

Sequence selection by ligation under non-equilibrium conditions

- science update -

Dieter Braun



Patrick Kudella

With Sergei Maslov and
Alexei Tkachenko, University of Illinois

upcoming hybridization kinetic code:
Bernhard Altaner and Ulrich Gerland, TUM

→ ⚙️ ↻ ⭐ ↓ <https://indico.physik.uni-muenchen.de/event/63/> Europe/Berlin English

Molecular Origins of Life, Munich 2021

26-27 August 2021
Literaturhaus München
Europe/Berlin timezone

The biannual Molecular Origins of Life, Munich addresses one of the most fundamental questions of science: How could life originate on Earth? With more than 20 lectures accompanied by discussion sessions and a virtual element, this international conference brings together scientists from wide range of disciplines, namely: astrophysics, biochemistry, biophysics, chemistry, geobiology, geochemistry and theoretical physics. Only the combined effort from renowned experts from various disciplines can be successful in retracing the origins of life under experimental conditions and pave the way towards answering some of the most pertinent questions: What were the conditions on early Earth? Which chemicals could serve as precursors for the synthesis of living systems on Earth and on other planets? How did the very first genetic material in lifeforms develop? How could Darwinian evolution emerge? What were the first metabolic pathways? The conference's aim is to represent and to discuss the state of the art in the Origin of Life field.

The Molecular Origins of Life, Munich 2021 is sponsored by DFG funded Collaborative Research Center 235 Emergence of Life.

Attendance to the conference is free of charge!

- Home
- Speaker List
- Poster Presentation
- Pre-conference BBQ
- Venue
- Accommodation
- Registration

Contact

✉ emergenceoflife@lmu.de

☎ +49 89 2180 3514

🕒 **Starts** 26 Aug 2021, 08:30
Ends 27 Aug 2021, 18:00
Europe/Berlin

📍 **Literaturhaus München**
Salvatorplatz 1,
80333 Munich,
Germany
[Go to map](#)

Important dates (2021)

July 20th, Tue -> *Poster abstract submission deadline*

Aug 15th, Sun..... -> *Registration deadline*

Aug 25th, Wed..... -> *Conference start with BBQ*

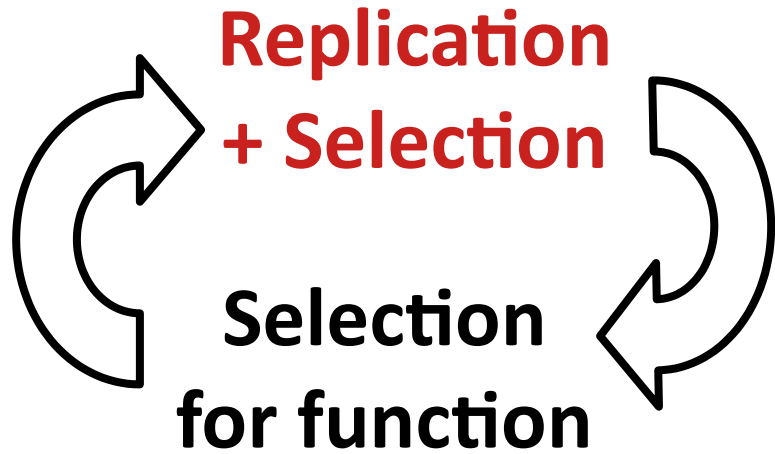


indico.physik.lmu.de/event/63/

(In)stability of Evolution

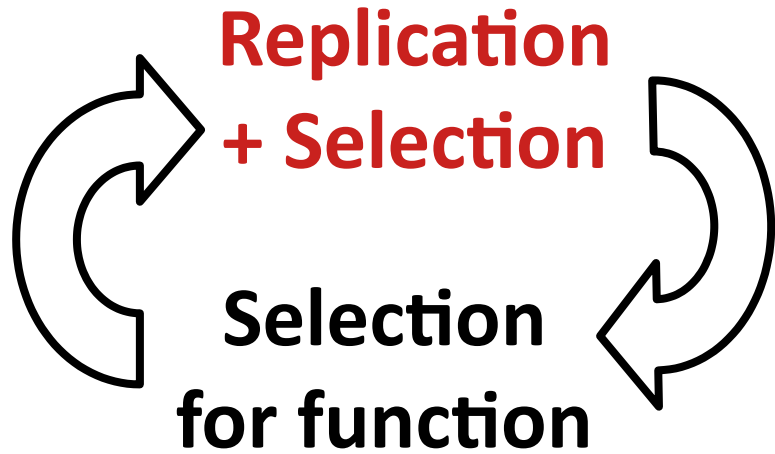


(In)stability of Evolution



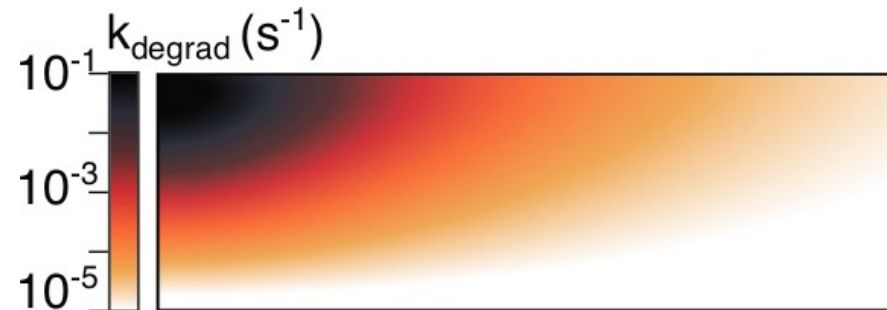
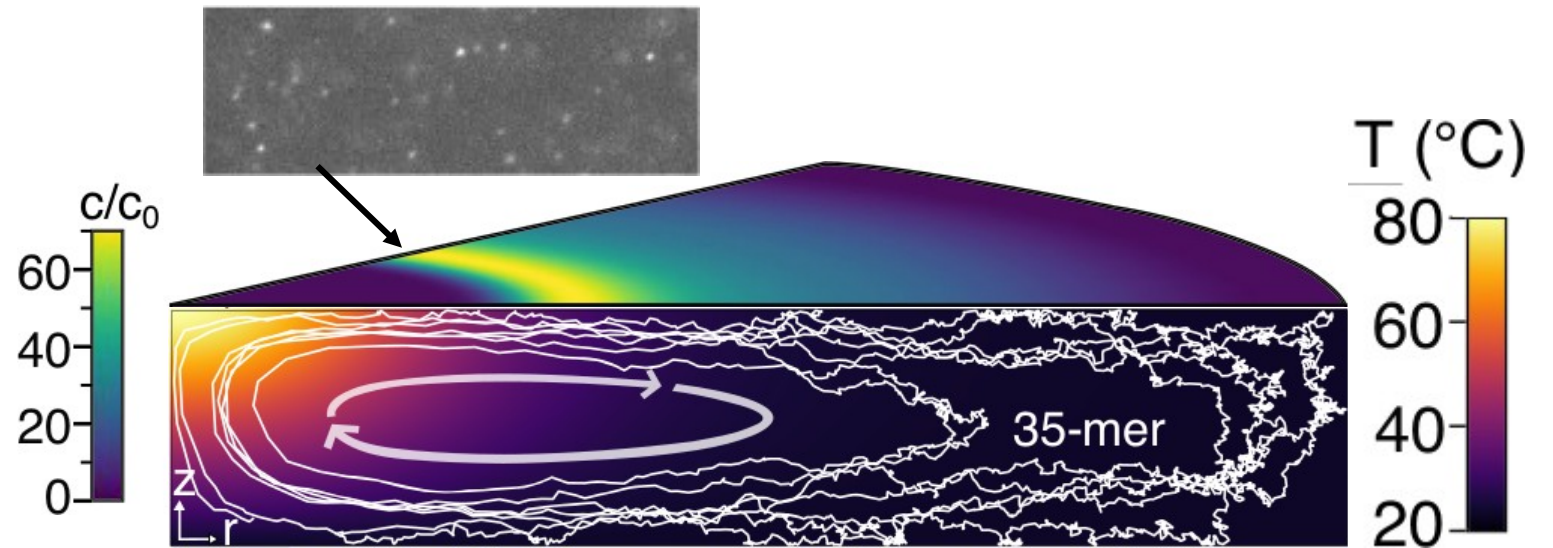
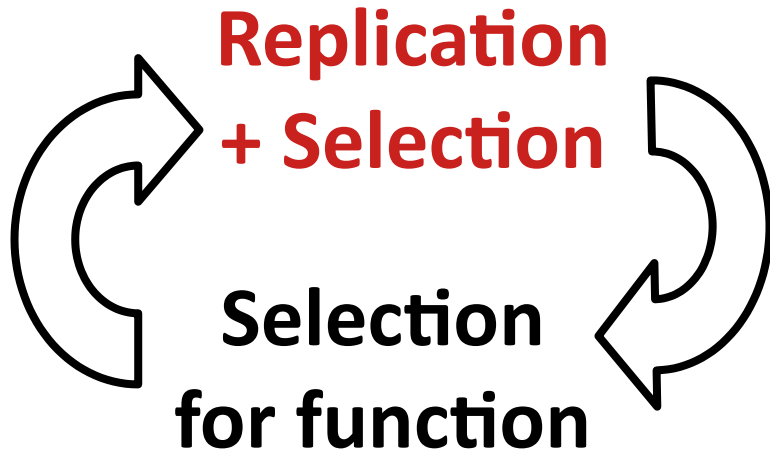
(In)stability of Evolution

- Tyranny of the shortest (Spiegelman)



(In)stability of Evolution

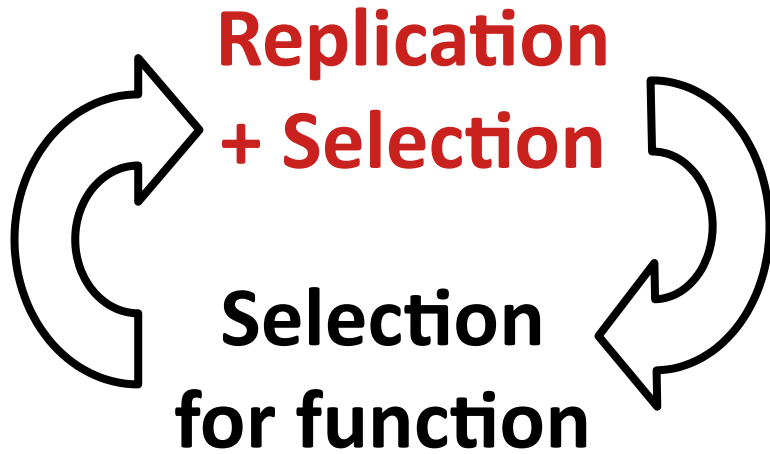
- Tyranny of the shortest (Spiegelman)
Lack of non-primer replication in Ribo-PCR



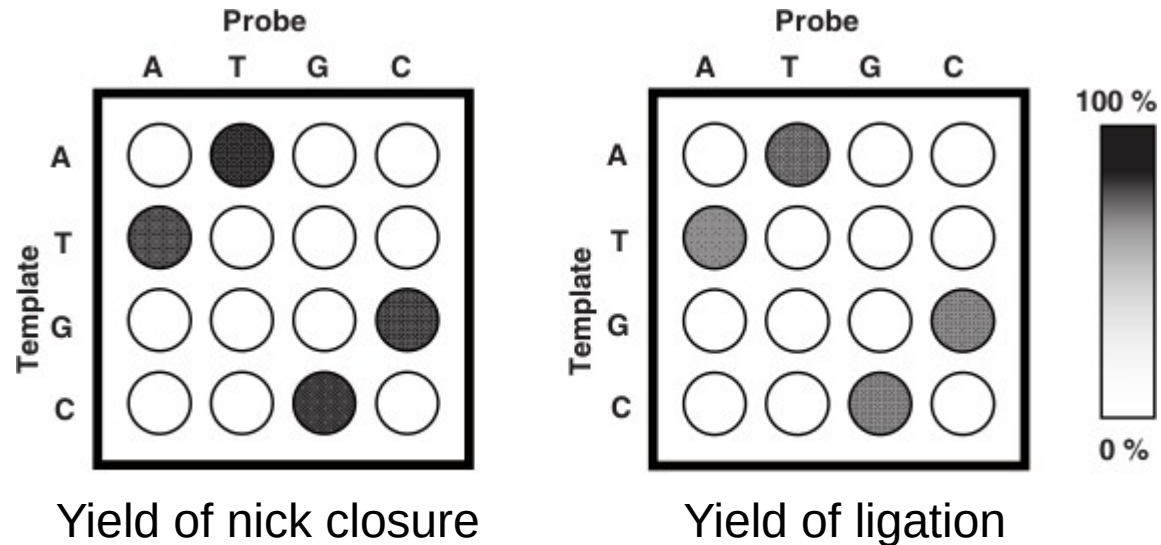
Salditt, Keil, Horning,
Mast, Joyce and Braun,
Physical Review Letters
125, 048104 (2020)

(In)stability of Evolution

Study templated ligation



Taq-Ligase: precision and low temperature performance



Profiling the selectivity of DNA ligases in an array format with mass spectrometry, **Kim and Mrksich**, Nucleic Acid Research, doi:10.1093/nar/gkp827 (2010)

Illumina sequencing with Swift kit and LMU Gene Center facility

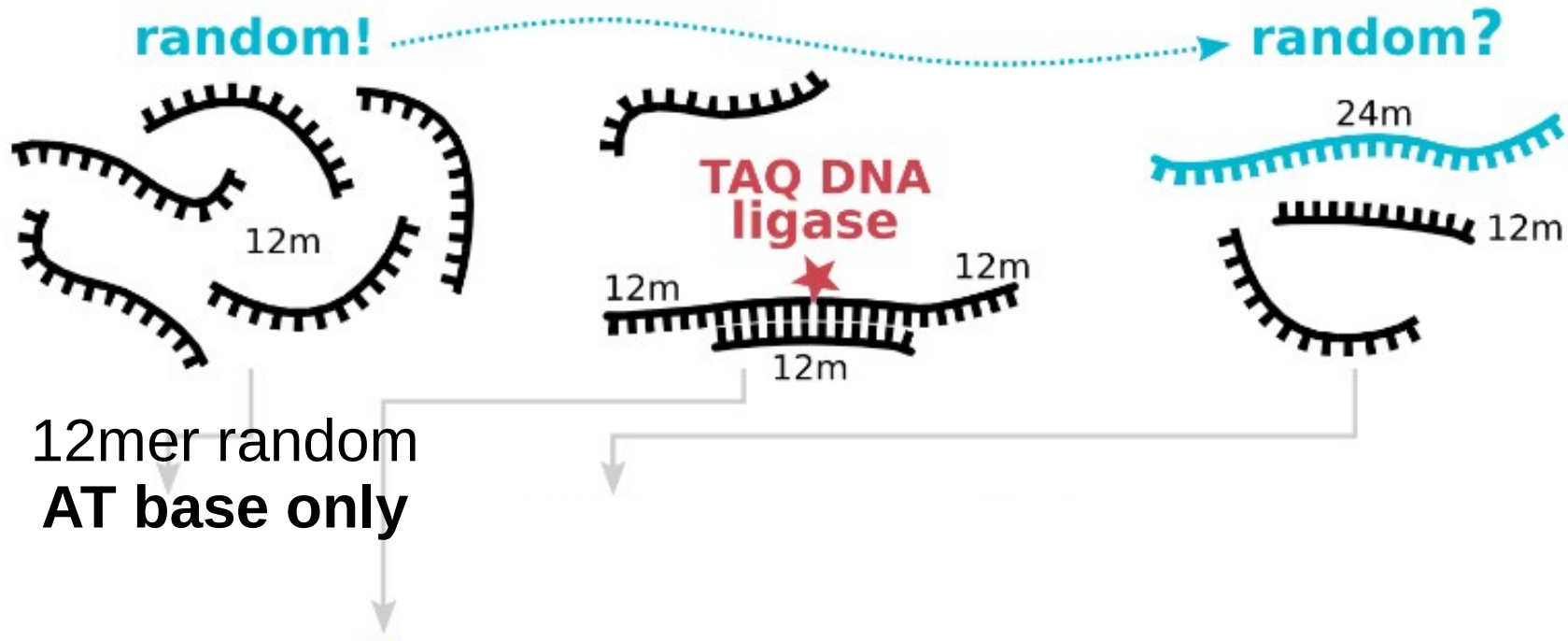
Thanks for discussions with Daniel Duzdevich and Irene Chen

