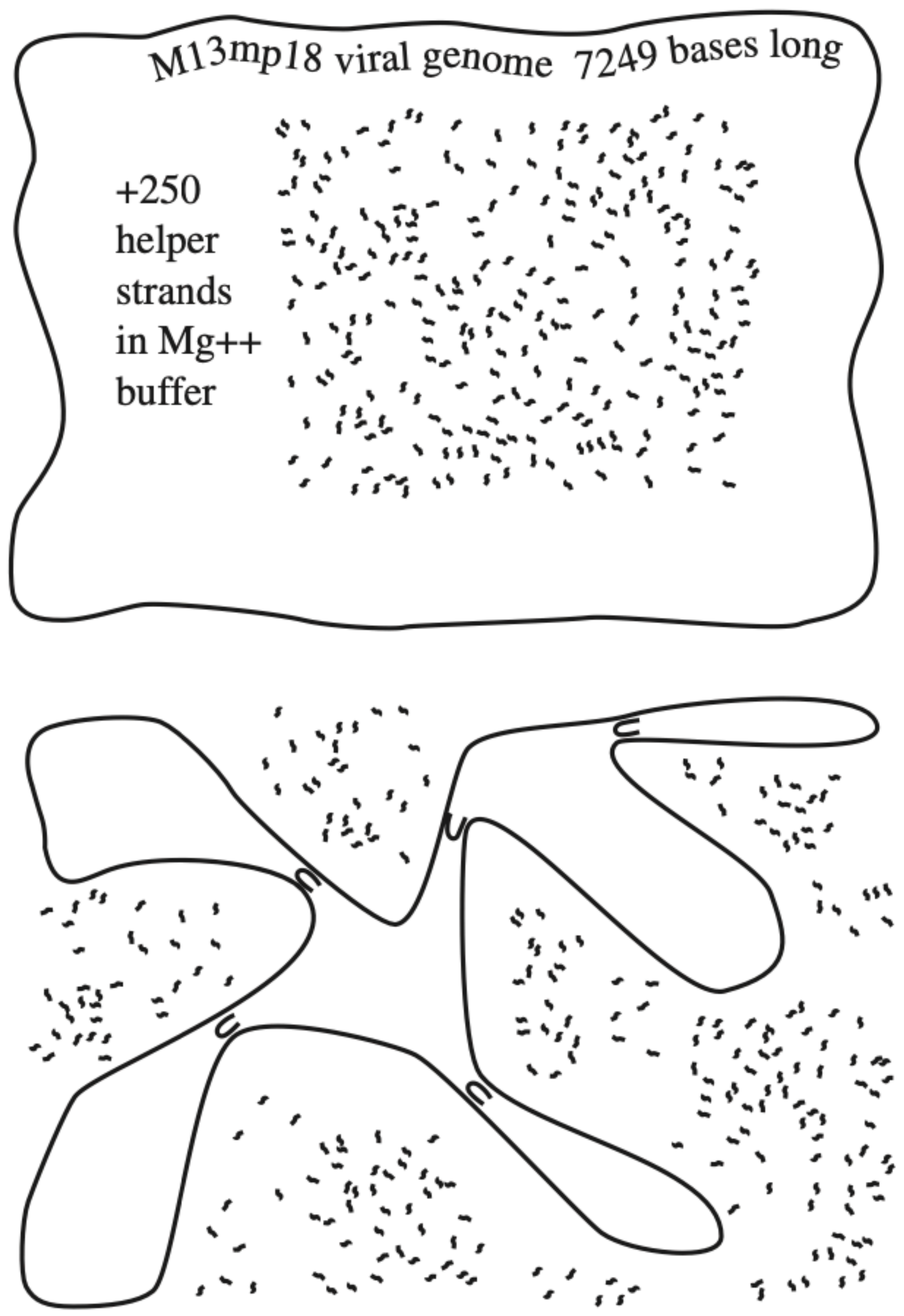
Robert Xi

Basic Principles

DNA Origami

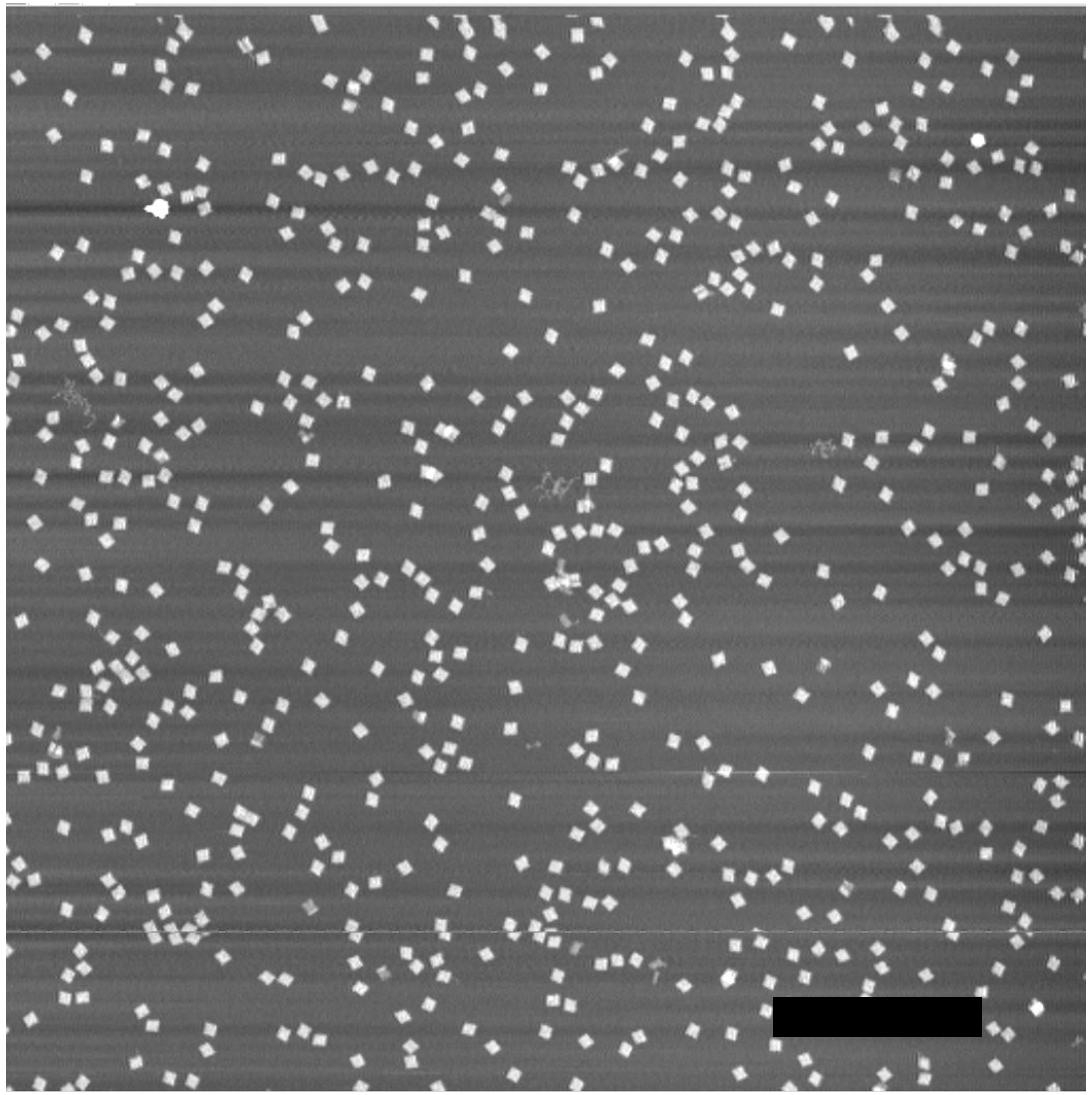
- Long single-stranded DNA M13 “Scaffold” + short single strand DNA “staple strand”