Repeated templated ligation of random pools

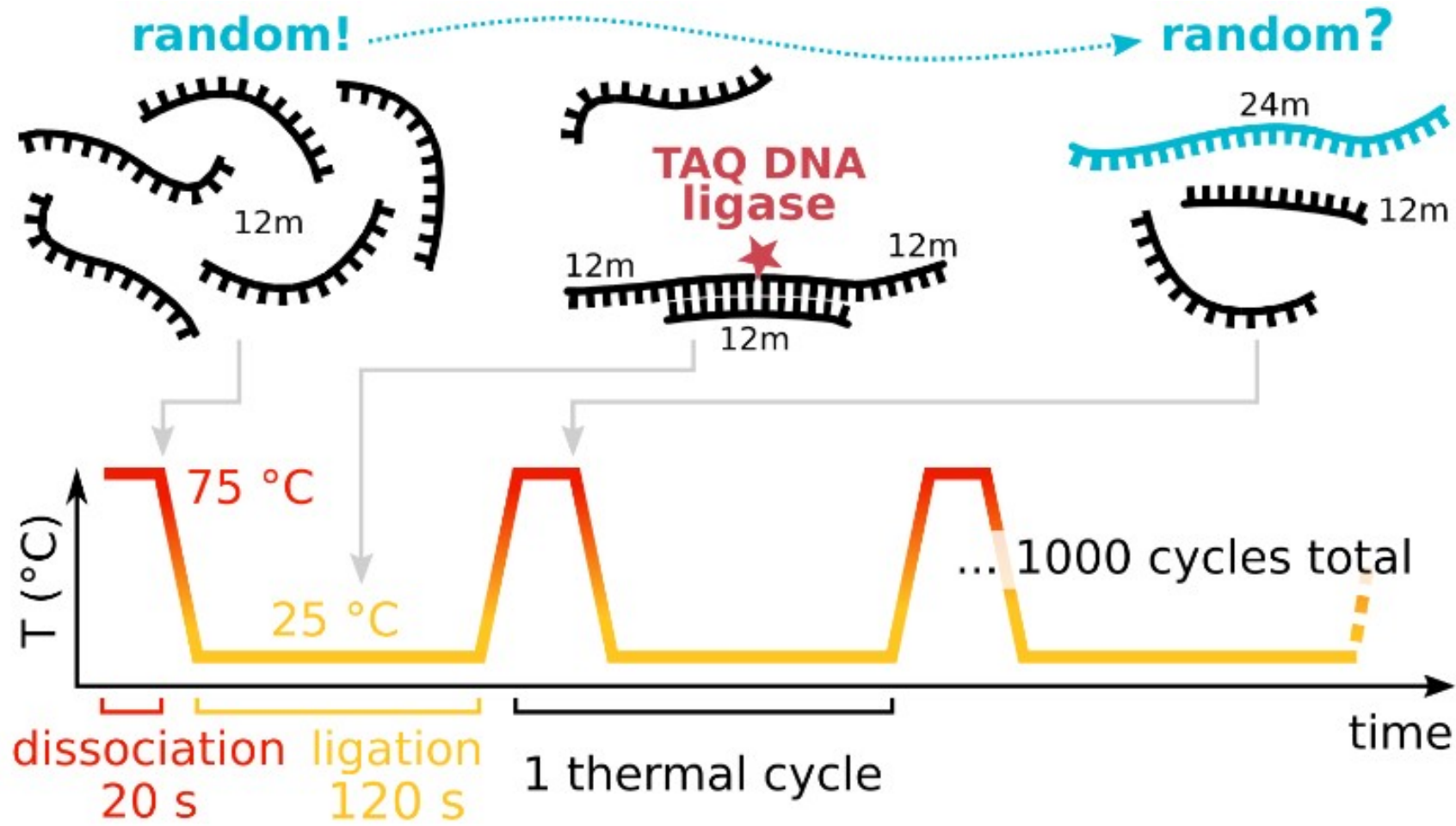


12mer random
AT base only

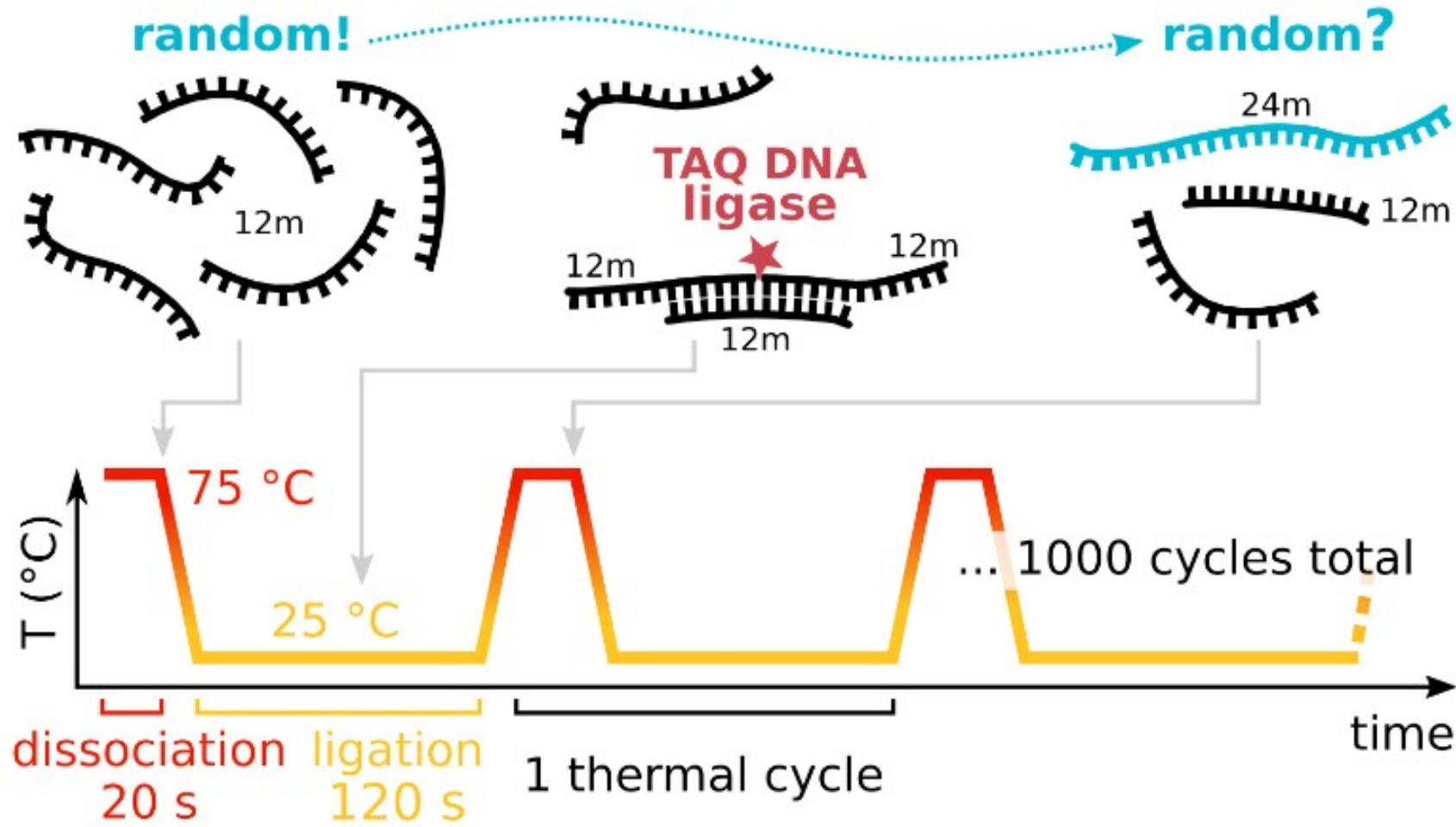
Repeated templated ligation of random pools



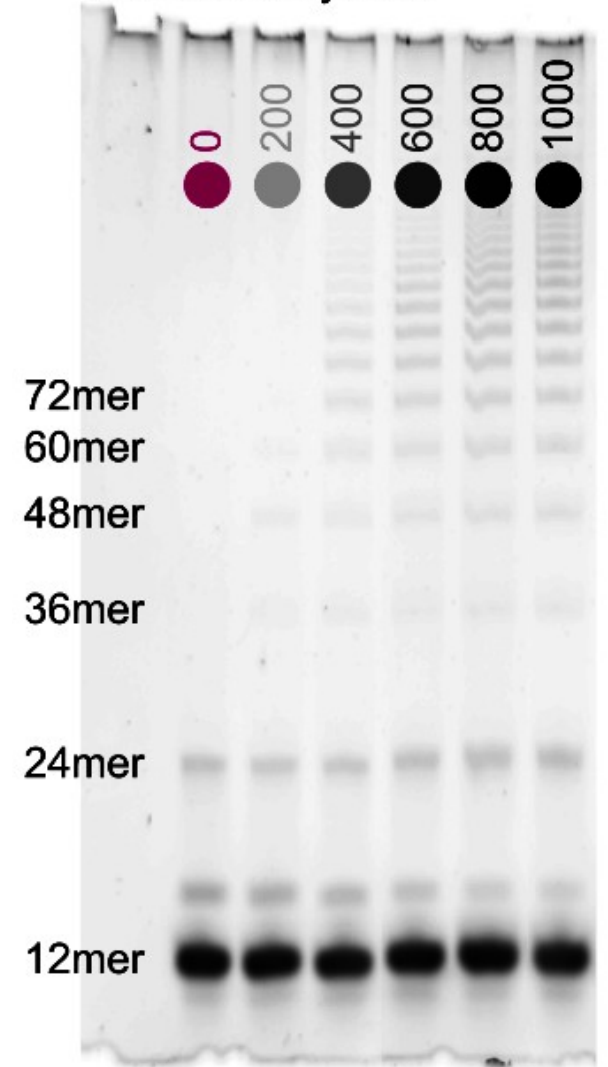
Repeated templated ligation of random pools



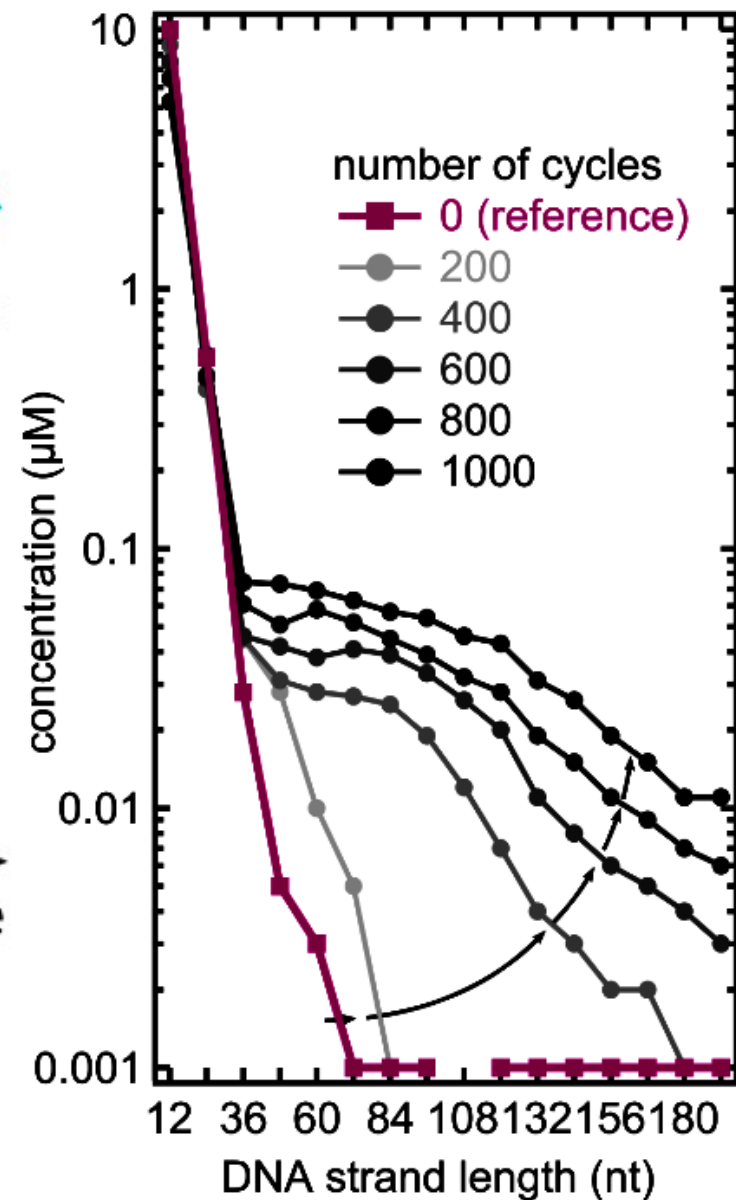
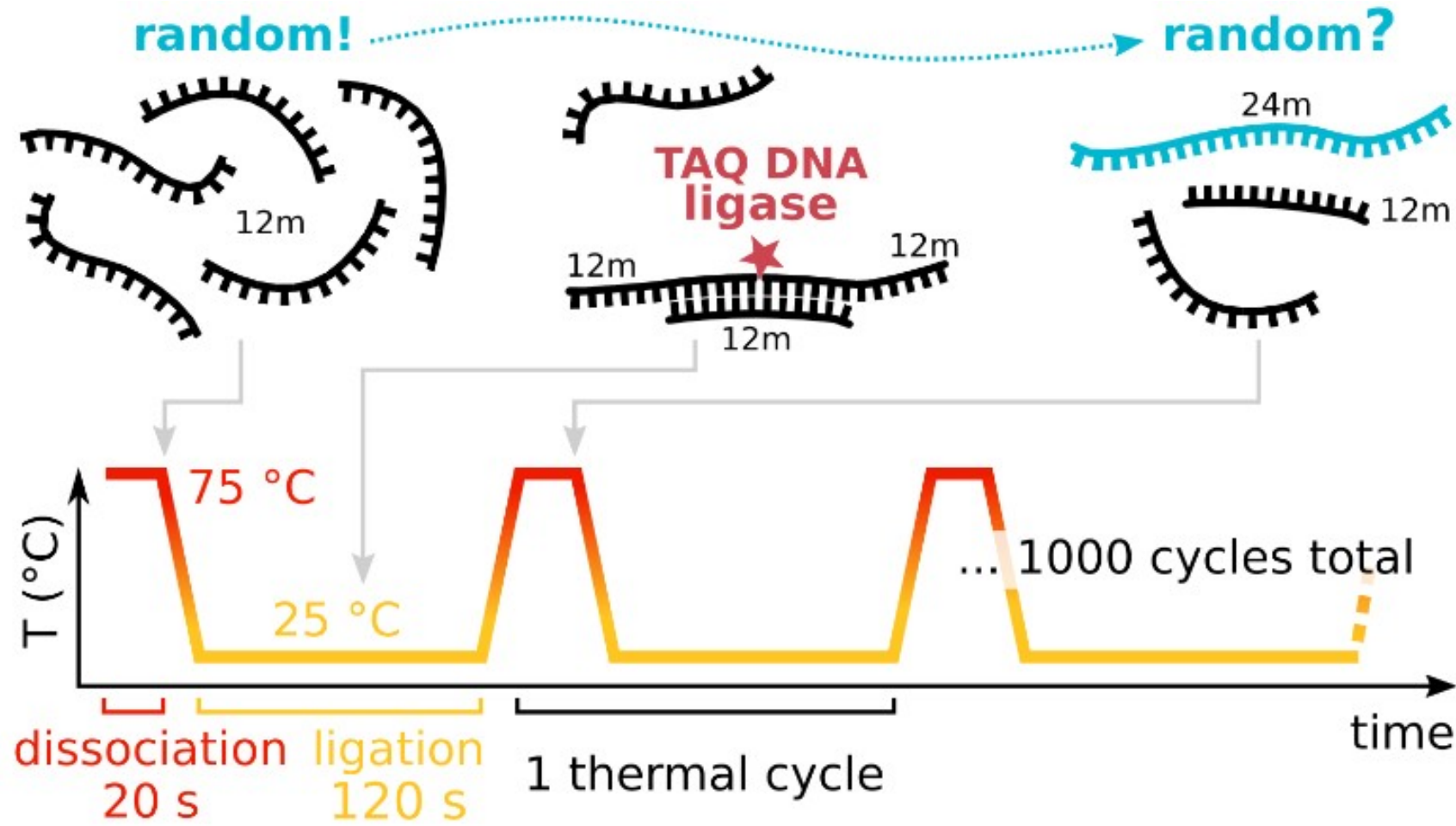
Repeated templated ligation of random pools