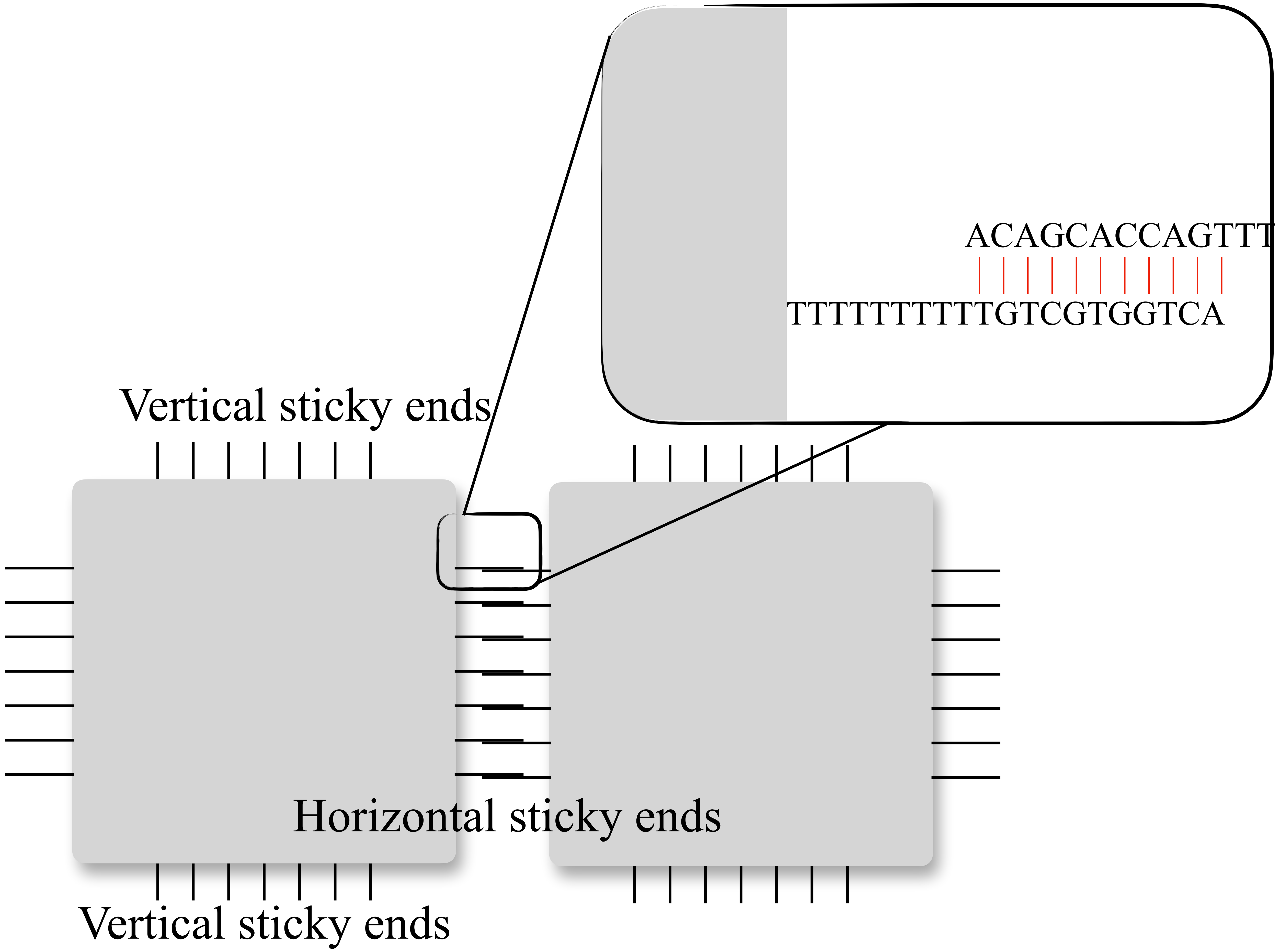


Basic Principles

DNA Origami — square tile



Square Tile without sticky ends Under AFM, scale bar length 1µm



Basic Principles

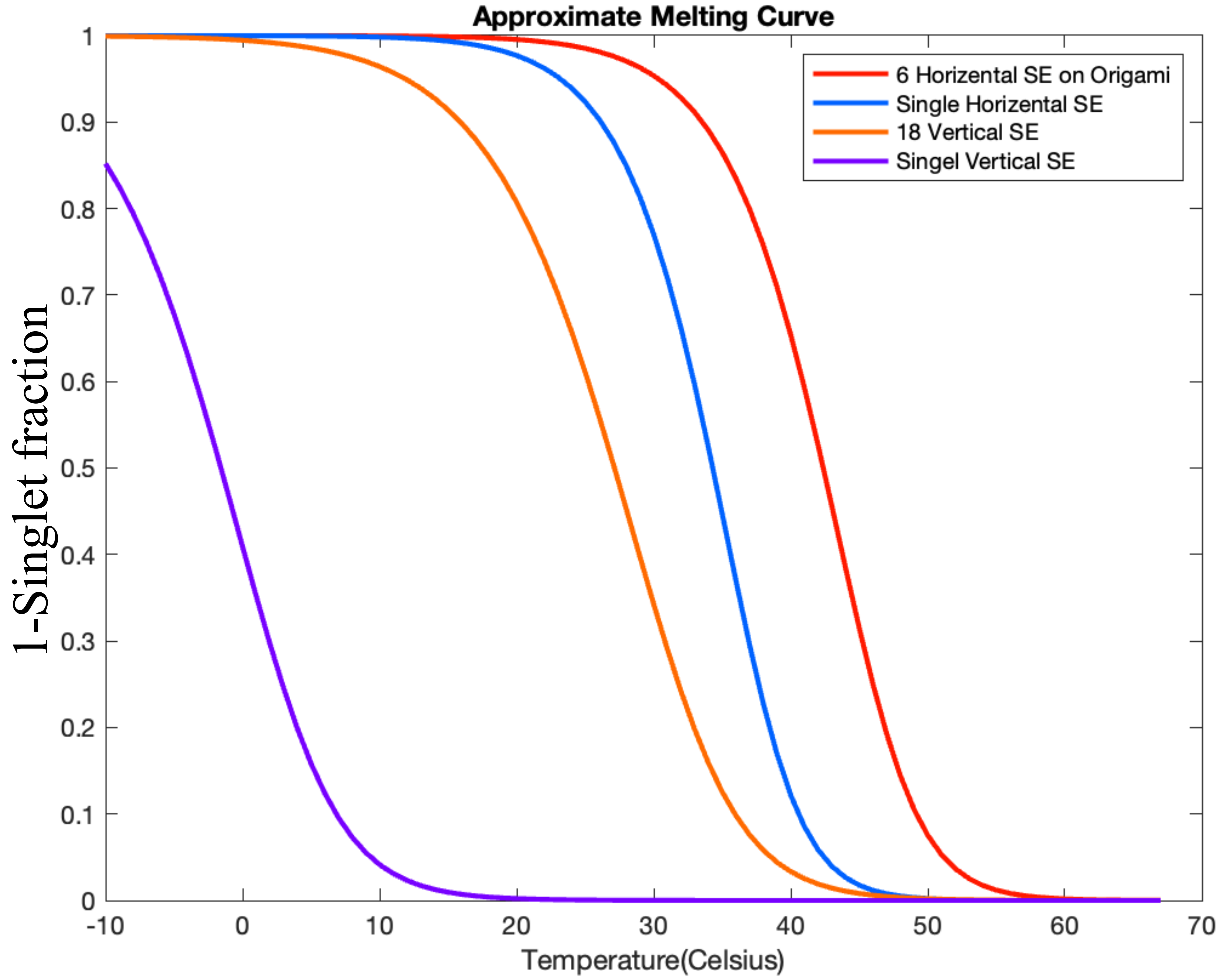
Melting Curve & Melting Temperature

- 1-Fraction of singlet f

$$f = 1 - \frac{-1 + \sqrt{4x+1}}{2x}$$

$$x = Ce^{-\frac{\Delta H - T\Delta S}{k_B T}}$$

- C — Concentration
- T — Temperature

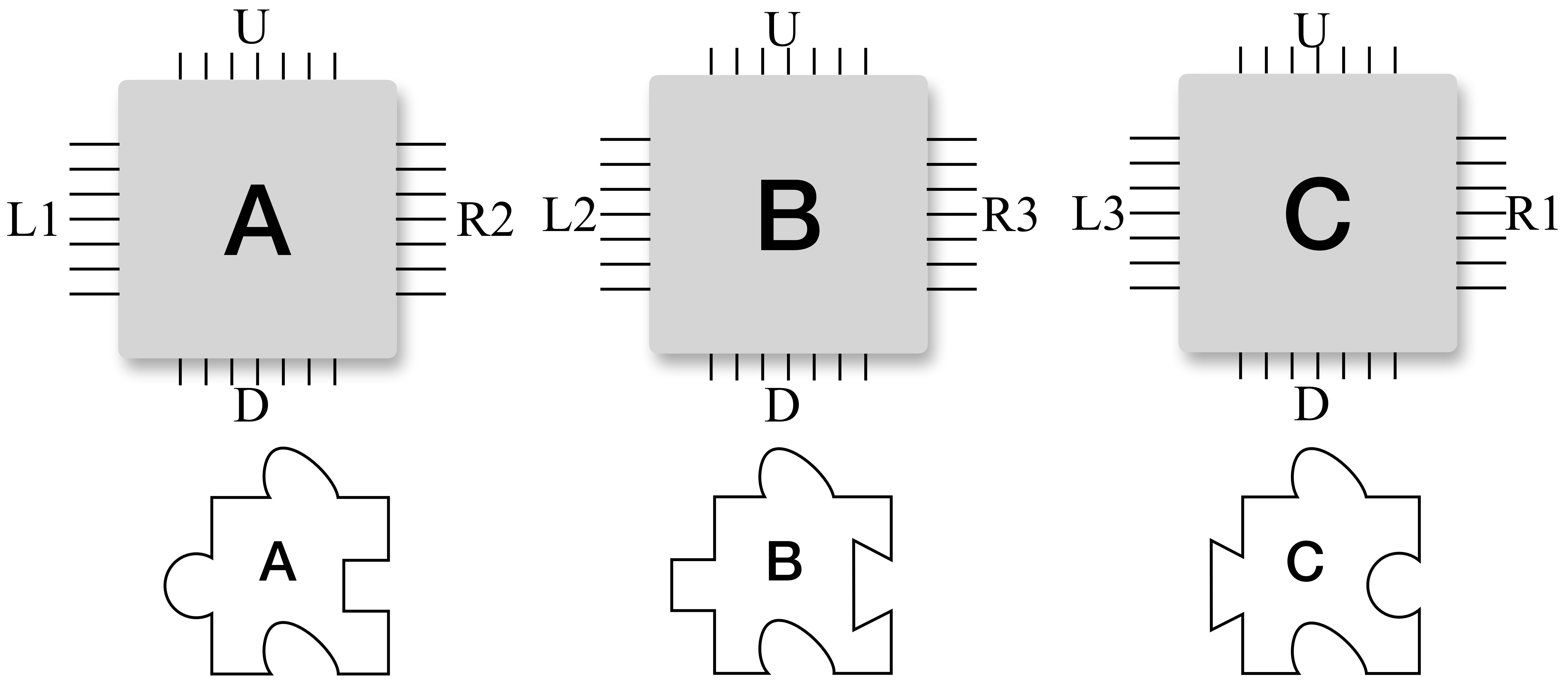


- Melting temperature is defined as the temperature when $f = 0.5$.

Single horizontal sticky ends : 45°C
Single Vertical sticky ends: 14.4°C

Basic Principles

A, B, C Square Tiles

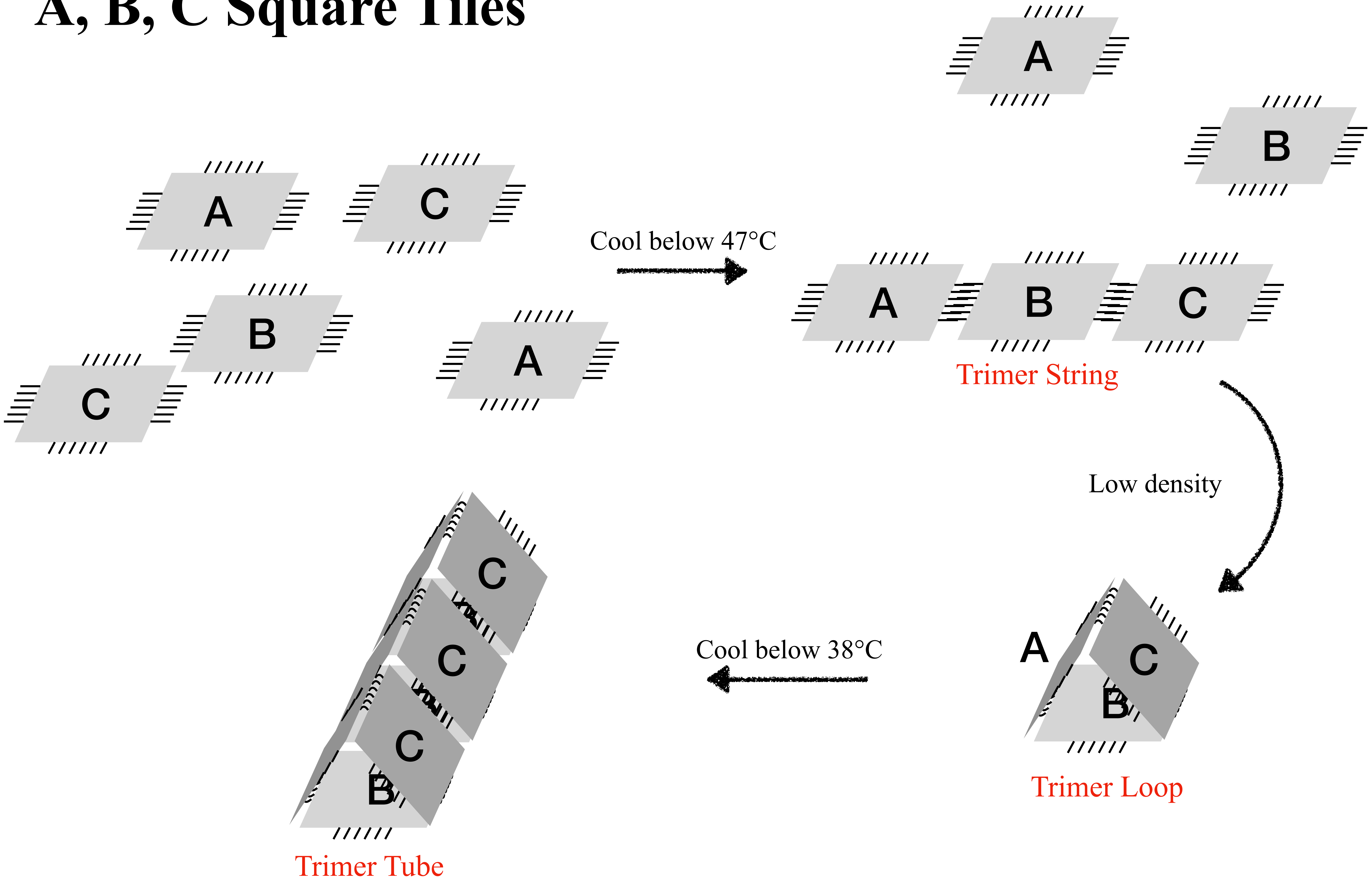


Approx. Conjugate DNA strands pairs Melting Temp

47°C	38°C
L1-R1	
L2-R2	U-D
L3-R3	

Basic Principles

A, B, C Square Tiles

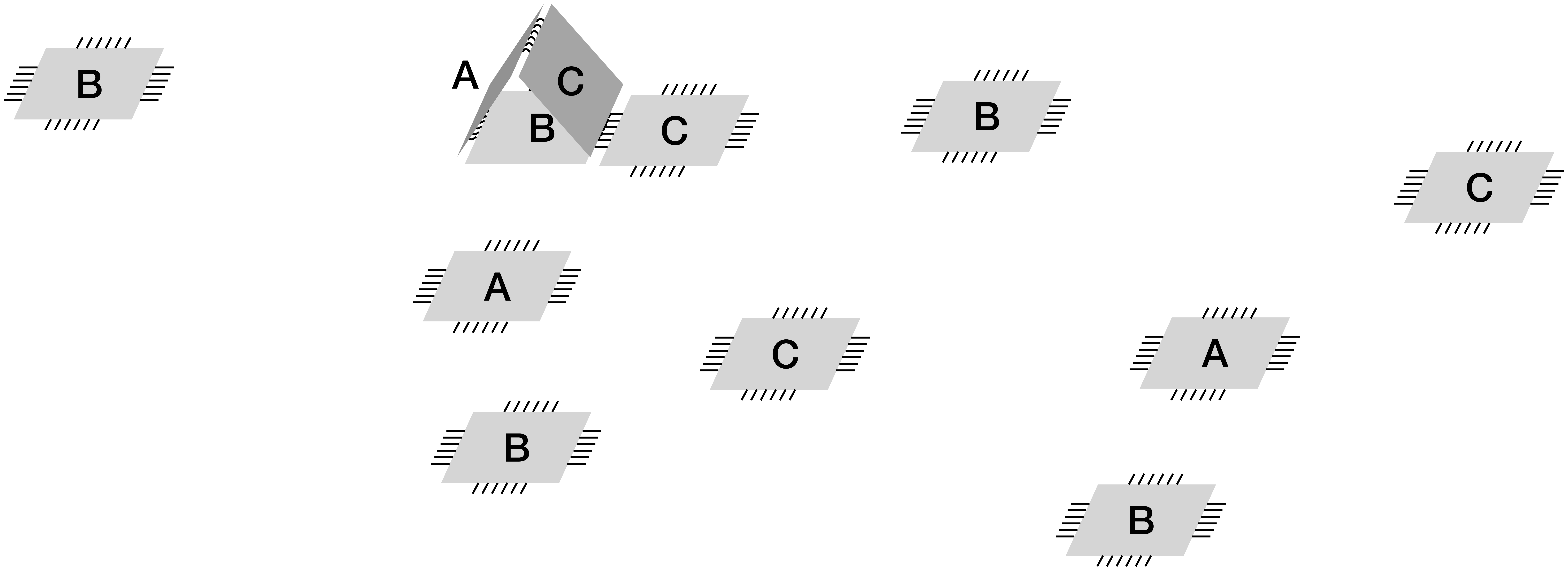


Approx. Conjugate DNA strands pairs Melting Temp

47°C	38°C
L1-R1	
L2-R2	U-D
L3-R3	

Basic Principles

Formation of ABC Seed (PolyT)



Formation of ABC seed

Theoretical Calculation

Number of square tiles consist in a single string: i, j, r. (Smoluchowski coagulation equation)

$$\textbf{Assumption: } J_r = \underbrace{\frac{1}{2}\sum_{i+j=r} k_{ij} C_i C_j f^2}_{\textbf{form into r}} - \underbrace{\sum_{n=1}^{\infty} k_{rn} C_r C_n f^2}_{\textbf{form into r+}} - \underbrace{\alpha_r C_r}_{\textbf{form loop}} \quad \textbf{(rate of forming / loosing string)}$$

J_r — number of length string r increased/decreased per m^3 per sec, $[1/m^3 s]$;

k_{ij} — constant depends on i, j, $[m^3/s]$, ($k_{ij} = k_{ji}$);

C_i, C_j — concentration of i, j, $[1/m^3]$

f — 1-singlet fraction given by melting curve

$$K = \begin{bmatrix} 0 & 0 & \alpha_3 & \dots & 0 \\ 0 & k_{11} & k_{12} & \dots & k_{1j} \\ \alpha_3 & k_{21} & k_{22} & \dots & k_{2j} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & k_{i1} & k_{i2} & \dots & k_{ij} \end{bmatrix}$$

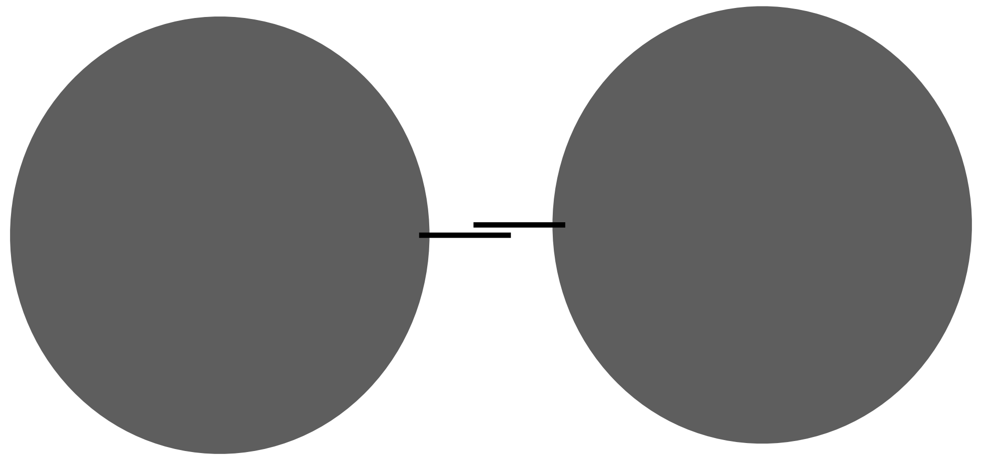
Assumption: $J_r = \alpha_r C_r$ **(rate of forming Loop)**

α_r — constant depends on r, $[1/s]$

Formation of ABC seed

Calculate k_{ij}

$J_{ij} = k_{ij} C_i C_j$



Time for i, j combined into i + j. $\tau_{ij} = \tau_l(\underbrace{1}_{\text{time for them to meet for the first time}} + \underbrace{\frac{\tau_r}{\tau_c}}_{\text{\# of times for them to meet until combined}}), [sm^3]$:

— translational search time $\tau_l = \frac{3 l_i l_j \mu}{2 k_B T (l_i + l_j)^2} \frac{1}{C_i C_j}, [sm^3]$

— rotational search time $\tau_r = \frac{1}{D_\theta} \frac{ln4}{\bar{\alpha}} = \frac{8\pi\mu}{k_B T} \frac{ln4}{\bar{\alpha}} \frac{l_i^3 l_j^3}{l_i^3 + l_j^3}, [s]$

— collision time $\tau_c = \frac{H}{6 D_{ij}} = \frac{H\pi\mu}{k_B T} \frac{l_i l_j}{l_i + l_j}, [s]$

— DNA hybridization time assume instant

- D_θ: effective rotational diffusion constant
- D_{ij}: effective translational diffusion constant
- H: length square of a Sticky ends $\approx 2.5 \times 10^{-17} m^2$
- l_i: radius of i, which is half the length of the string $i \times 2.5 \times 10^{-8} m$
- $\bar{\alpha}$: relative capture area ≈ 0.47
- μ: dynamic viscosity $\approx 0.6 \times 10^{-3} [Ns/m^2]$

Formation of ABC seed

Calculate k_{ij}

- τ_l: translational search time
- τ_c: collision time
- τ_r: rotational search time

Time for i, j combined into i + j, $\tau_{ij} = \tau_l(1 + \frac{\tau_r}{\tau_c})$

$$\tau_{ij} = \frac{1}{M}\left(\frac{l_i l_j}{(l_i + l_j)^2} + N\frac{l_i^3 l_j^3}{(l_i^3 + l_j^3)(l_i + l_j)}\right)\frac{1}{C_i C_j}, \quad M = \frac{2k_B T}{3\mu}, N = \frac{16ln2}{H\bar{\alpha}}$$