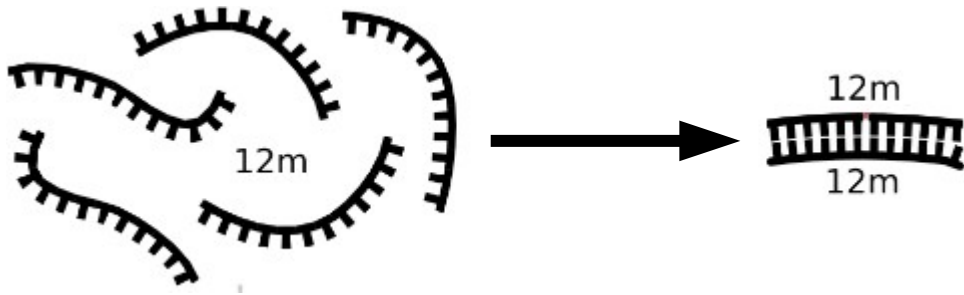
AT random 12mer, 10 μ M
33 °C ligation temperature
number of cycles:



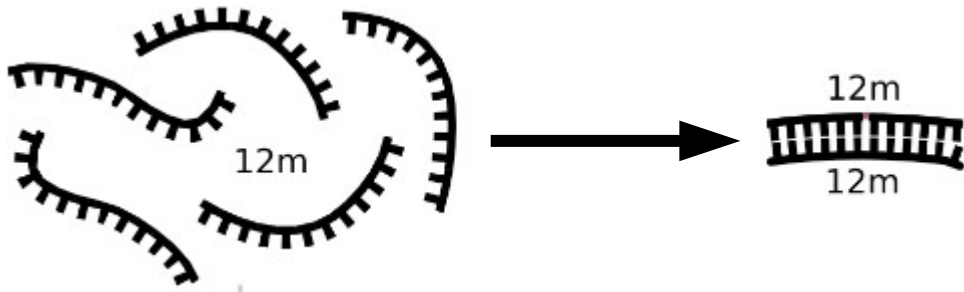
Repeated templated ligation of random pools



Why templated ligation is out of equilibrium

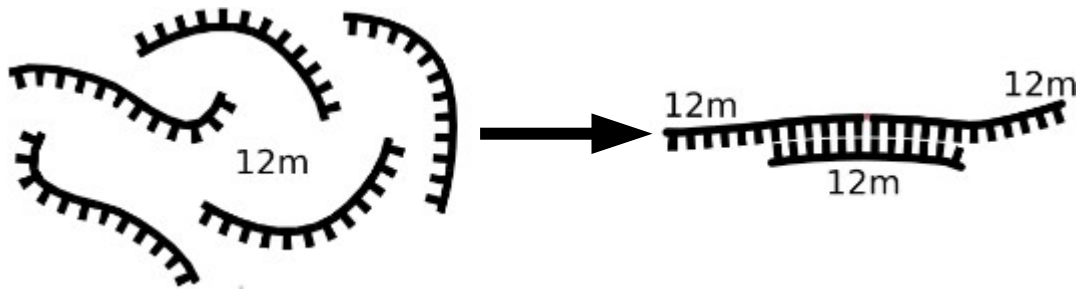


Why templated ligation is out of equilibrium



Hybridization
no competition

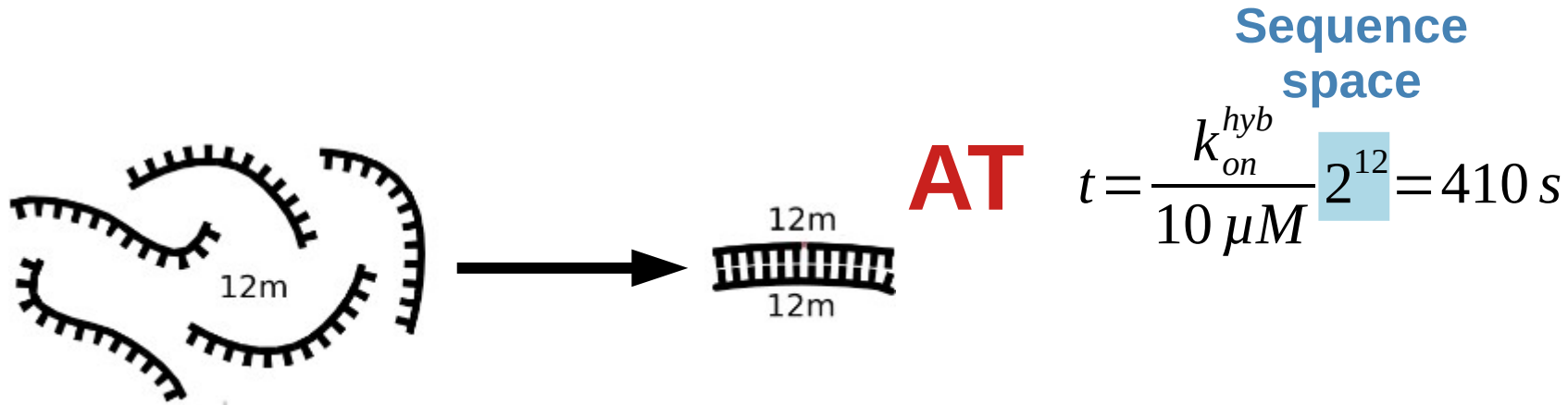
$$k_{on}^{\hat{h}yb} = 1 \mu M^{-1} s^{-1}$$



Gao, Wolf, Georgiadis, Nucleic acids research, 34(11), 3370-3377 (2006)

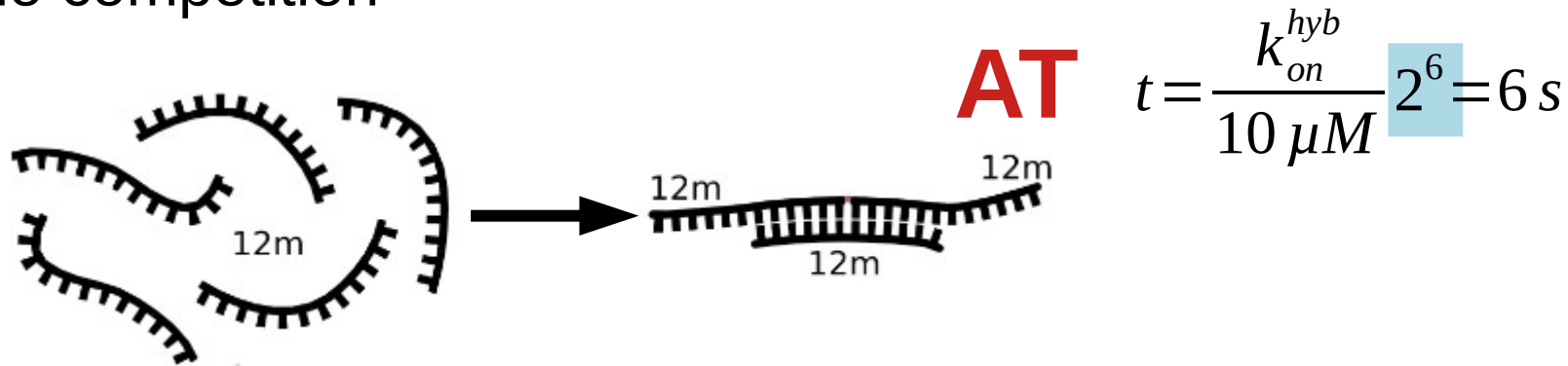
Ouldrige, Šulc, Romano, Doye, Louis, Nucleic acids research, 41(19), 8886-8895 (2013)

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Hybridization
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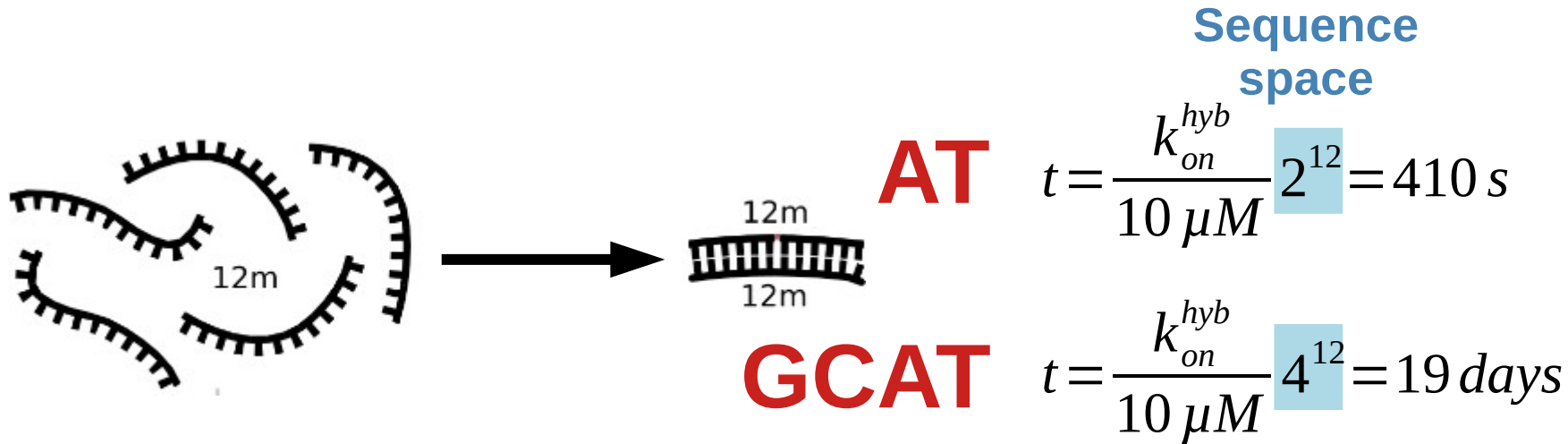
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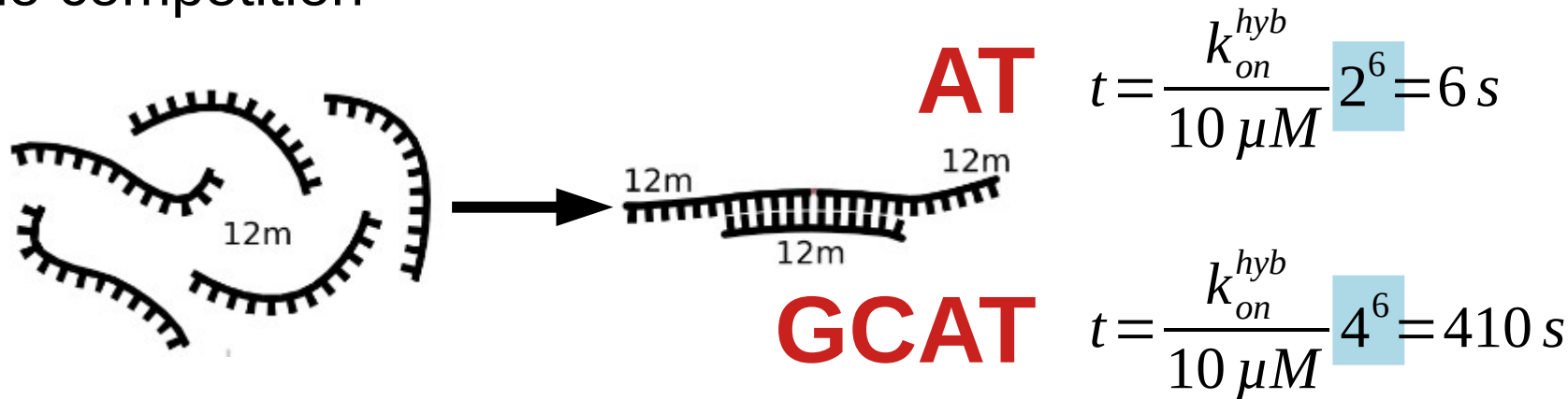
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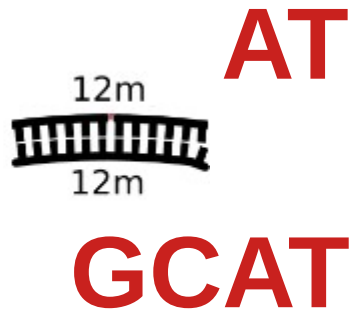
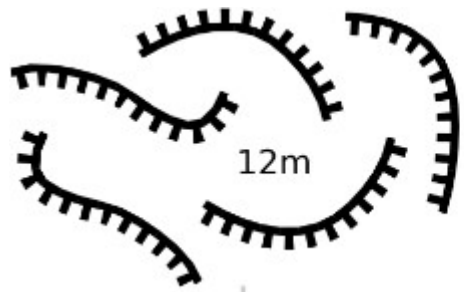
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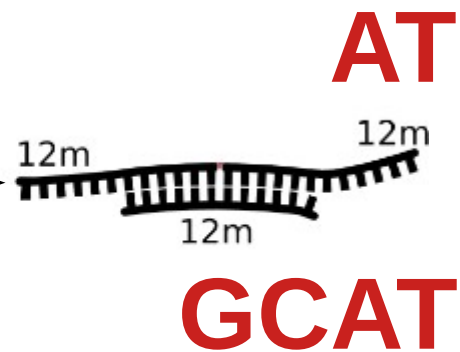
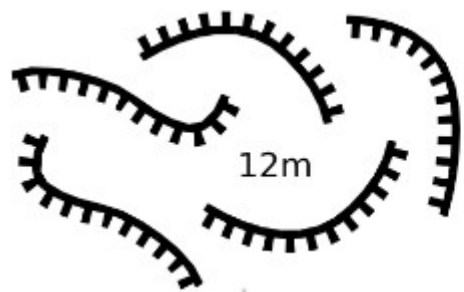
Ouldrige, Šulc, Romano, Doye, Louis, Nucleic acids research, 41(19), 8886-8895 (2013)

Why templated ligation is out of equilibrium



Hybridization
no competition

$$k_{on}^{\hat{hyb}} = 1 \mu M^{-1} s^{-1}$$



Sequence
space

$$t = \frac{k_{on}^{hyb}}{10 \mu M} 2^{12} = 410 s$$

$$t = \frac{k_{on}^{hyb}}{10 \mu M} 4^{12} = 19 \text{ days}$$

$$t = \frac{k_{on}^{hyb}}{10 \mu M} 2^6 = 6 s$$

$$t = \frac{k_{on}^{hyb}}{10 \mu M} 4^6 = 410 s$$

$T_{lig} (^{\circ}C) =$ 25 30 35 40

GCAT

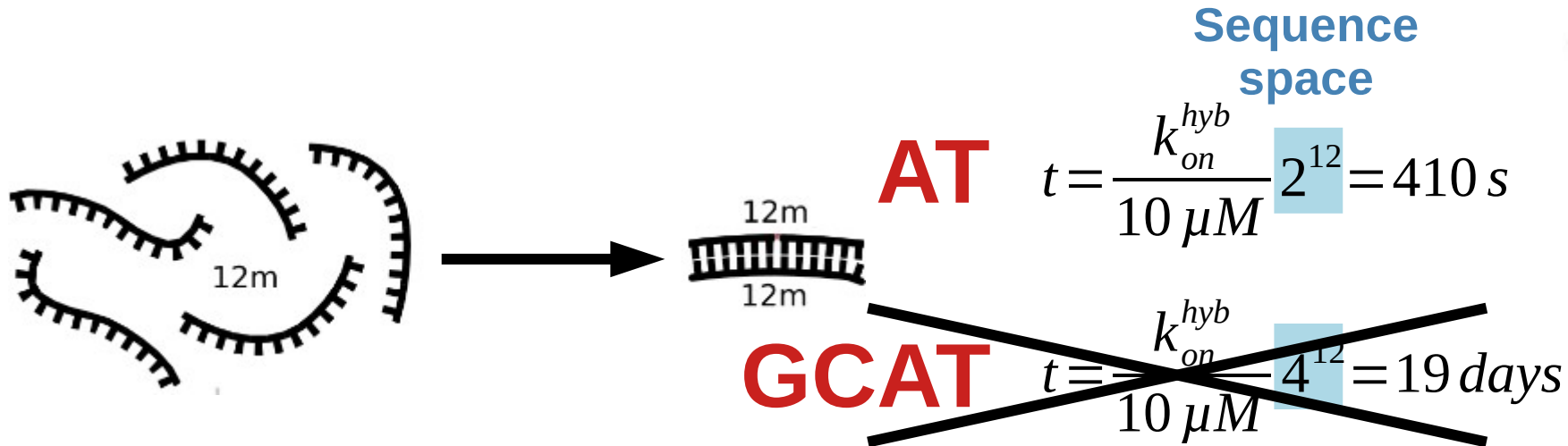
DNA strand length (nt)