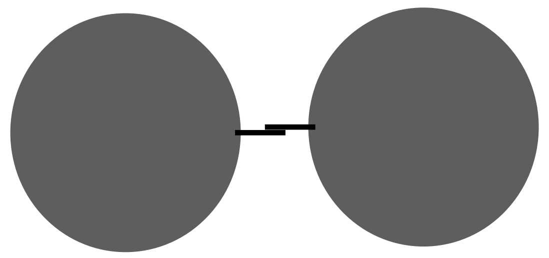
since $J_{ij} = 1/\tau_{ij}$, and $J_{ij} = k_{ij}C_iC_j$ J_{ij} formation of (i+j) string by combining i, j string

$$J_{ij} = \left(\frac{M(l_i + l_j)^2}{l_i l_j + N\frac{l_i^3 l_j^3 (l_i + l_j)}{(l_i^3 + l_j^3)}}\right)C_iC_j = k_{ij}C_iC_j \quad \Rightarrow \quad \boxed{k_{ij} = \frac{M(l_i + l_j)^2}{l_i l_j + N\frac{l_i^3 l_j^3 (l_i + l_j)}{(l_i^3 + l_j^3)}}}$$

Formation of ABC seed

Calculate k_{ij}

$$k_{ij} = \frac{M(l_i + l_j)^2}{l_i l_j + N\frac{l_i^3 l_j^3 (l_i + l_j)}{(l_i^3 + l_j^3)}}$$



For one sticky end on each particle

In our case, there are three pairs of different sticky ends.

$$k_{ij} = \frac{M(l_i + l_j)^2}{l_i l_j + N\frac{l_i^3 l_j^3 (l_i + l_j)}{(l_i^3 + l_j^3) \cdot n_{ij}}} \cdot \frac{1}{3}$$

A+BC = ABC/BCA

A+B = AB

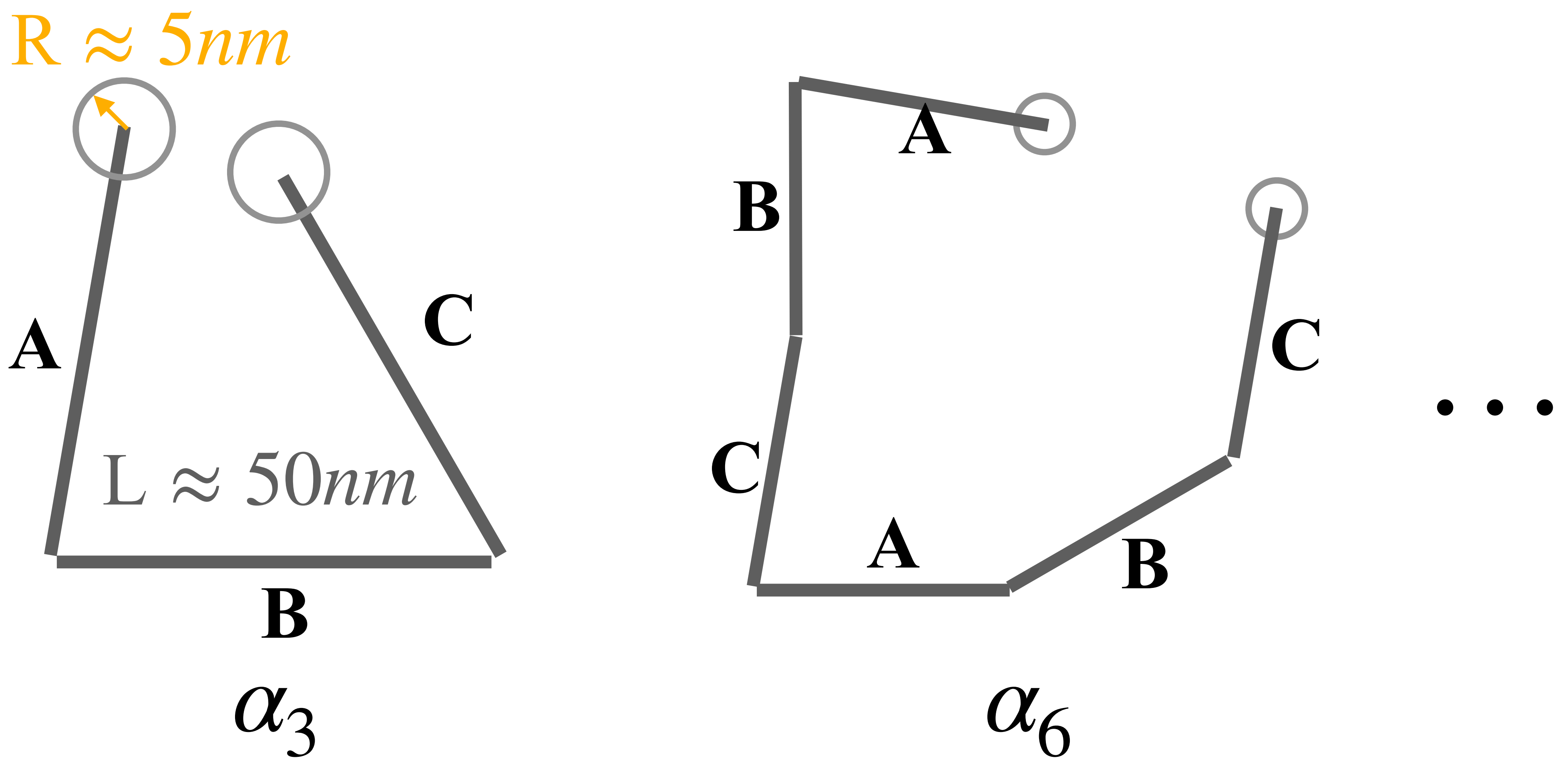
Configurational constant $n_{ij} = \begin{cases} 2, & \text{if } \mathrm{mod}(\mathrm{i} + \mathrm{j}, 3) = 0 \\ 1, & \text{else.} \end{cases}$

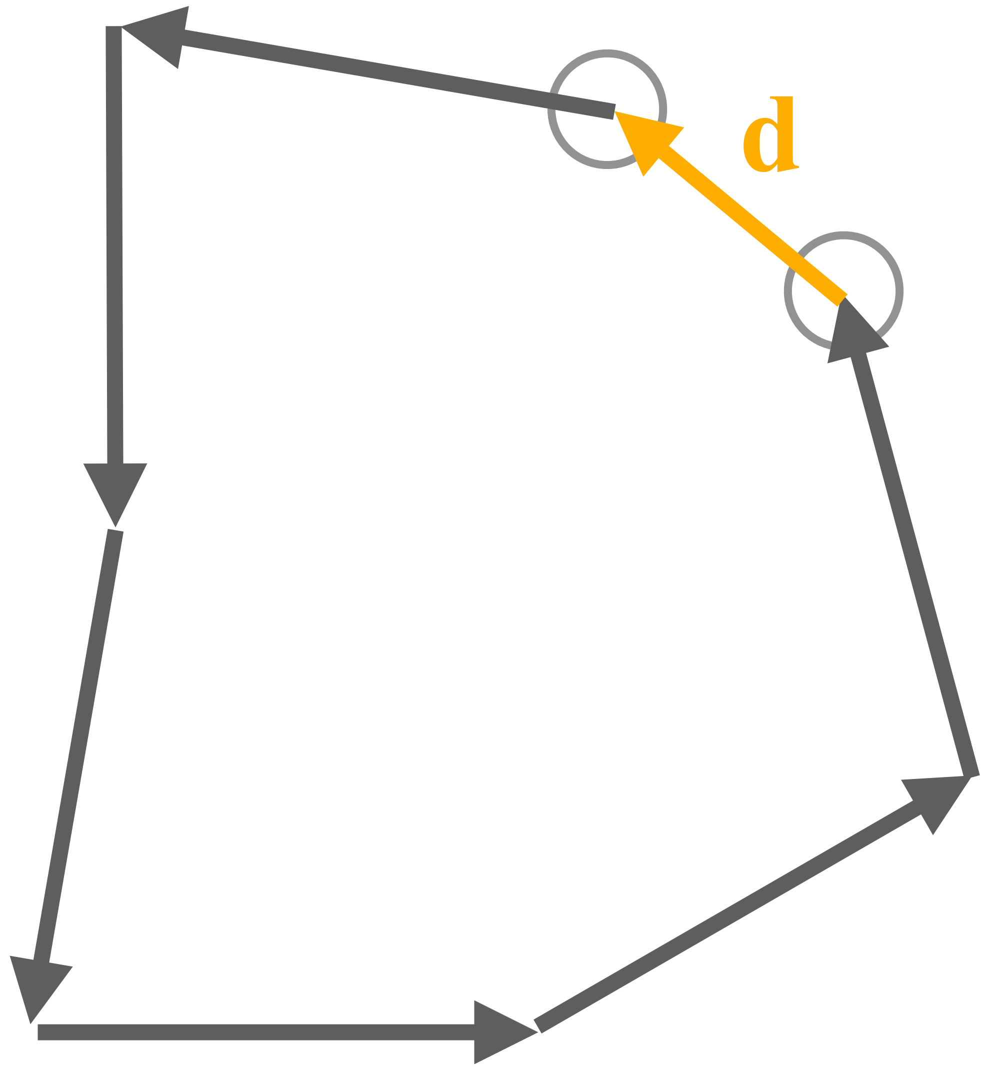
Formation of ABC seed

Calculate α_r — proportion of string at given time that their two ends are close enough to form a loop

$$J_r = k_{0r} C_r = \alpha_r C_r,$$

$$\alpha_r = \begin{cases} 0 < \alpha_r < 1, & \text{if mod(r, 3) = 0} \\ 0, & \text{else.} \end{cases}$$