24

12

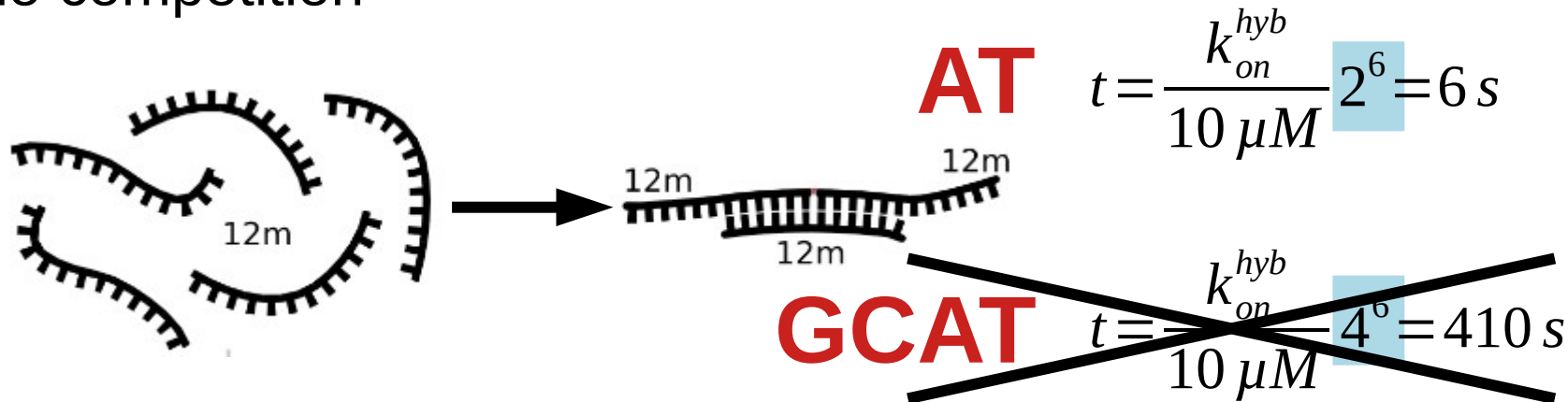


Why templated ligation is out of equilibrium

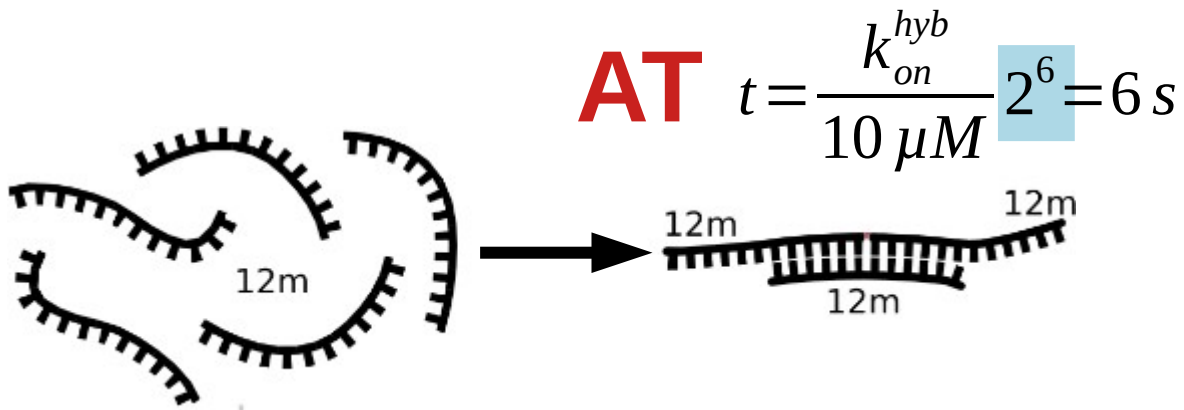
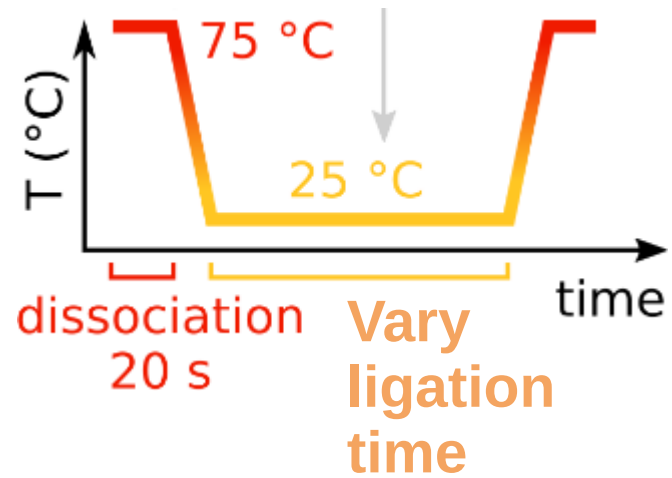


Hybridization
no competition

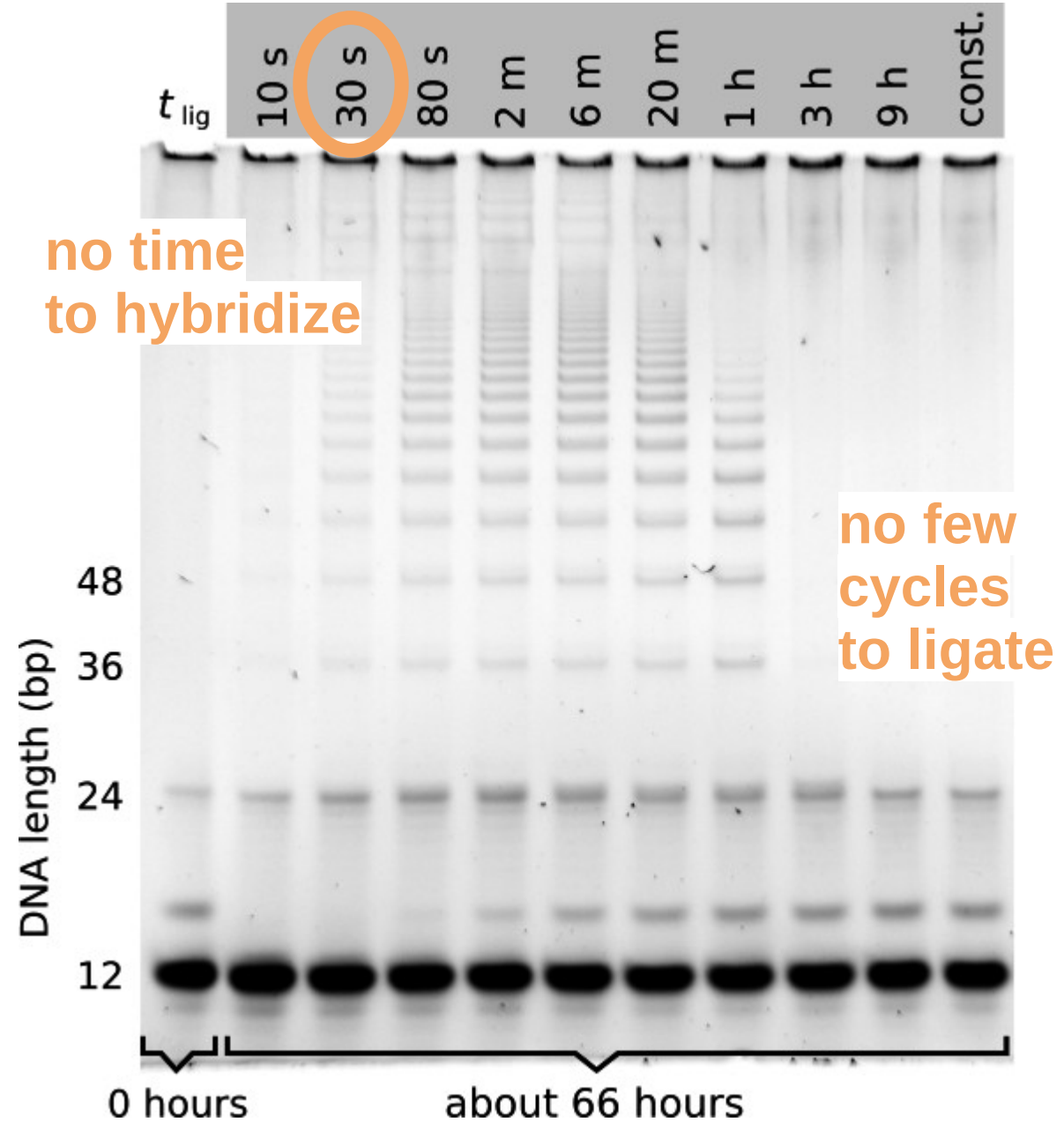
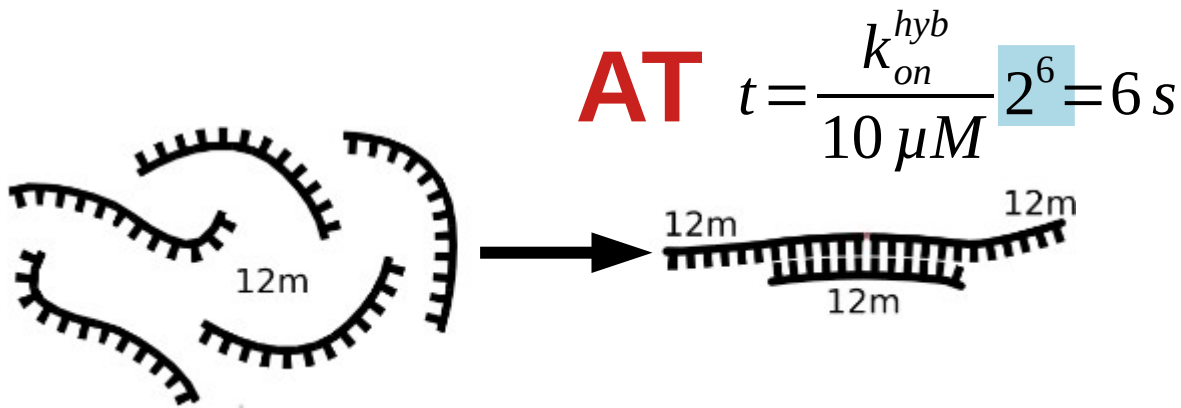
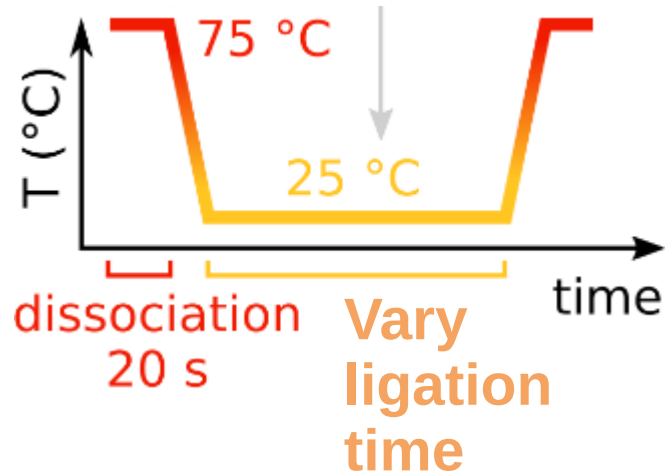
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Why templated ligation is out of equilibrium



Why templated ligation is out of equilibrium



Dynamics in sequence space

Spontaneous emergence of autocatalytic information-coding polymers, J. Chem. Physics (2015)
Onset of natural selection in populations of autocatalytic heteropolymers, J. Chem. Physics (2018)

With Sergei Maslov and Alexei Tkachenko, University of Illinois

Dynamics in sequence space

**Replication amplifies
patterns at the ligation site**

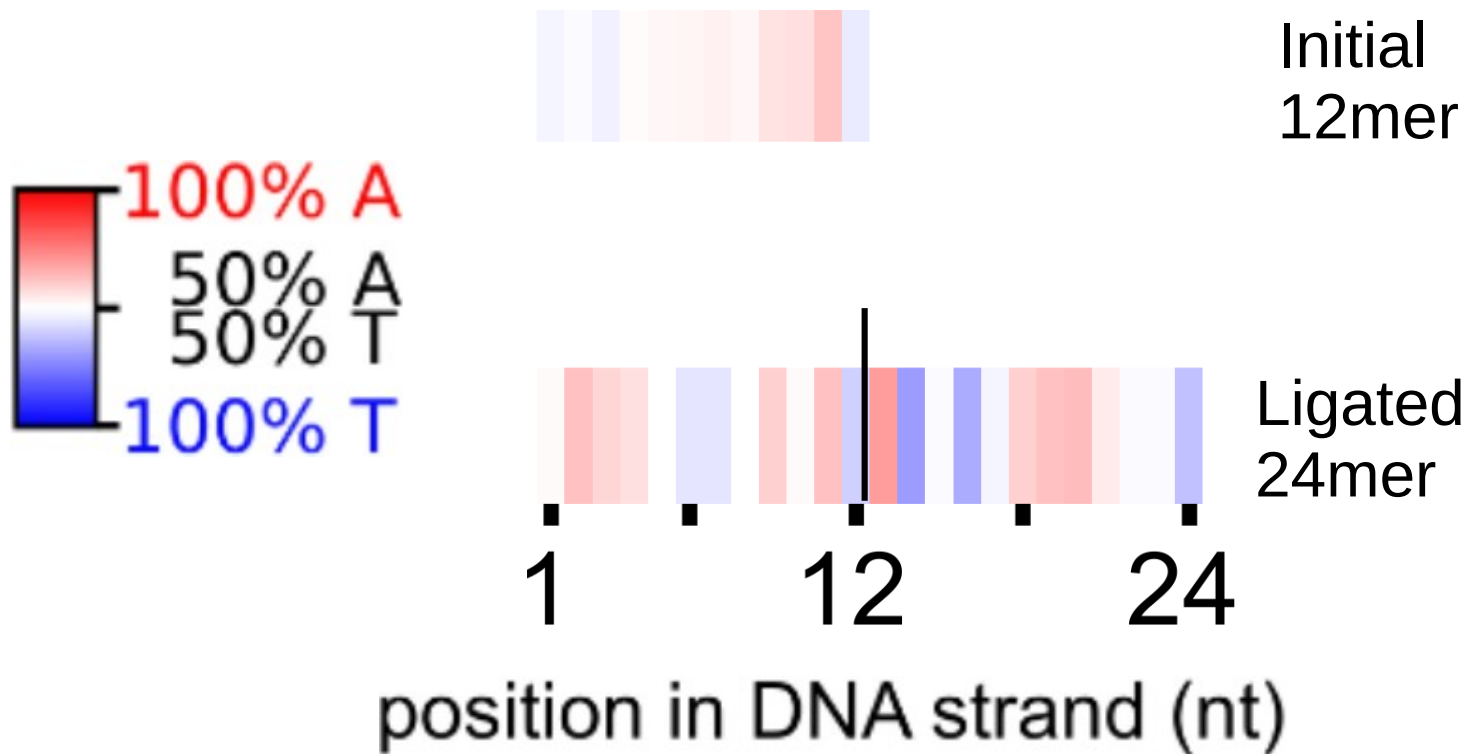
**Replication avoids hairpins by
evolving complementary pools**