each vector has random orientation in 2D

if $d < 2R$, it form loop;
if $d > 2R$, it doesn't;
Compute using Matlab

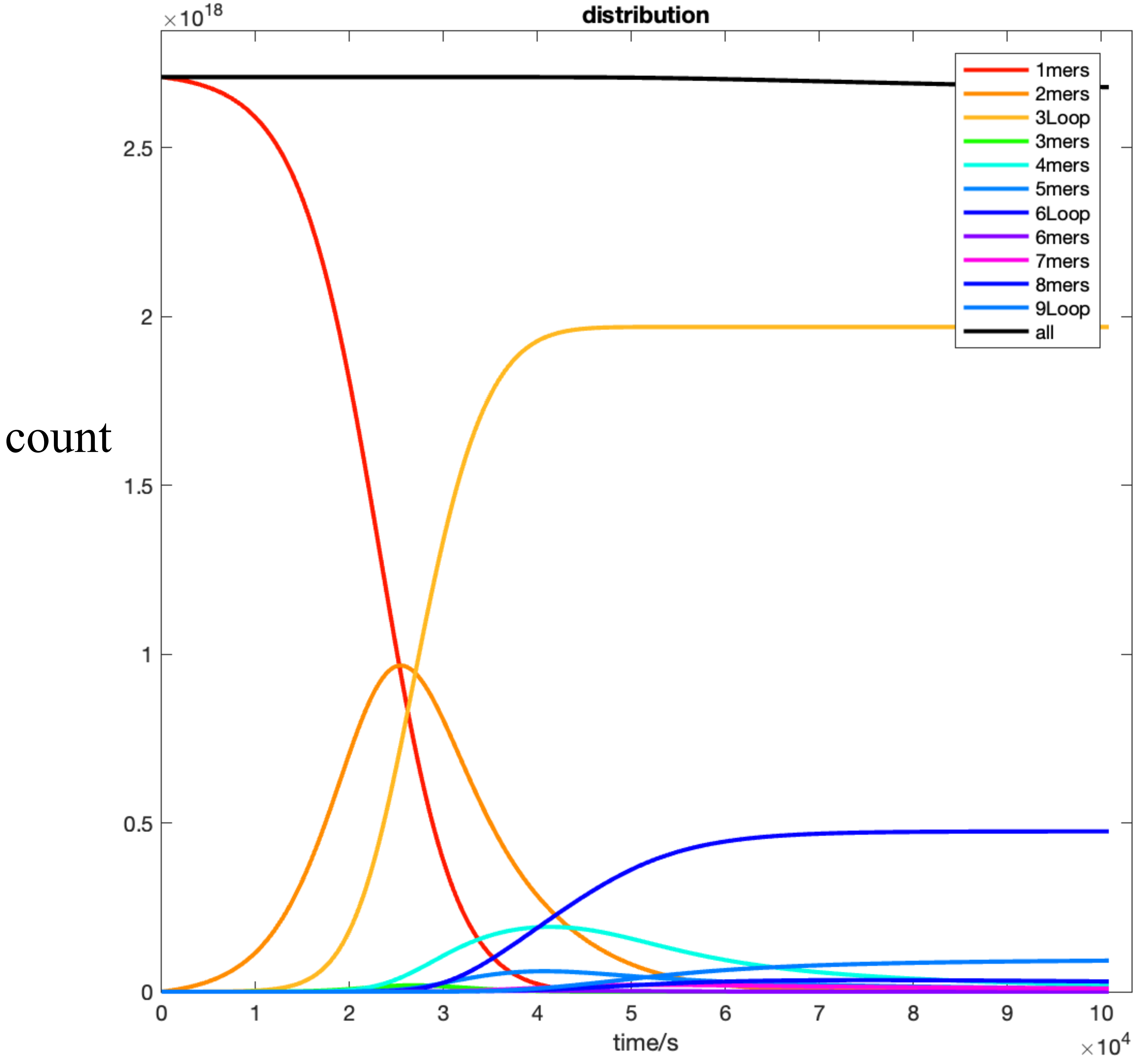
α_3	0.0074
α_6	0.0065
α_9	0.0041
α_{12}	0.0031
α_{15}	0.0025

$$K = \begin{bmatrix} 0 & 0 & \alpha_3 & \dots & 0 \\ 0 & k_{11} & k_{12} & \dots & k_{1j} \\ \alpha_3 & k_{21} & k_{22} & \dots & k_{2j} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & k_{i1} & k_{i2} & \dots & k_{ij} \end{bmatrix}$$

Assumption: 1. hinge is free, 2. They will bind when closer than $2R$

Formation of ABC seed

Simulation



Distribution of sizes across time, 2nM, 1°C/hour, 53°C to 25°C

Assumption:

for horizontal sticky ends,

$\Delta H = -82.8[\text{kcal/mol}]$,

$\Delta S = -222.6[\text{cal/mol s}]$

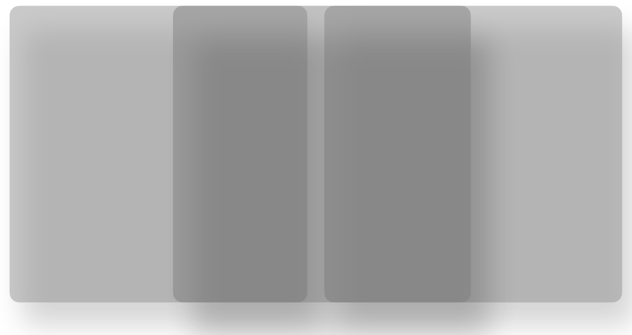
count right after annealing process ends

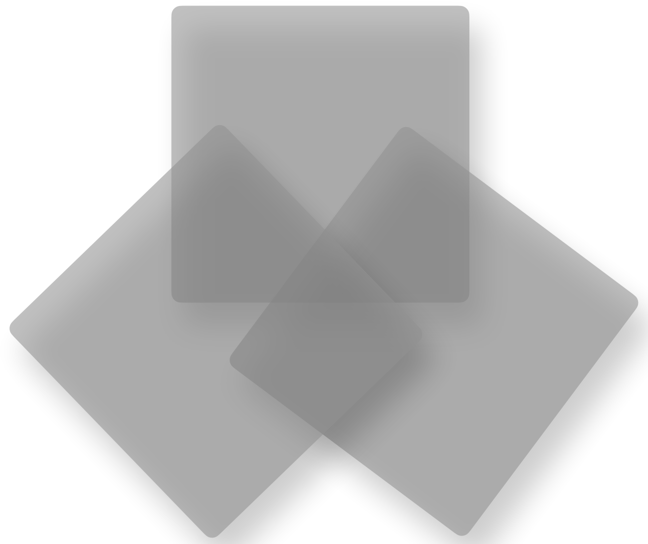
Formation of ABC seed

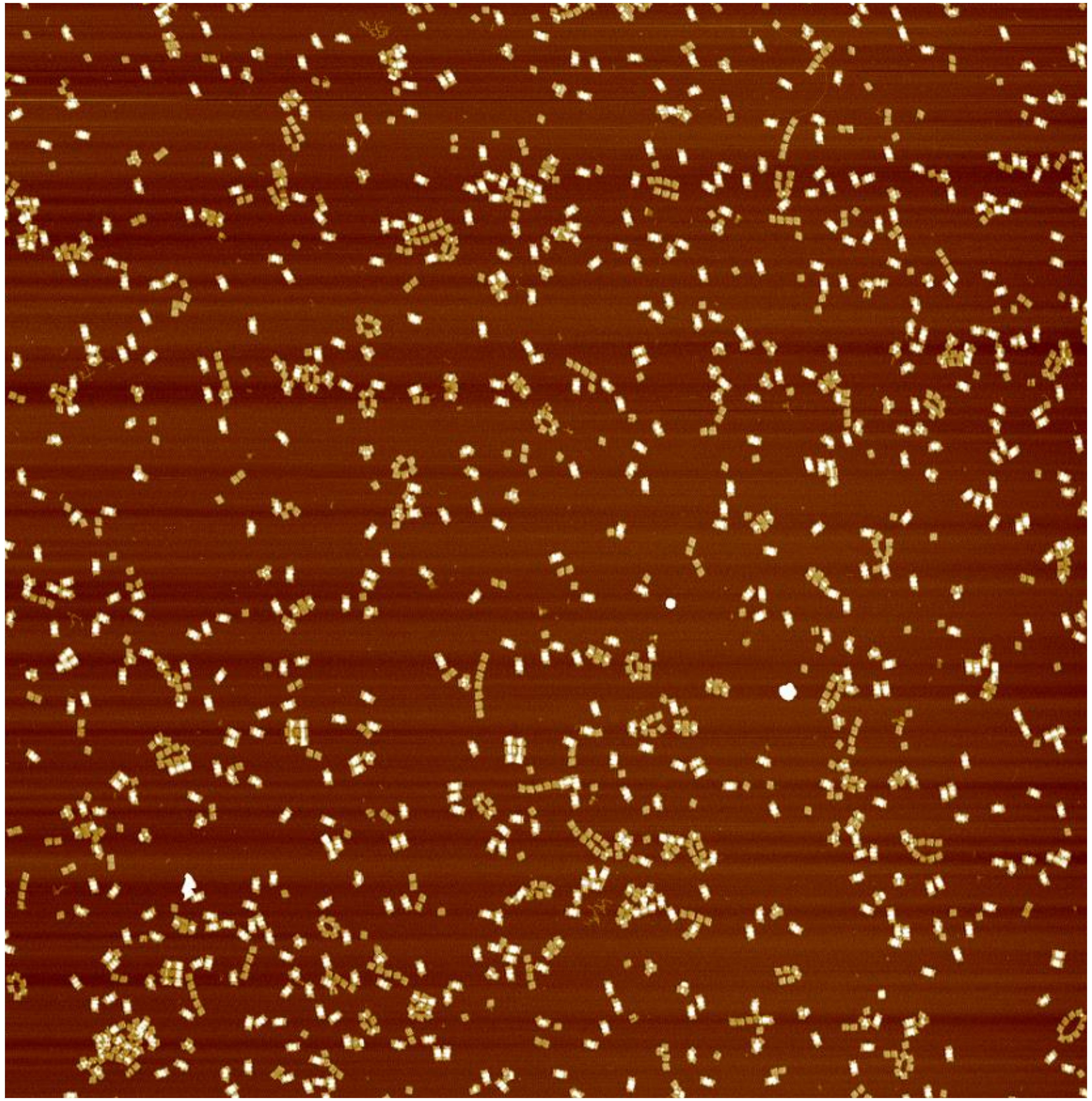
Experiment

AFM result example

1. 2nM /1.5nM A,B,C monomer mixture (that's 6nM monomer)
2. Annealing from 53°C to 25°C at 1°C/hour