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Dynamics in sequence space

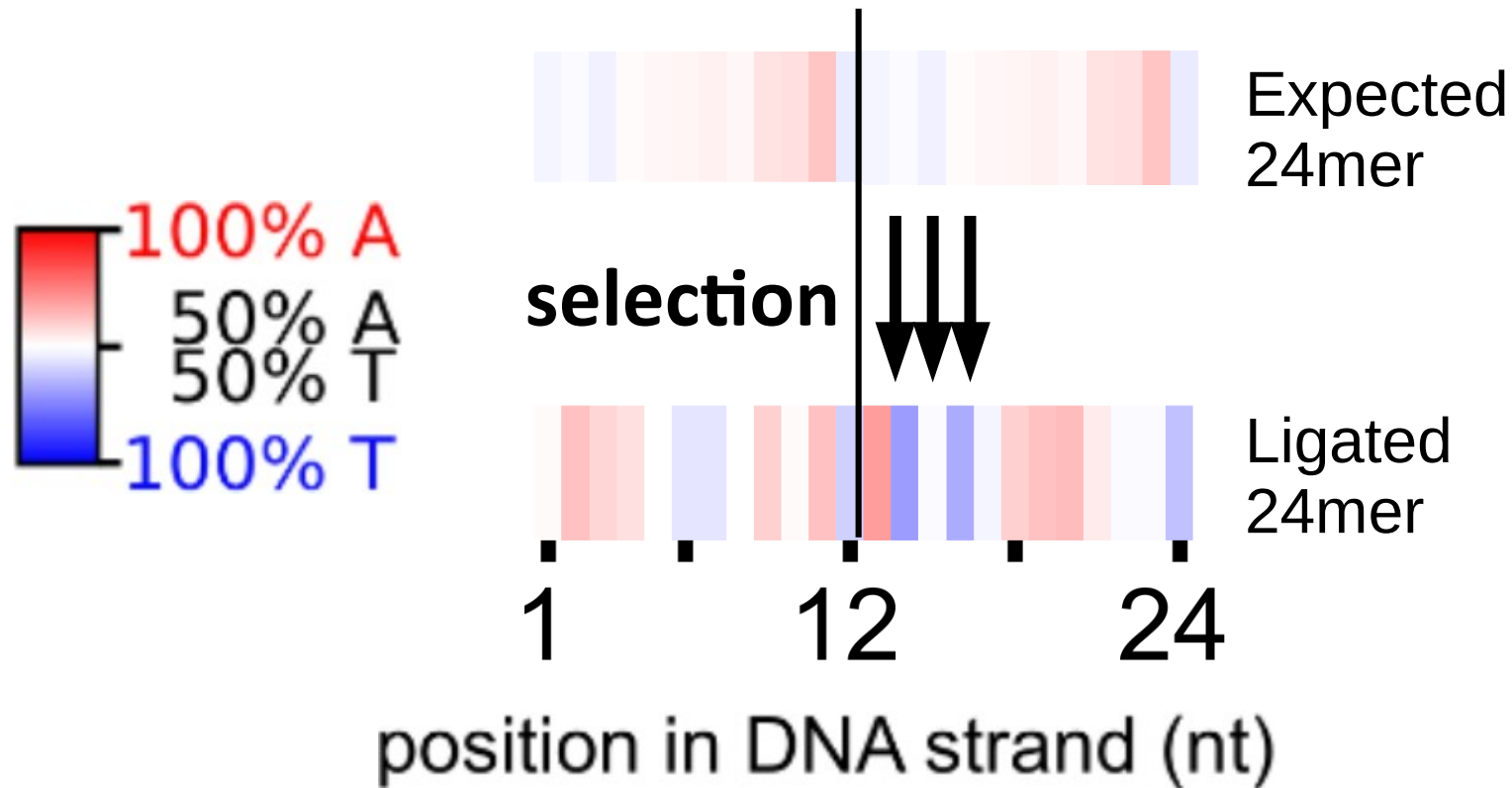
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Dynamics in sequence space

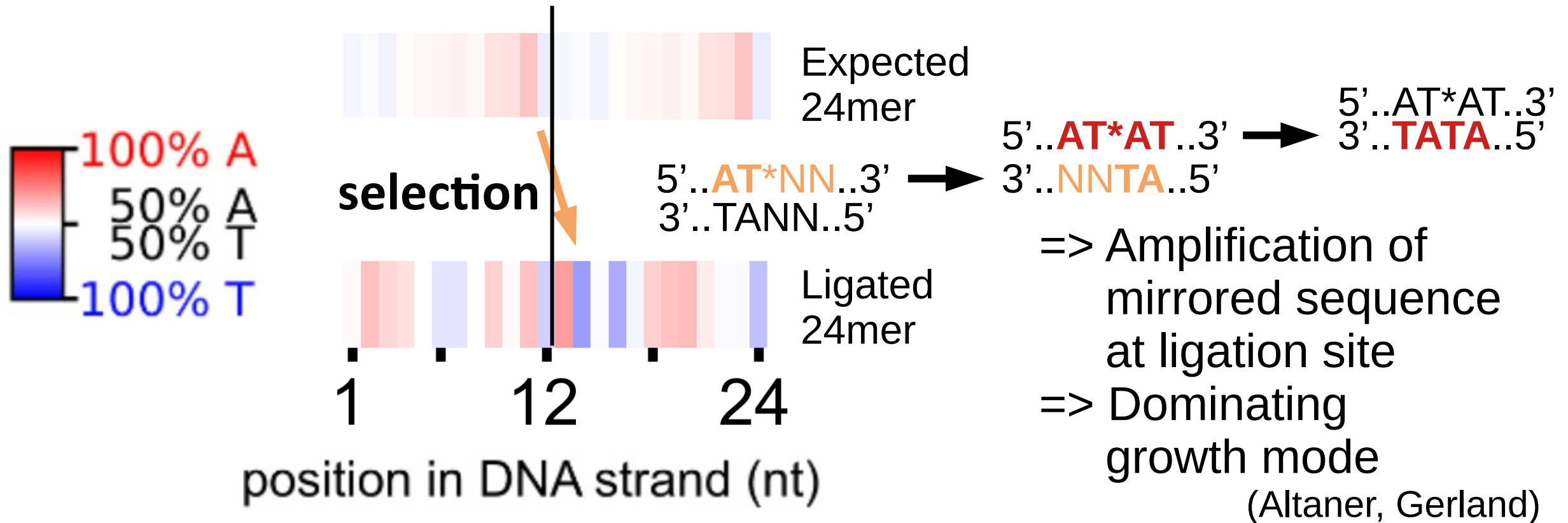
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With Sergei Maslov and Alexei Tkachenko, University of Illinois

Dynamics in sequence space

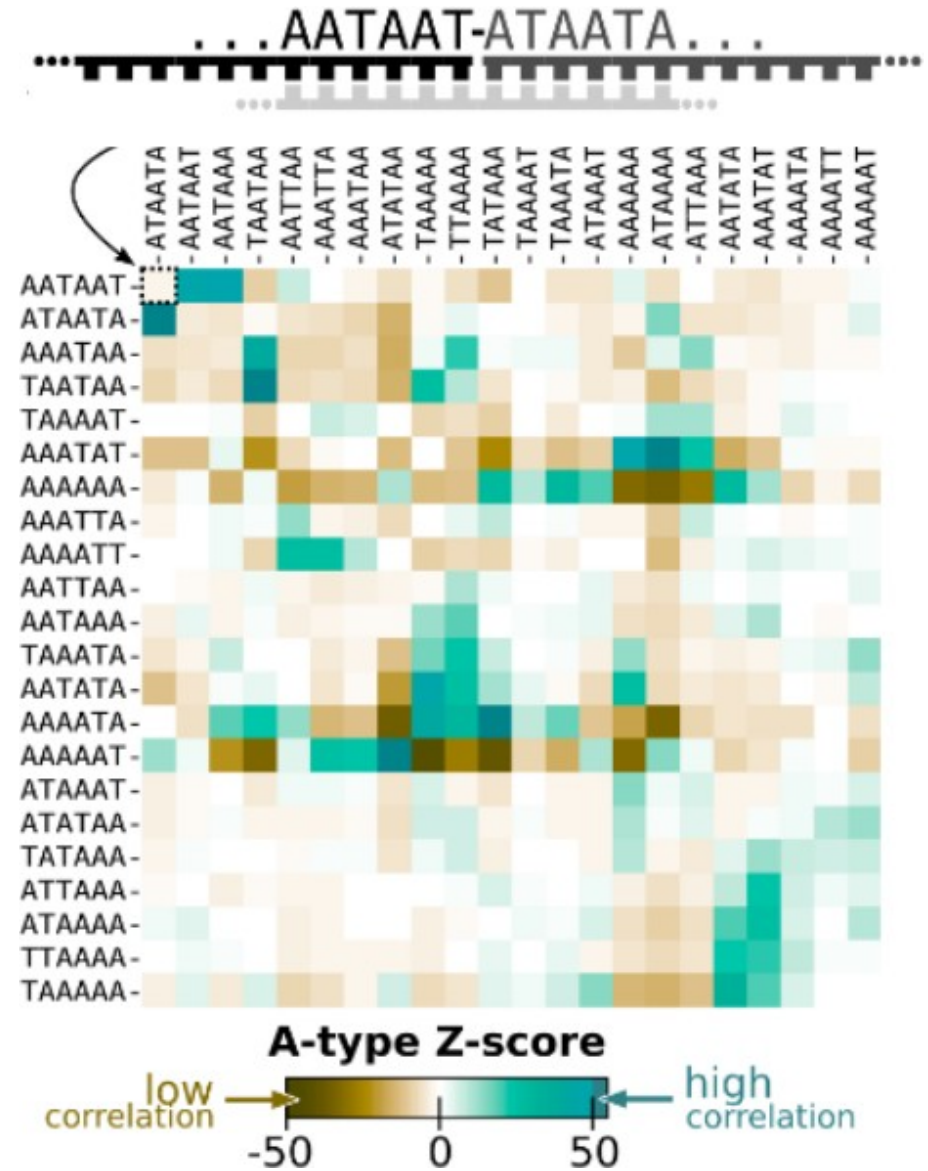
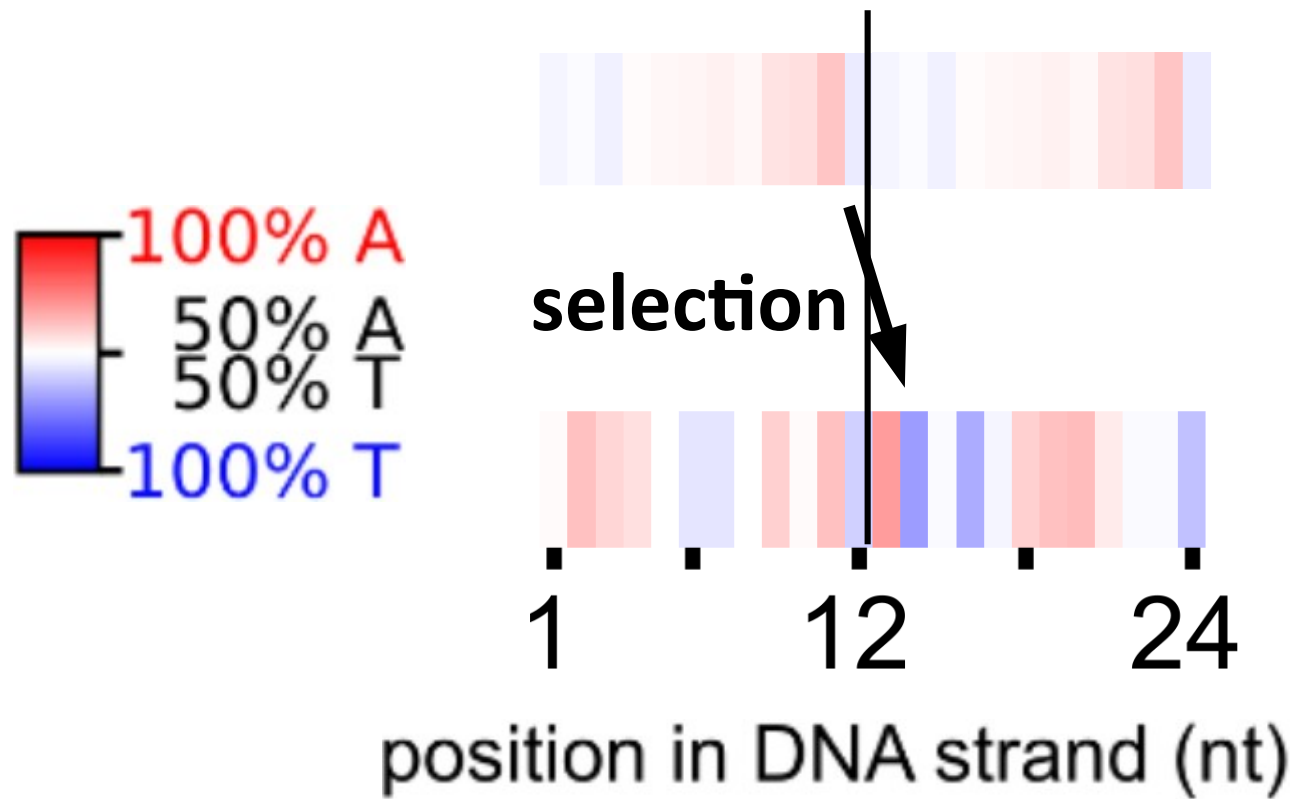
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Dynamics in sequence space

Replication amplifies patterns at the ligation site



With Sergei Maslov and Alexei Tkachenko, University of Illinois

Dynamics in sequence space

**Replication amplifies
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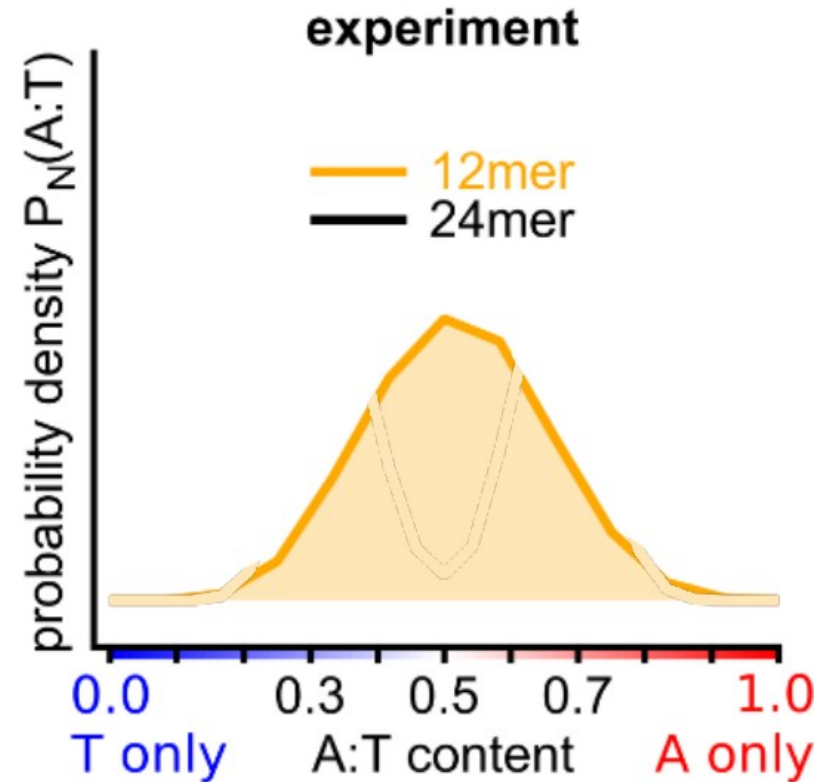
Dynamics in sequence space

**Replication amplifies
patterns at the ligation site**

**Replication avoids hairpins by
evolving complementary pools**

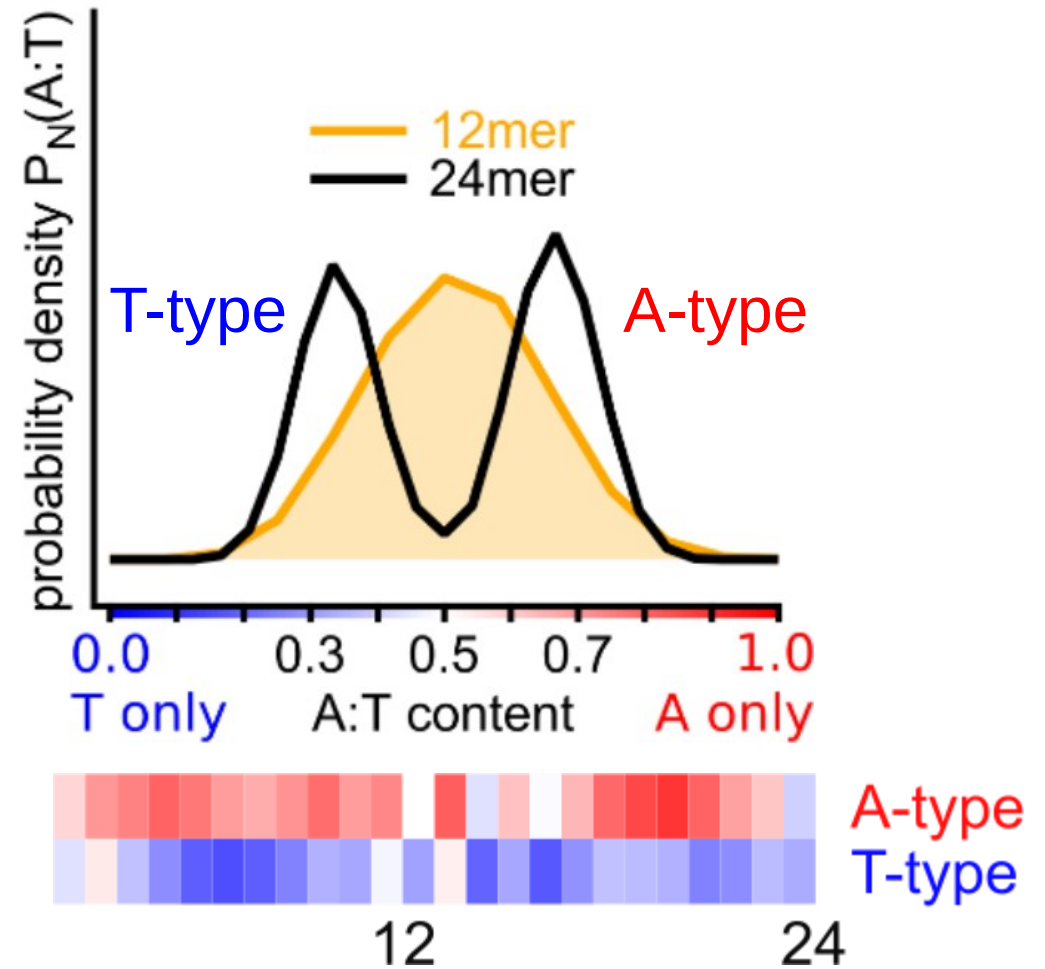
Dynamics in sequence space

Replication avoids hairpins by evolving complementary pools



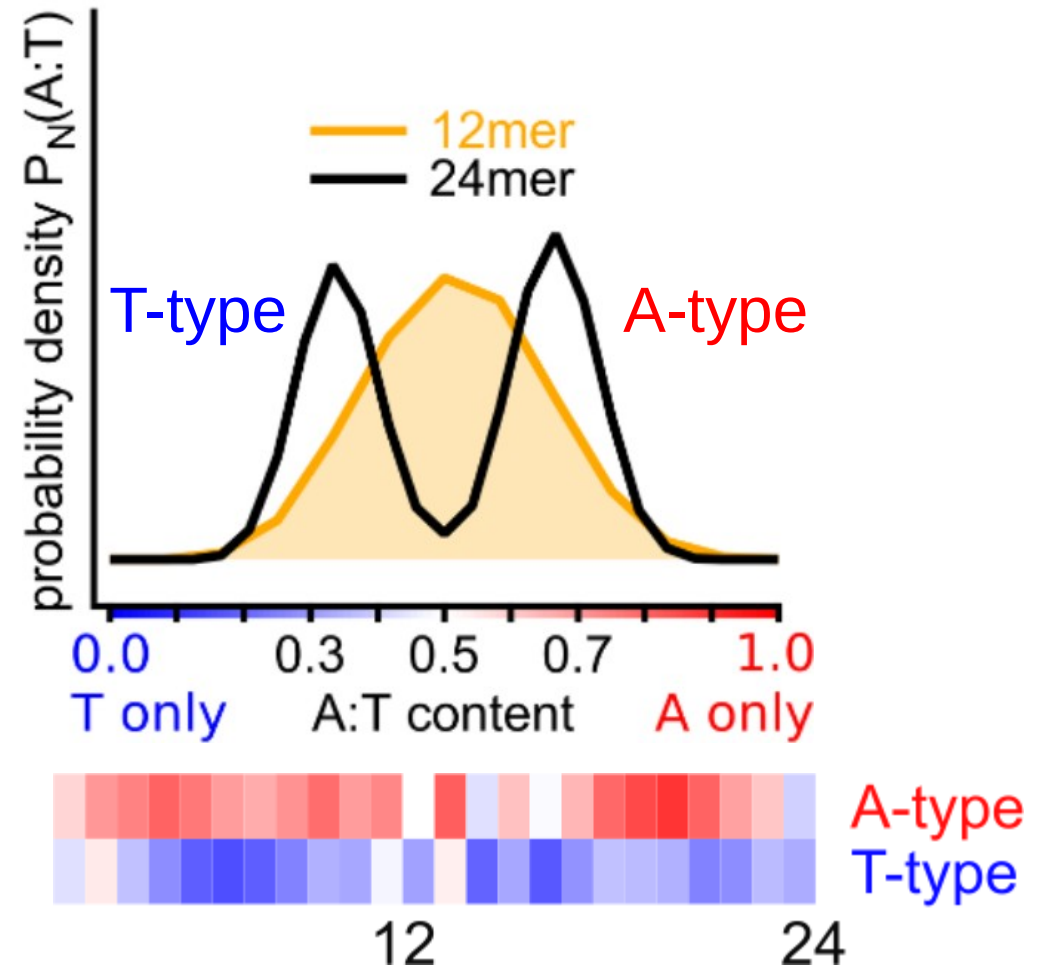
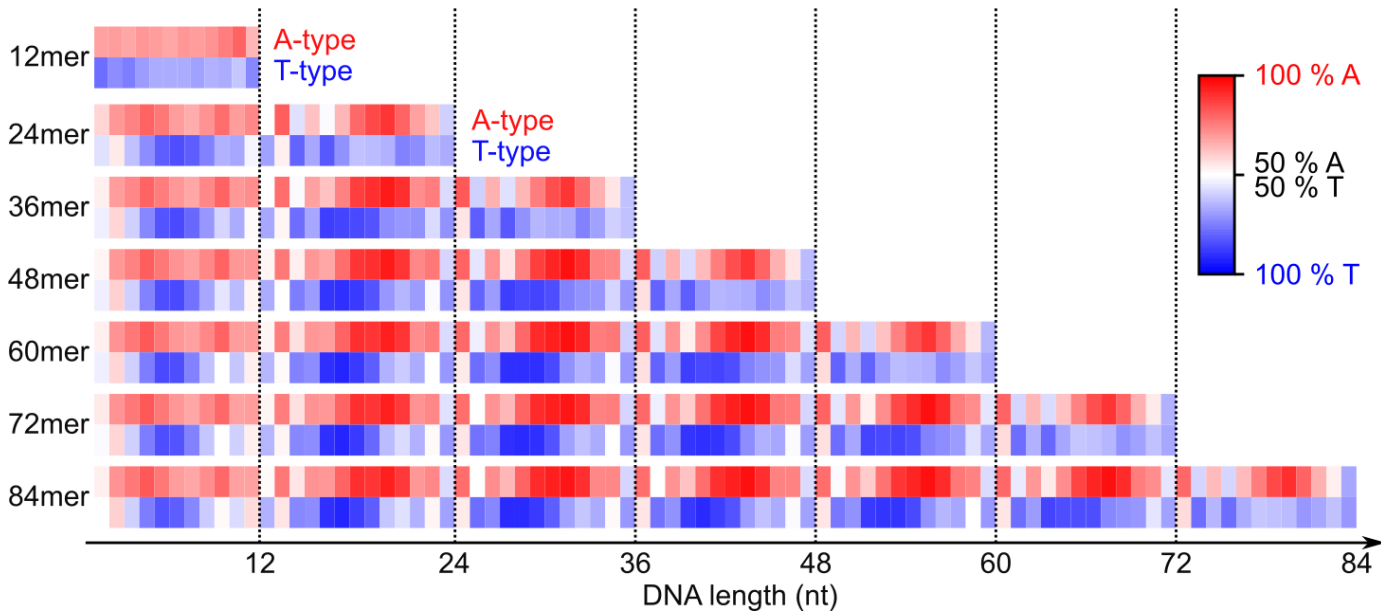
Dynamics in sequence space

Replication avoids hairpins by evolving complementary pools



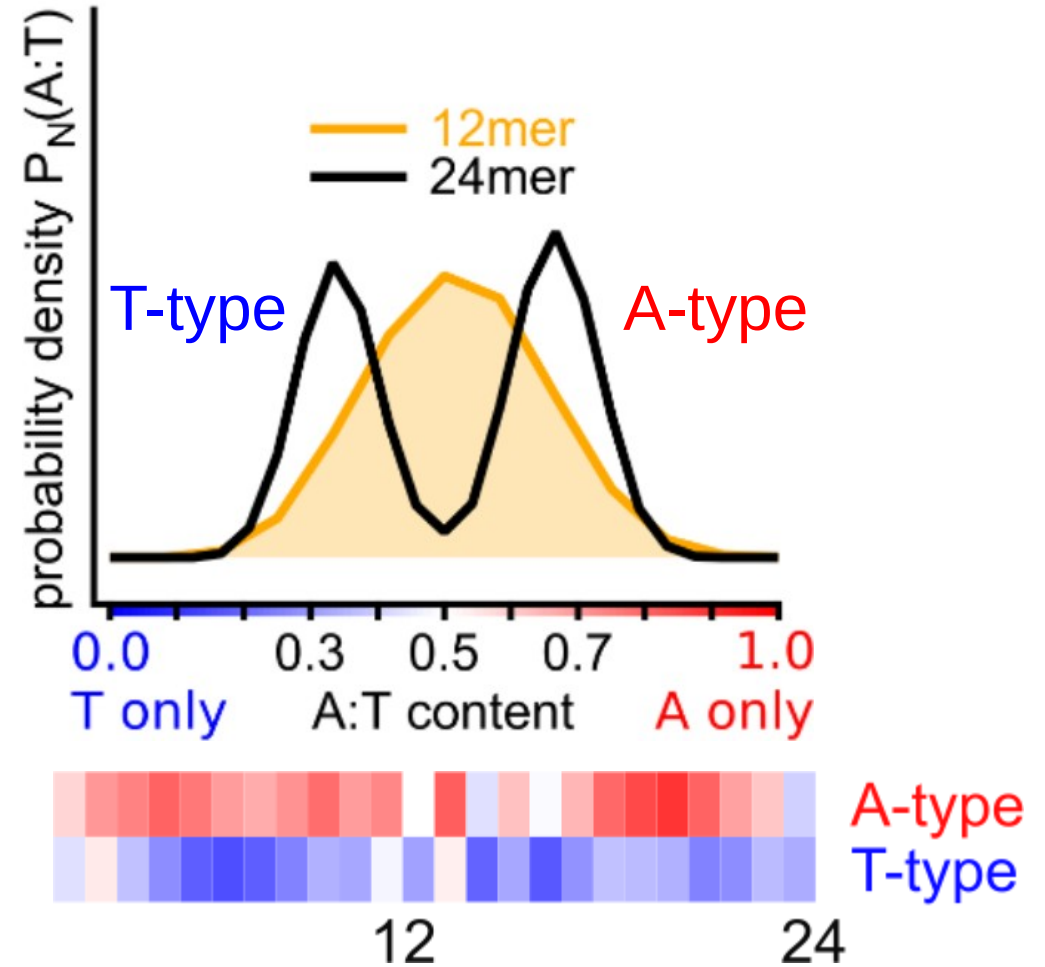
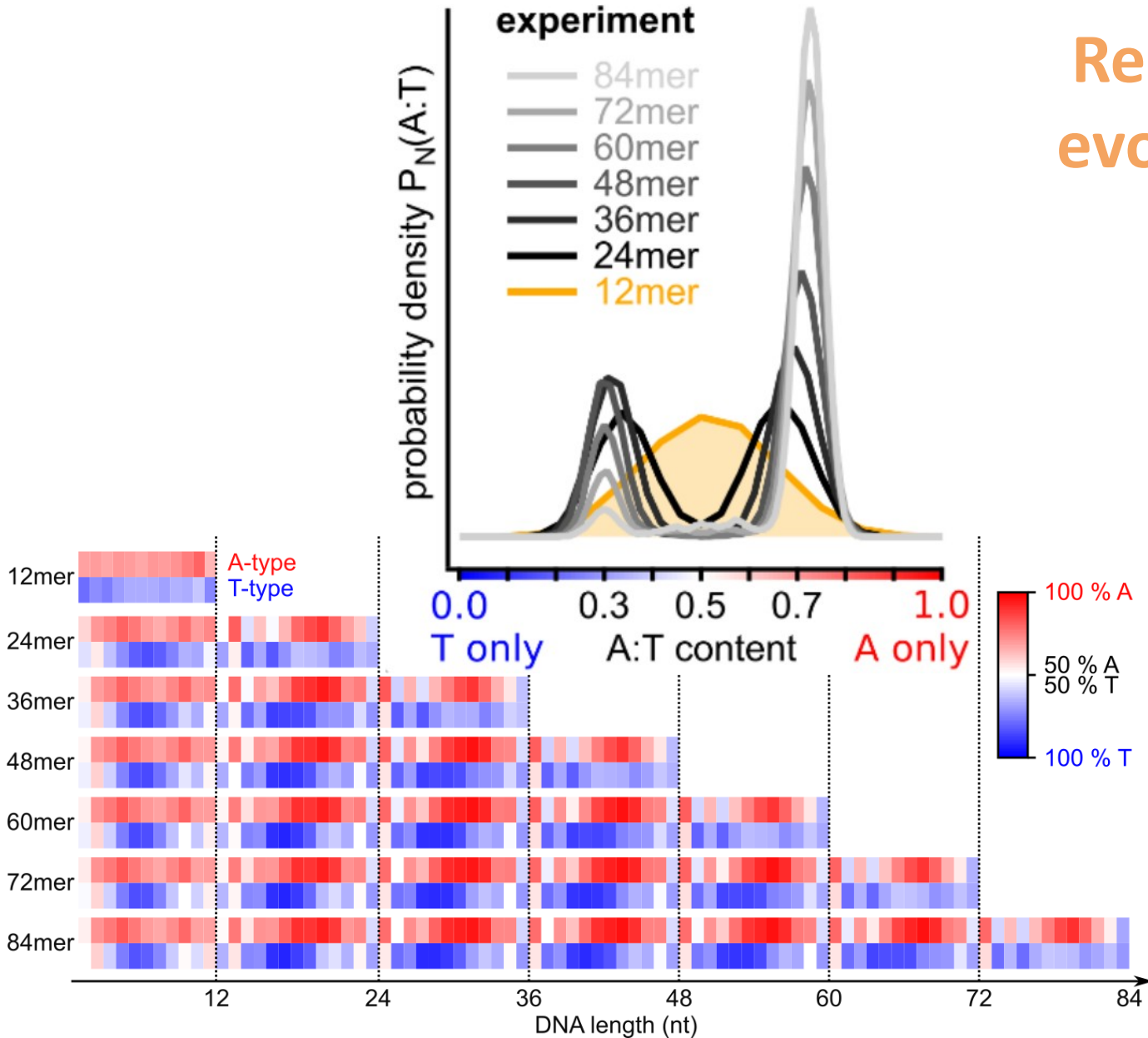
Dynamics in sequence space

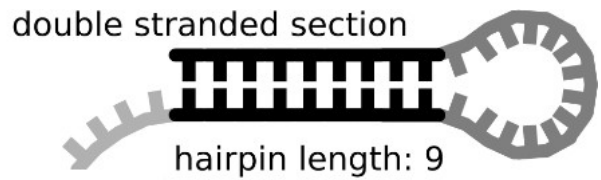
Replication avoids hairpins by evolving complementary pools