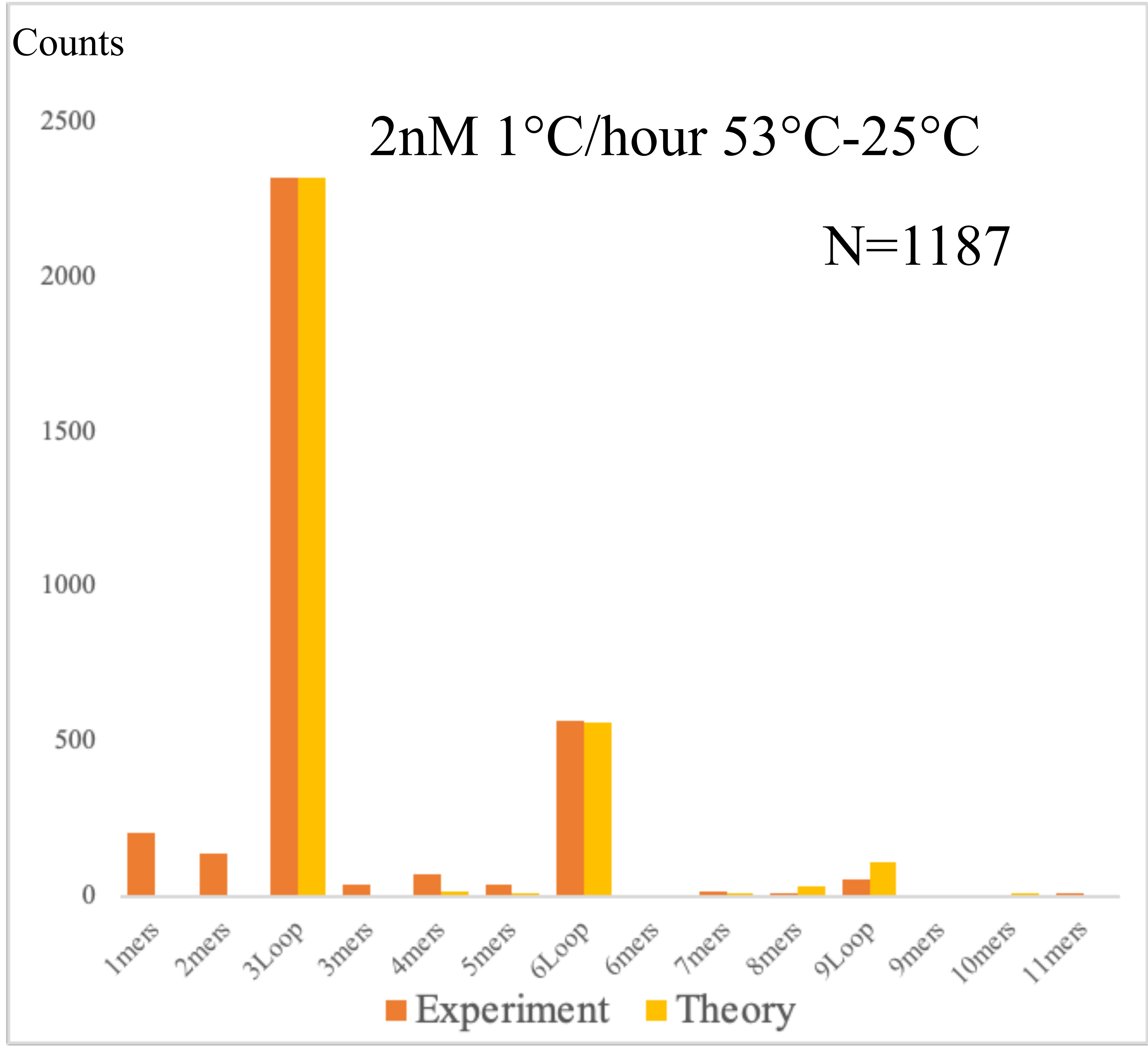
AFM of 2nM 1°C/hour 53°C to 25°C

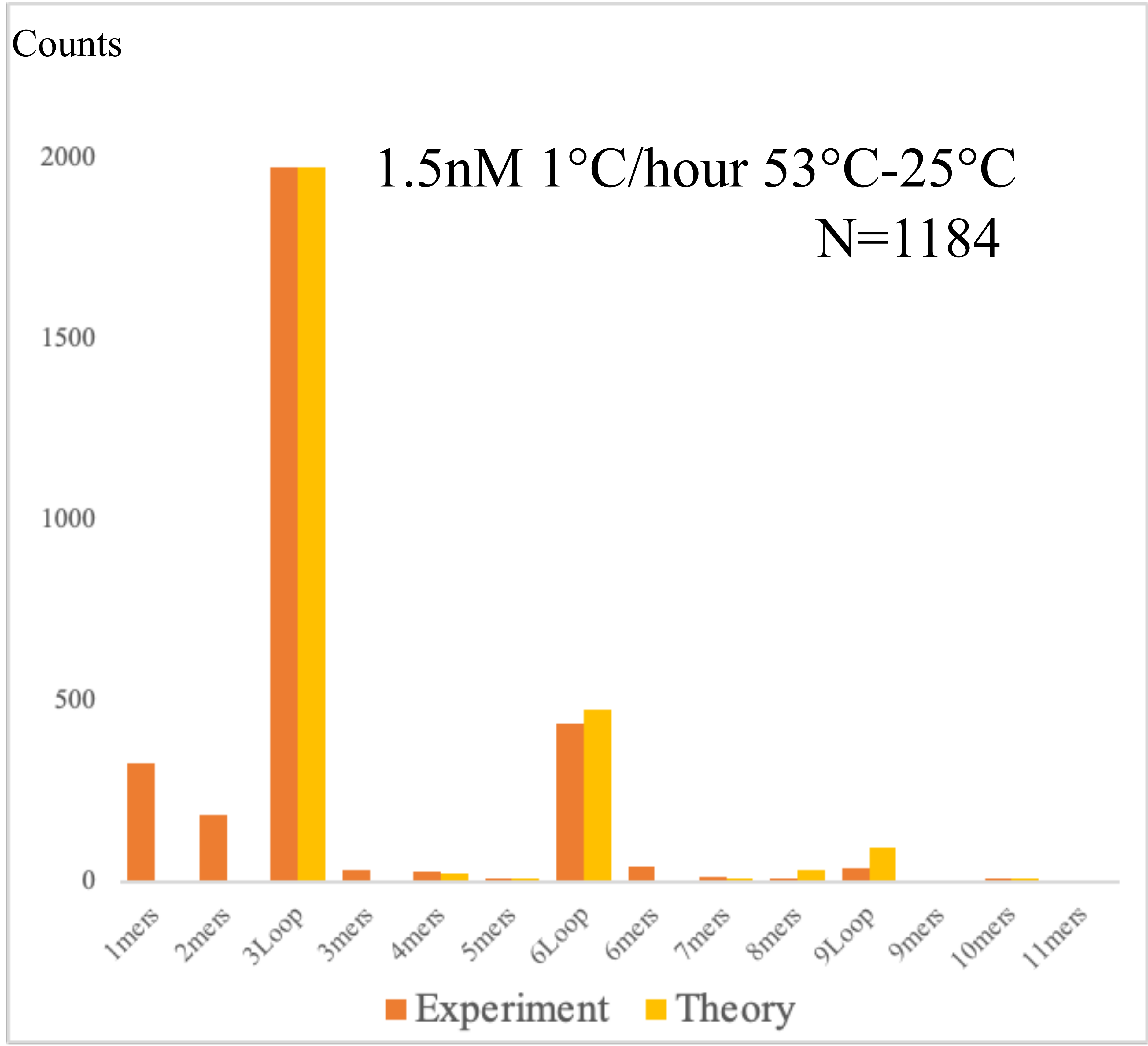
Formation of ABC seed

Simulation vs Experiment

1. 2nM /1.5nM A,B,C monomer mixture (that's 6nM monomer)
2. Annealing from 53°C to 25°C at 1°C/hour

Assumption:
for horizontal sticky ends,
$\Delta H = -82.8$[kcal/mol],
$\Delta S = -222.6$[cal/mol K]
$\bar{\alpha} = 0.47$
count right after annealing process ends





Formation of Trimer Tubes

Theoretical Calculation

Add vertical sticky ends back

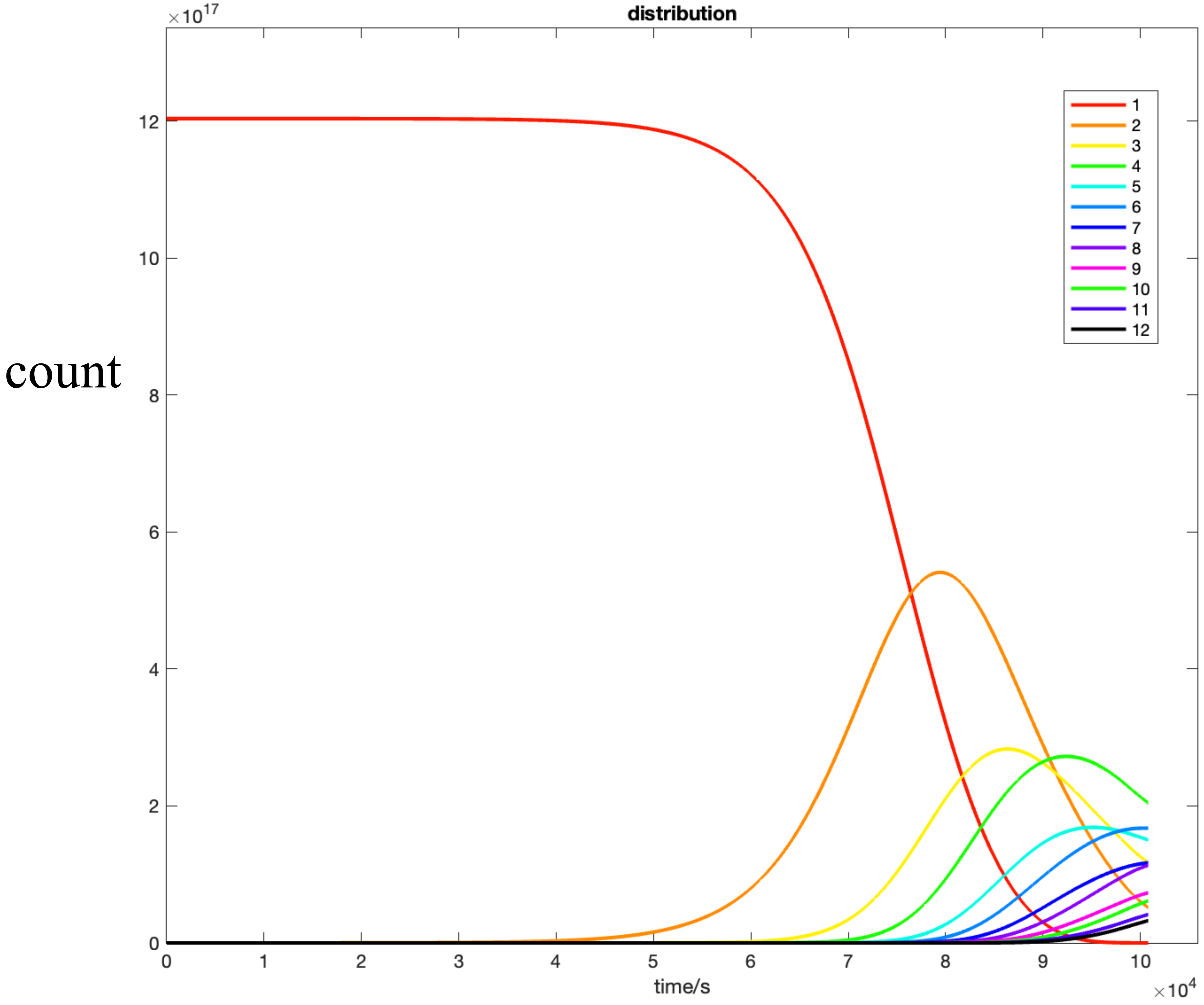
Similar to formation of seed (Smoluchowski coagulation equation)

$$J_r = \underbrace{\frac{1}{2}\sum_{i+j=r} k_{ij}C_iC_jf^2}_{\textbf{form into r}} - \underbrace{\sum_{n=1}^{\infty} k_{rn}C_rC_nf^2}_{\textbf{form into r+}} \longrightarrow k_{ij} = \frac{M(l_i + l_j)^2}{l_il_j + N\frac{l_i^3l_j^3(l_i + l_j)}{(l_i^3 + l_j^3)}} \qquad M = \frac{2k_BT}{3\mu}, N = \frac{16ln2}{H\bar{\alpha}}$$