Dynamics in sequence space

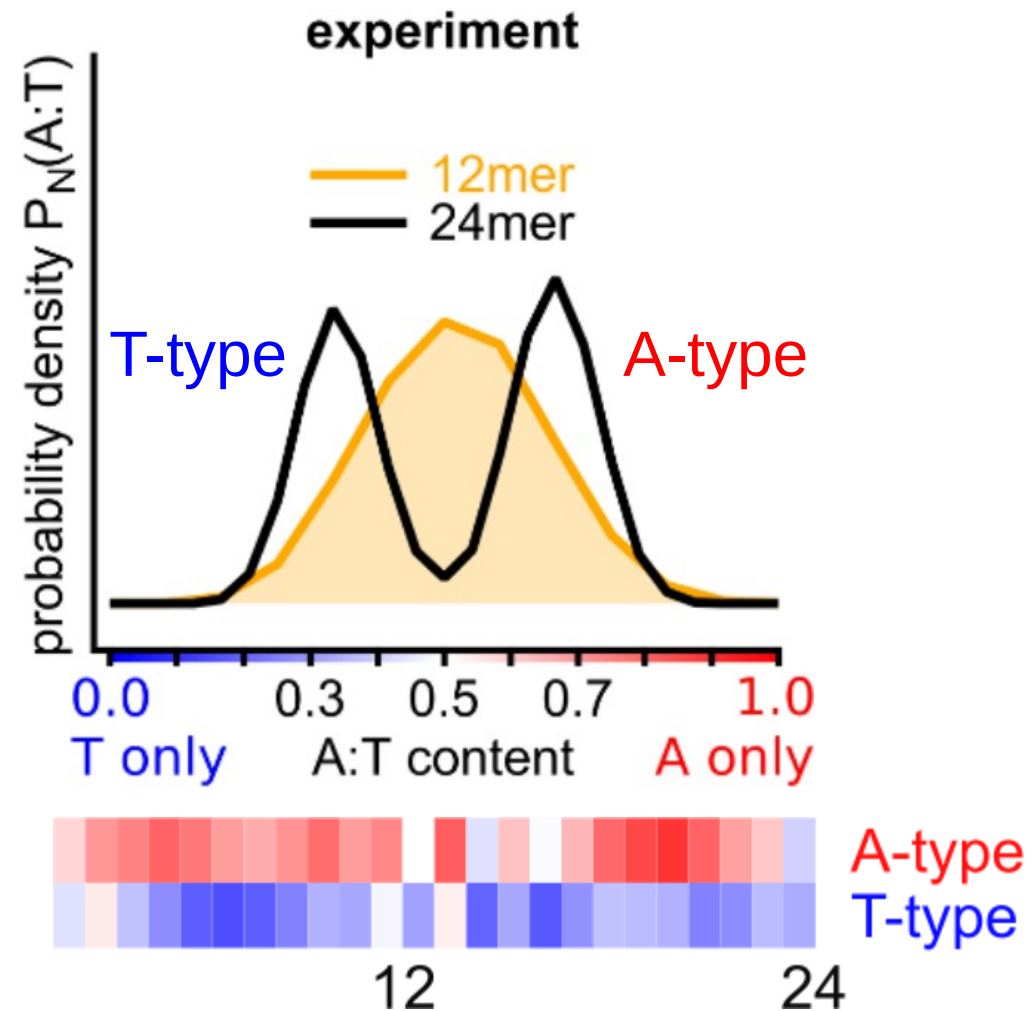
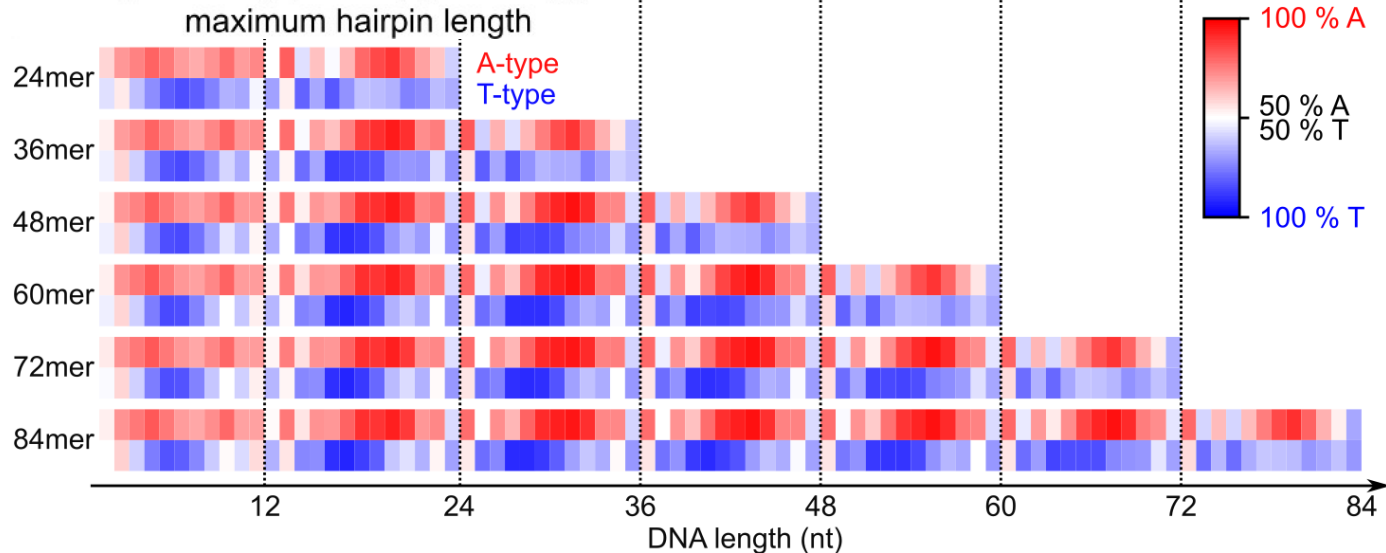
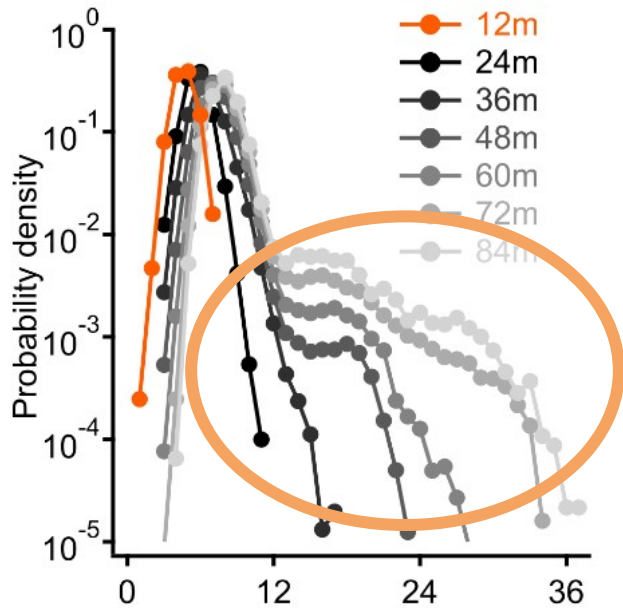
Replication avoids hairpins by evolving complementary pools





Dynamics in sequence space

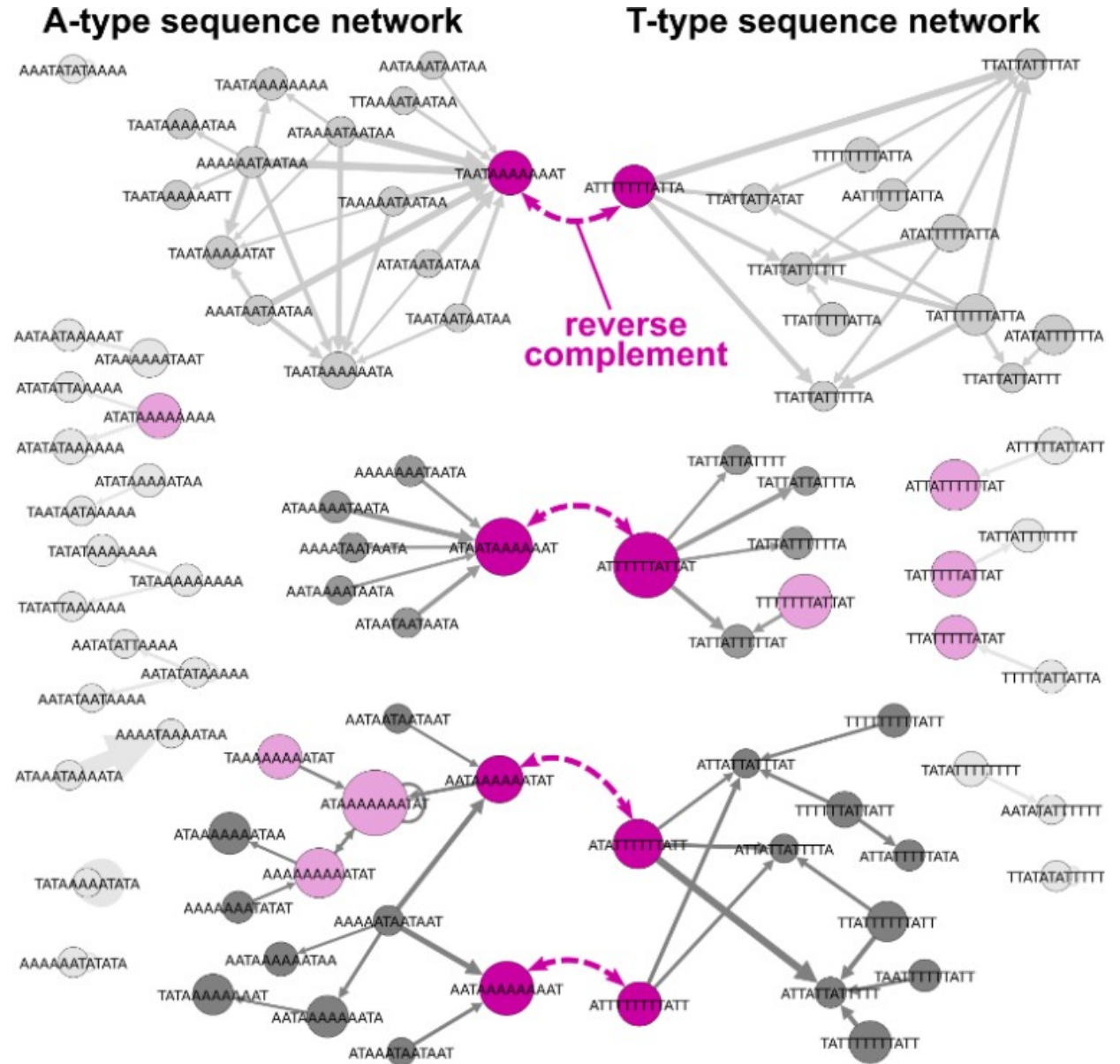
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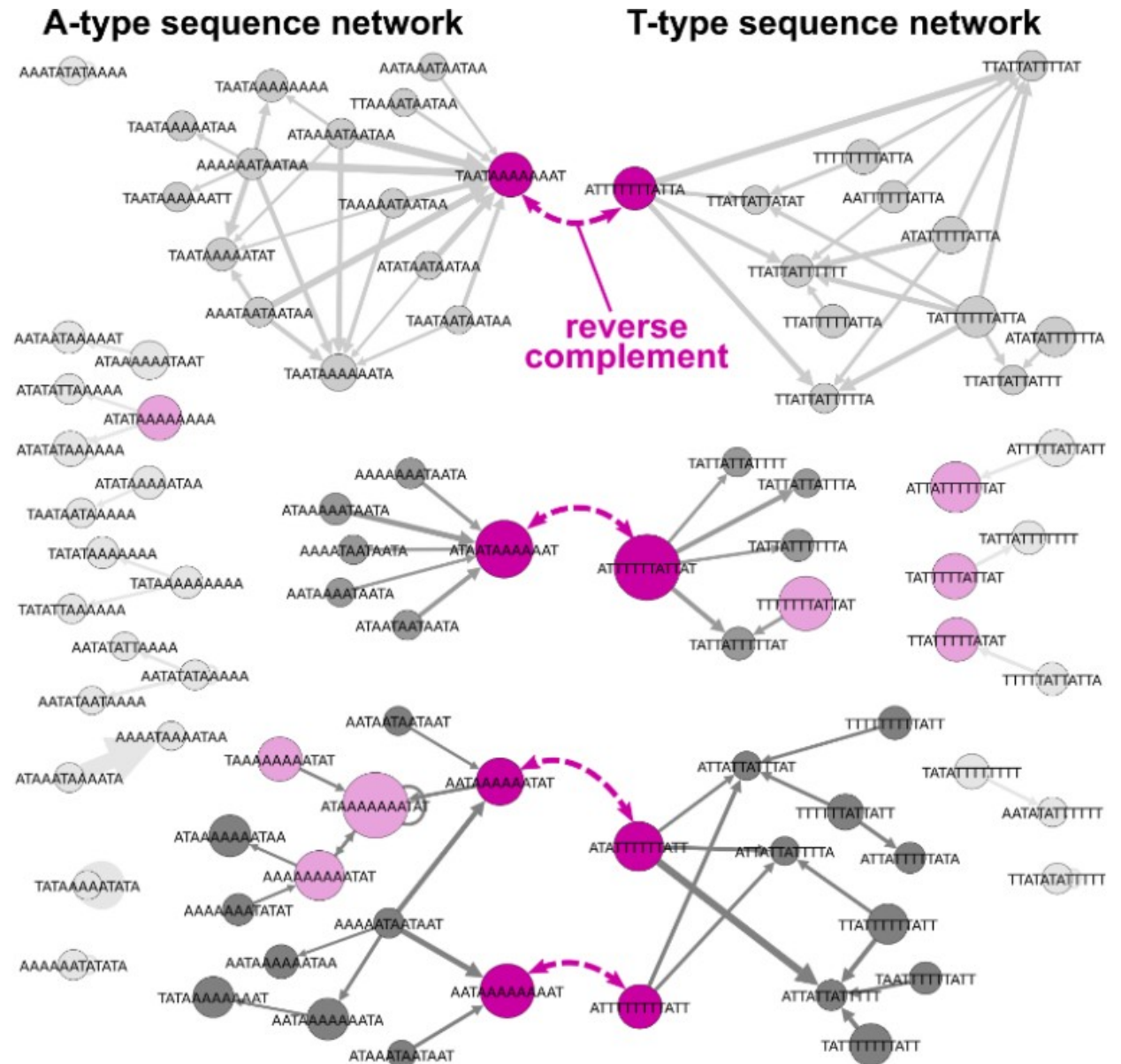
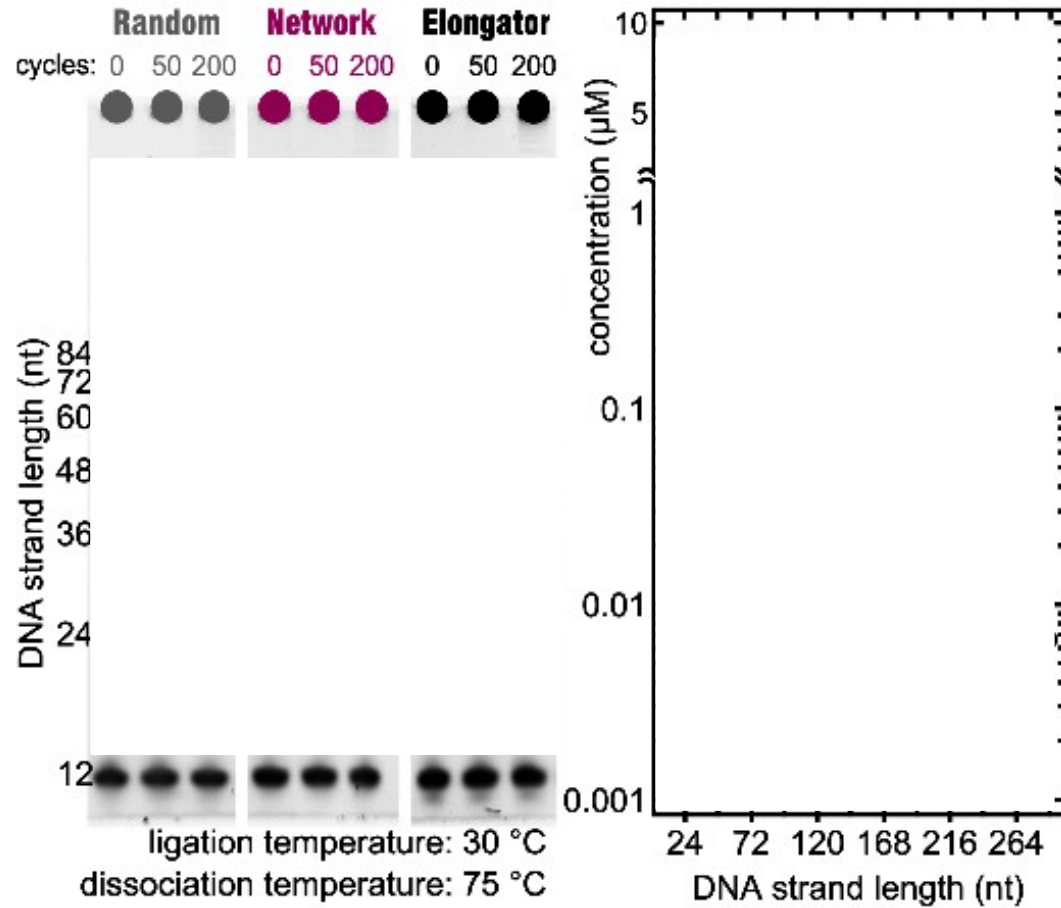
Dynamics in sequence space

Replication amplifies patterns at the ligation site

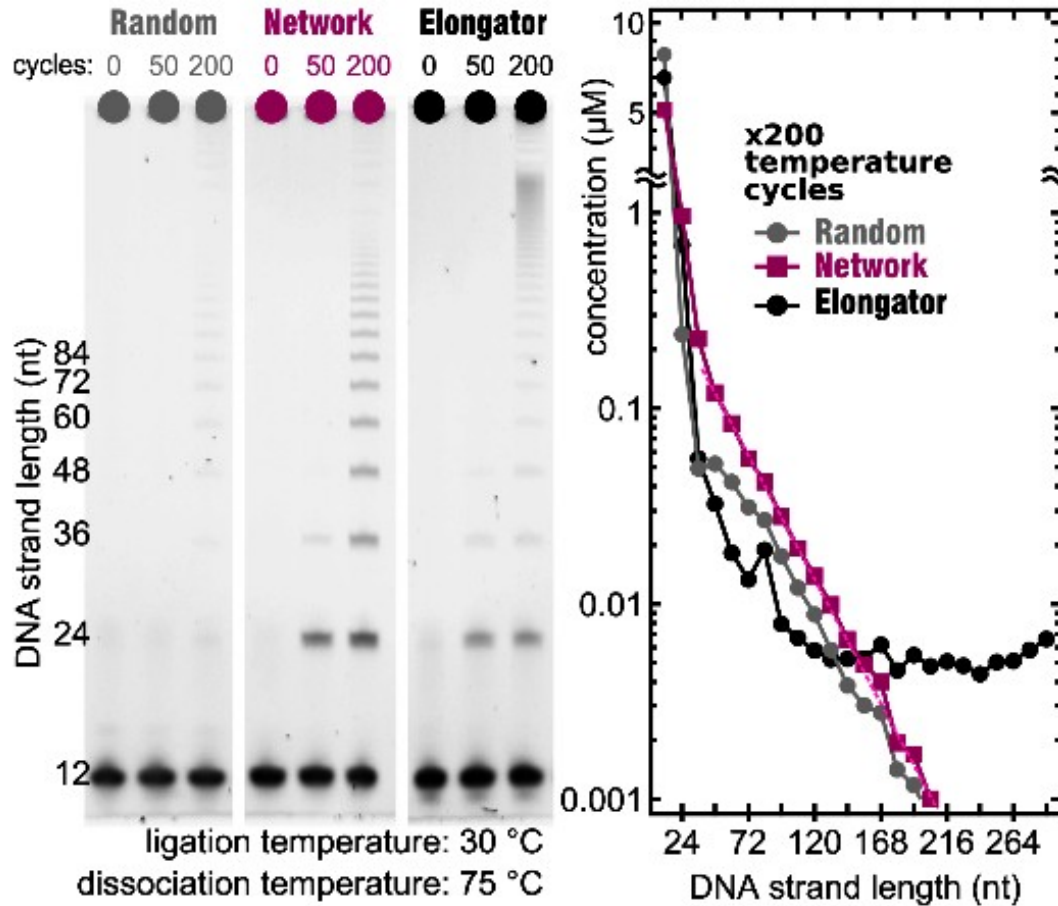
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Dynamics in sequence space



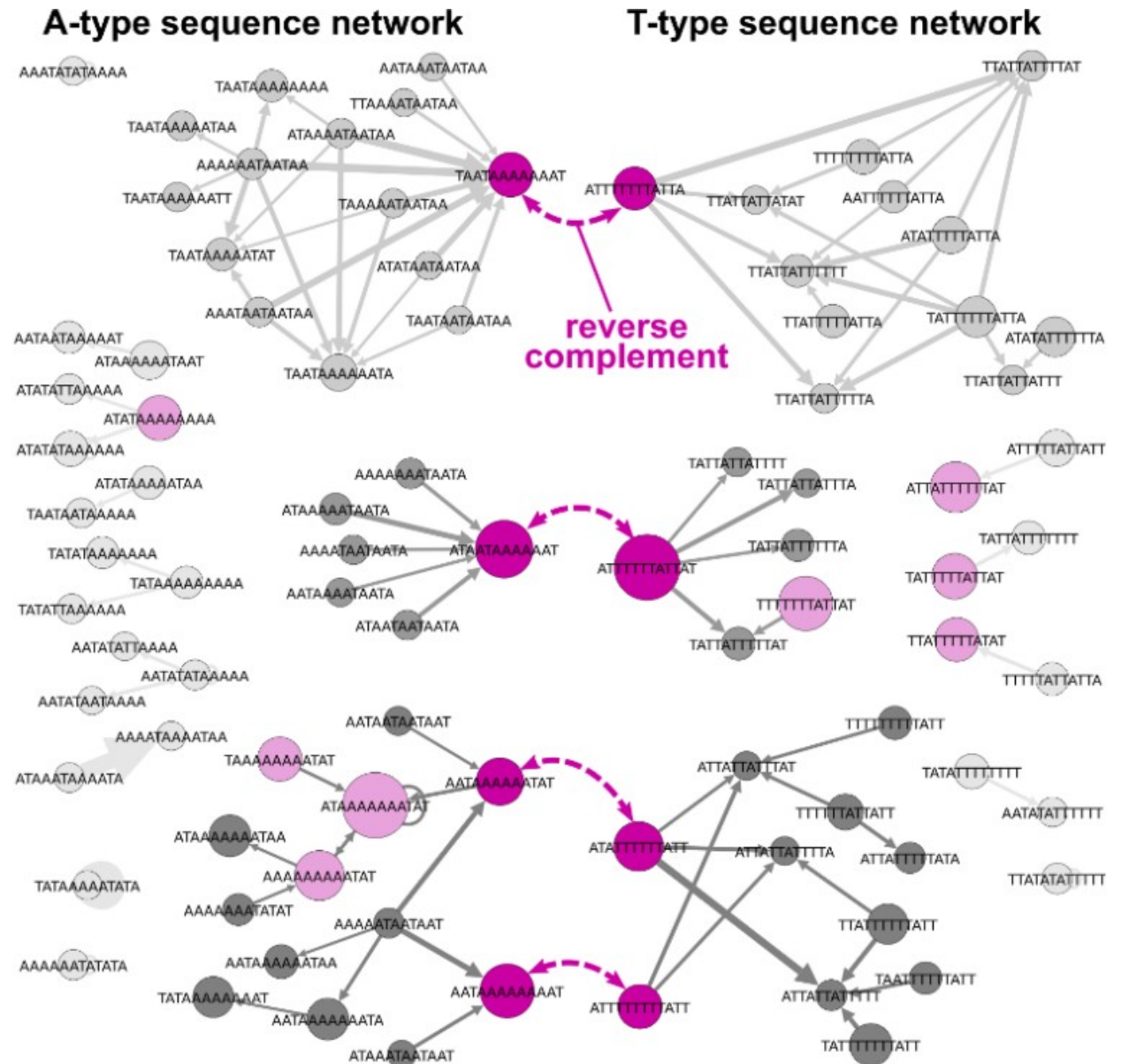
Dynamics in sequence space



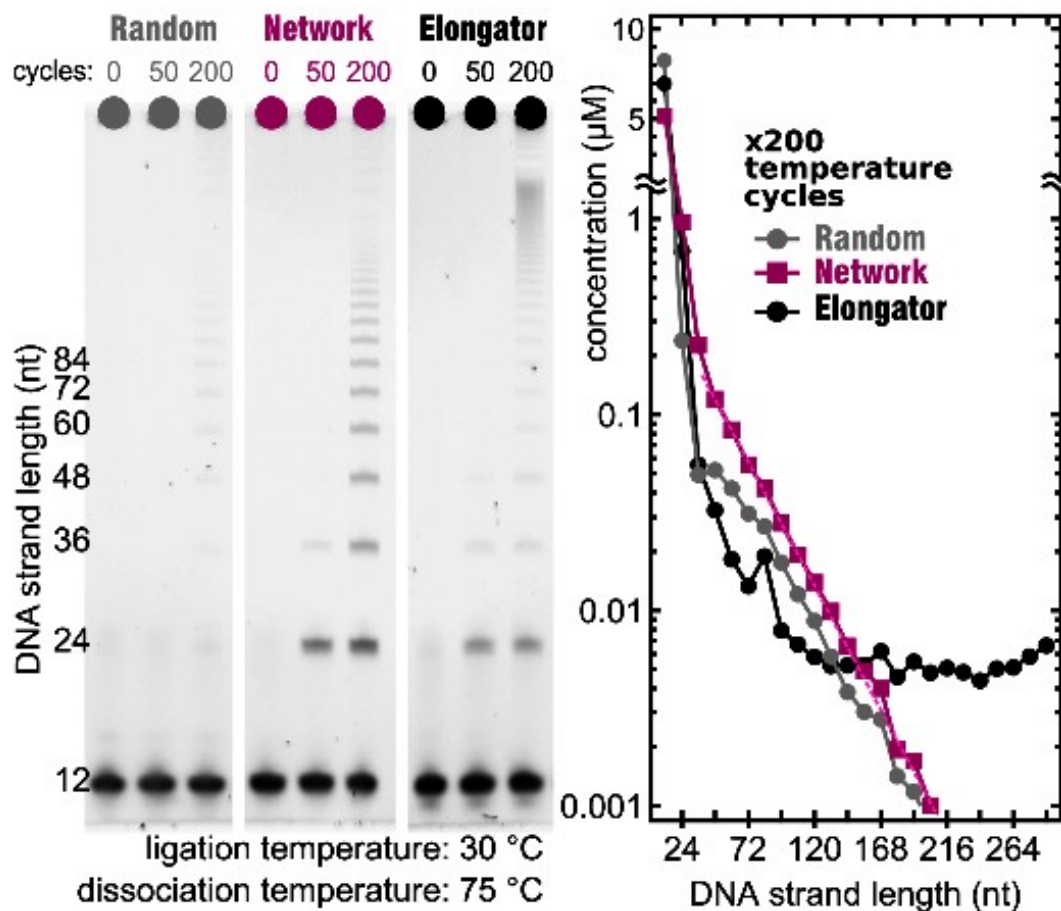
Random
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 ATAATTAAATAA
 TAAAAATTATTT
 TTAAATTTTATA
 TATTTAATTTTT
 TAAAAATTAATA
 AAAATAATTTAT
 TTATATAAAATA

Network
 ATAATAAAAAAT
 AATAAAAAAAAT
 AATAAAAAATAT
 TAATAAAAAAAT
 ATTTTTTATTAT
 ATATTTTTTATT
 ATTTTTTTTTATT
 ATTTTTTTTATTA

Elongator
 ATATTTTTTATA
 TATAAAAAATAT
 AAATATATAAAA
 TTTTATATATTT
 AAAATATATAAA
 TTTATATATTTT
 TATTTTTTTTTAT
 ATAAAAAAAATA



Dynamics in sequence space



Random

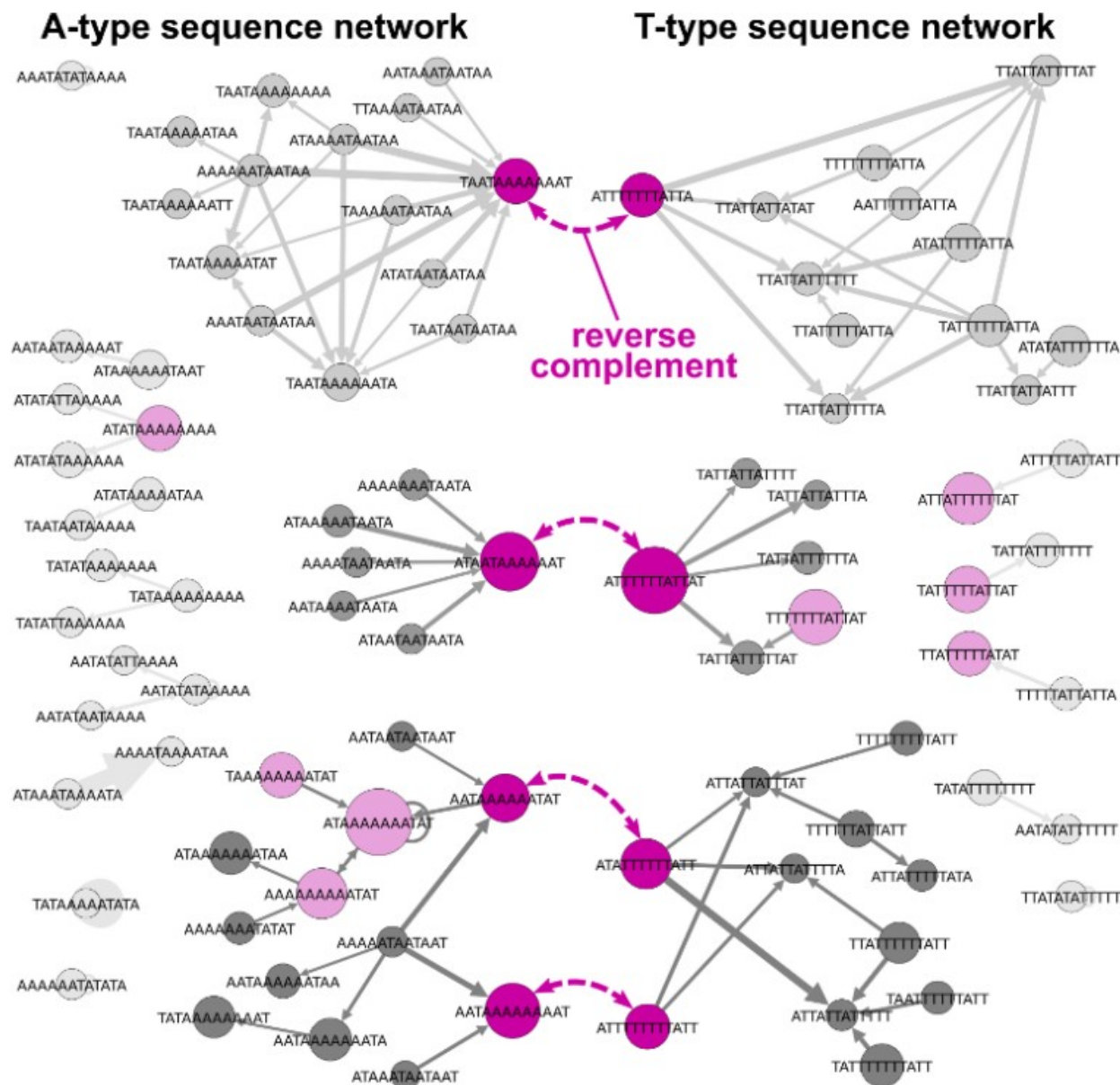
AAAATAAAATAT
ATAATTAAATAA
 TAAAAATTATTT
 TAAAATTTTATA
TATTTAATTTTT
 TAAAAATTAATA
 AAAATAATTTAT
 TTATATAAAATA

Network

ATAATAAAAAAT
 AATAAAAAAAAT
 AATAAAAAATAT
 TAATAAAAAAT
 ATTTTTTATTAT
 ATTTTTTTTATT
 ATTTTTTTTATT
 ATTTTTTTTATTA

Elongator

ATATTTTTTATA
 TATAAAAAATAT
 AAATATATAAAA
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 TTTATATATTTT
 TATTTTTTTTTAT
 ATAAAAAAAATA





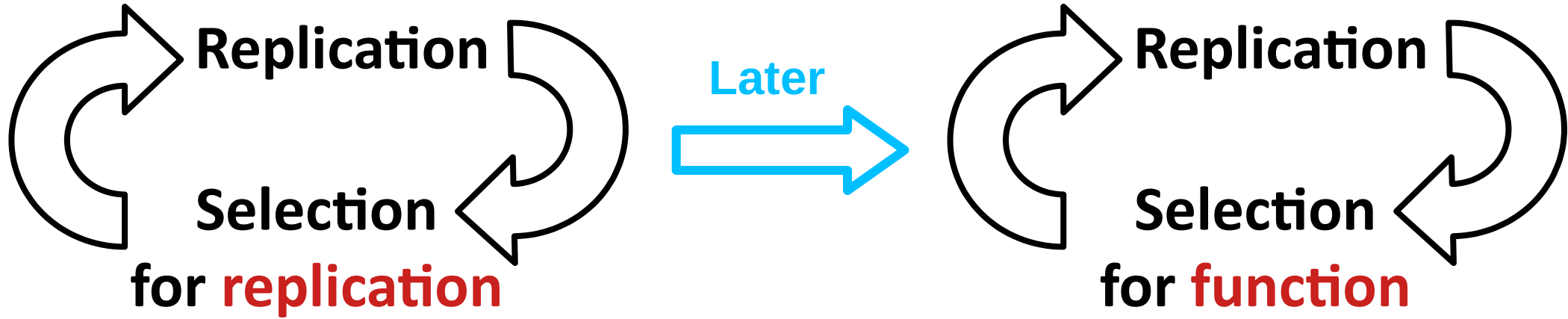


Later

A blue arrow pointing from the left diagram to the right diagram.



Fast replication selects small sequence spaces



Fast replication selects small sequence spaces