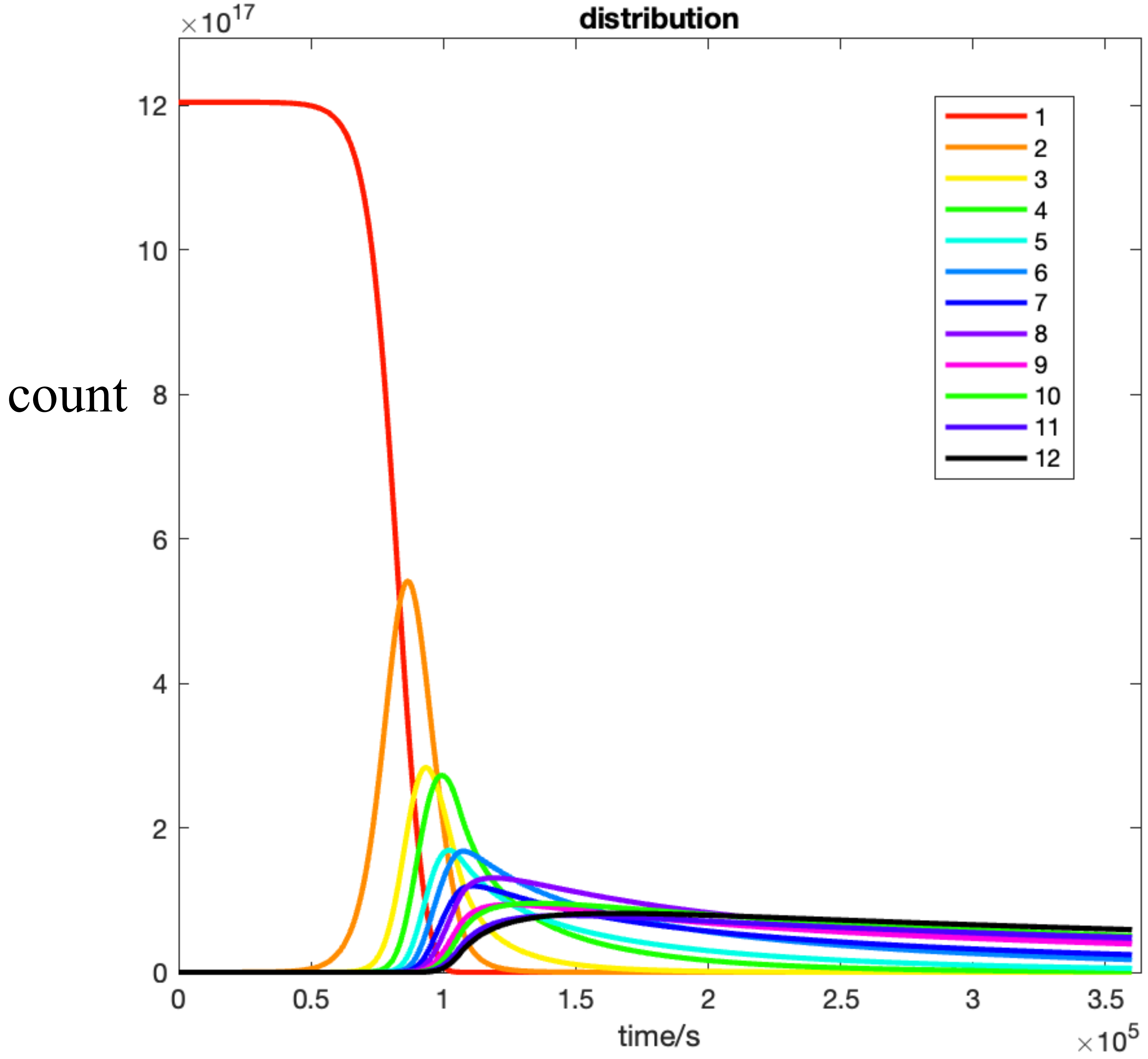
Formation of Trimer tubes

Simulation

Assumption:
for vertical sticky ends,
$\Delta H = -58.3$[kcal/mol],
$\Delta S = -154.3$[cal/mol K]
count right after annealing process ends



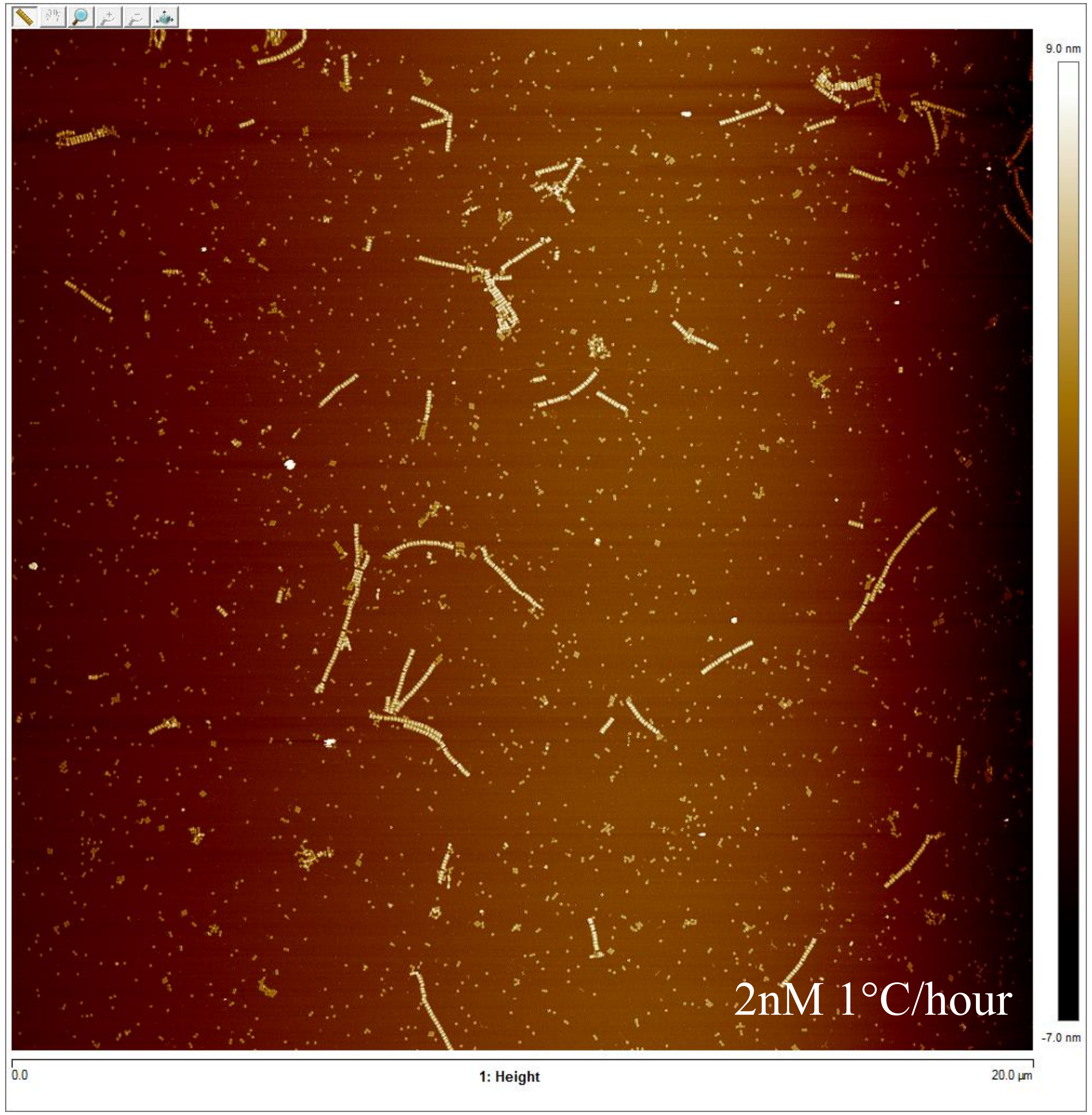
2nM 1°C/hour 53°C-25°C

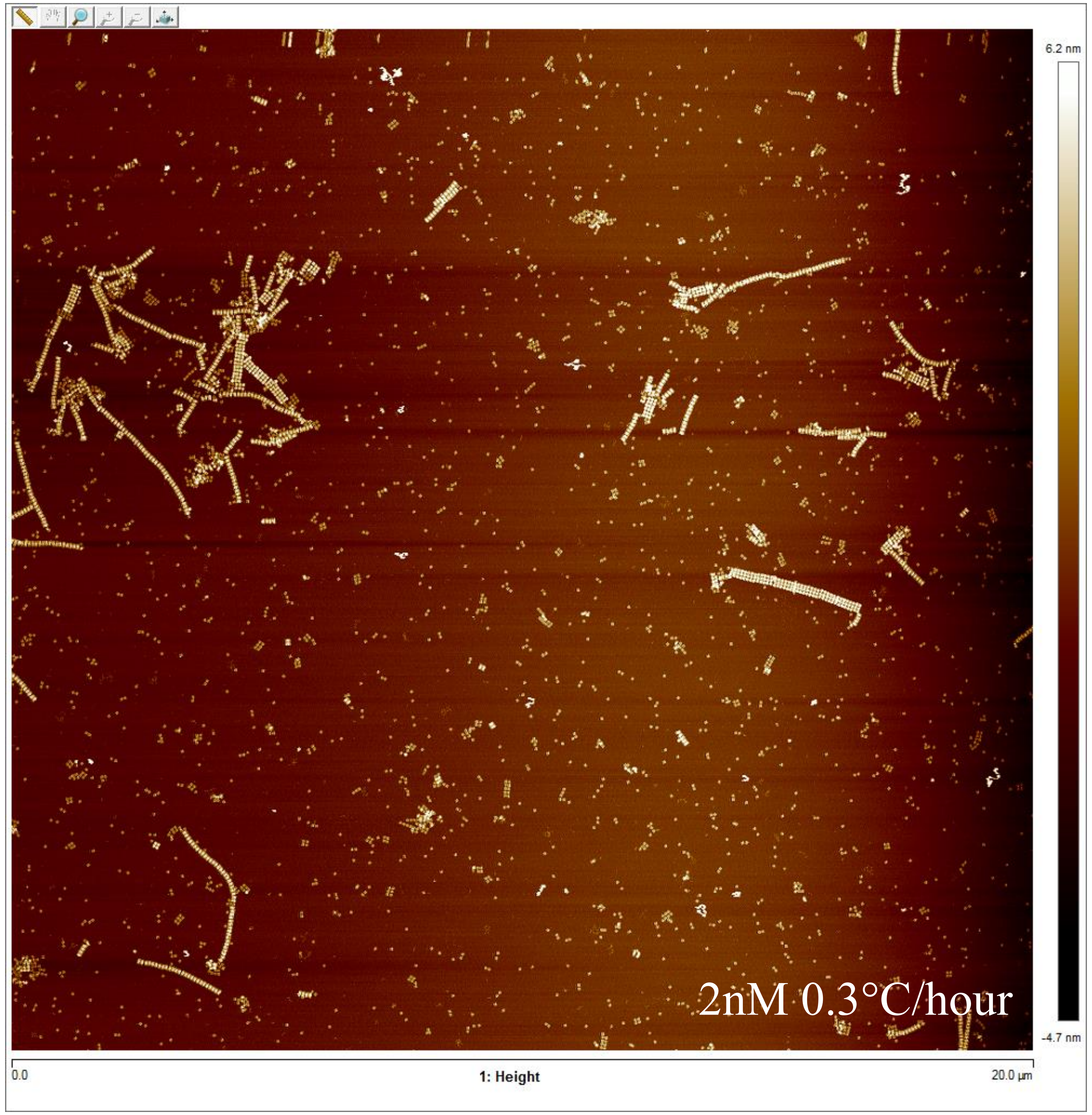


2nM 1°C/hour 53°C-25°C, wait another 70 hours after annealing.
Intensity plot (one length 5 string has intensity 5)

Formation of Trimer tubes

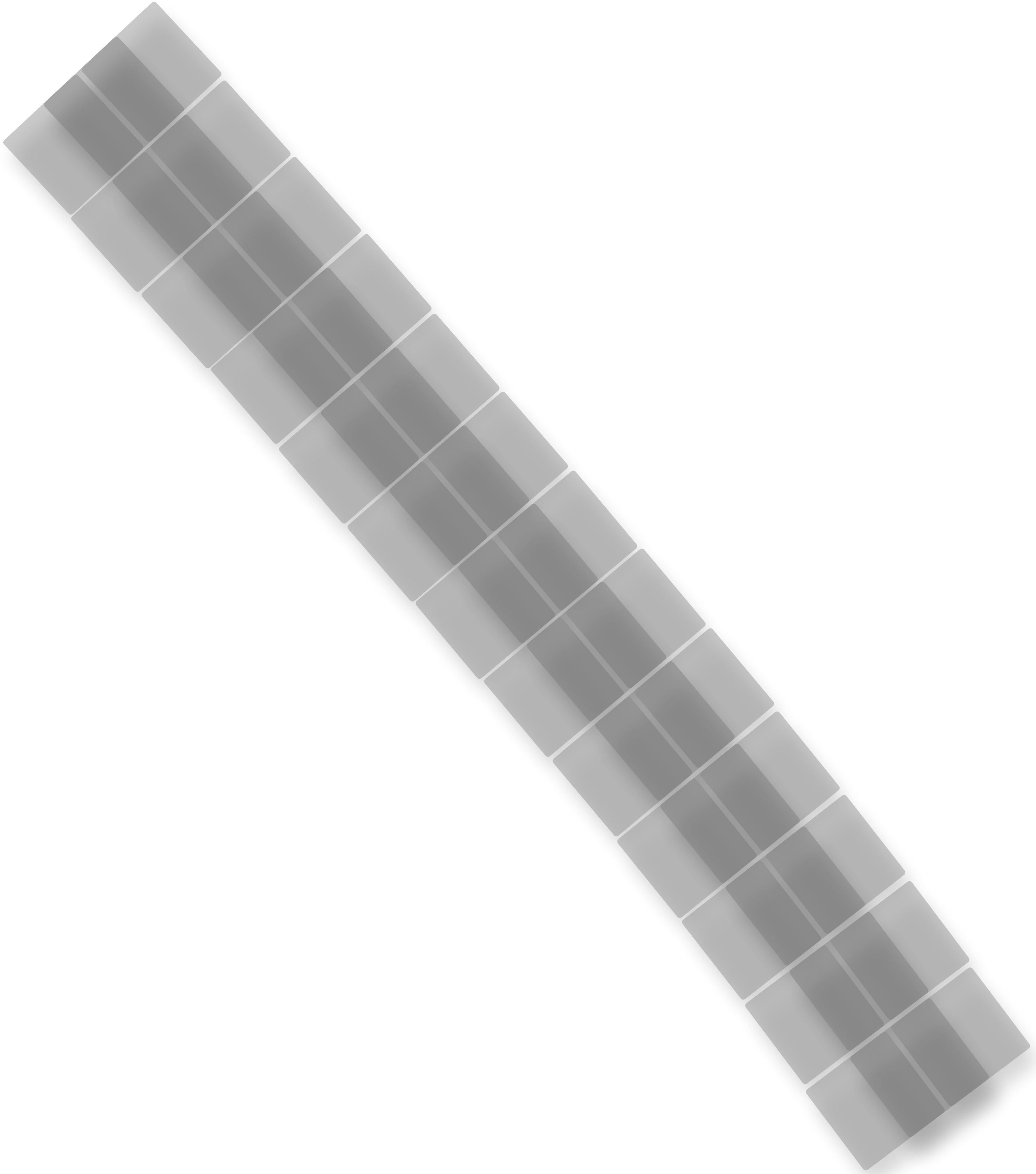
Experiment

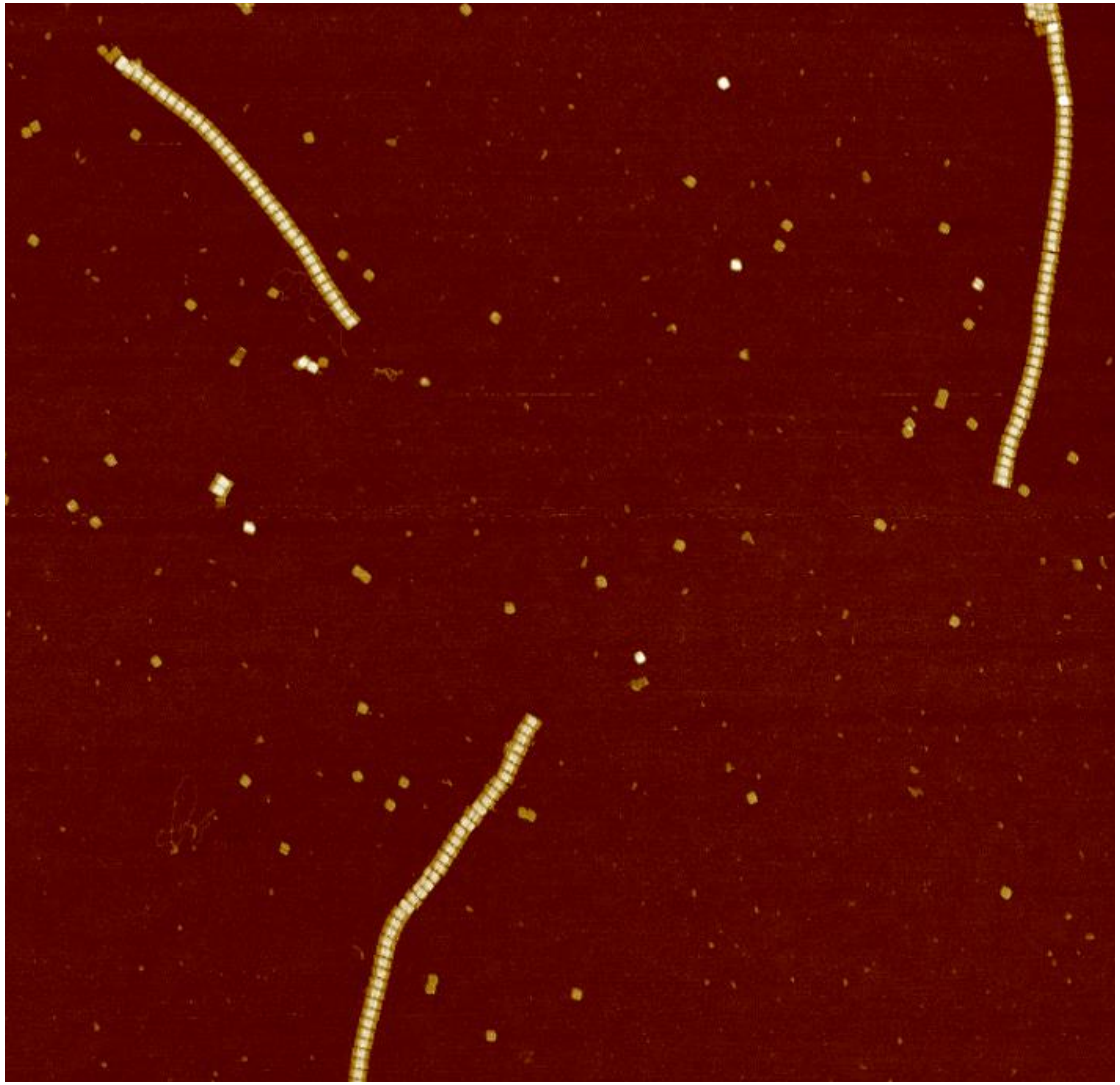




Formation of Trimer tubes

Experiment





Formation of Trimer tubes

Simulation vs Experiment

Assumption:
for horizontal sticky ends,
$\Delta H = -58.3$[kcal/mol],
$\Delta S = -154.3$[cal/mol K]
$\bar{\alpha} = 0.67$
count right after annealing process ends