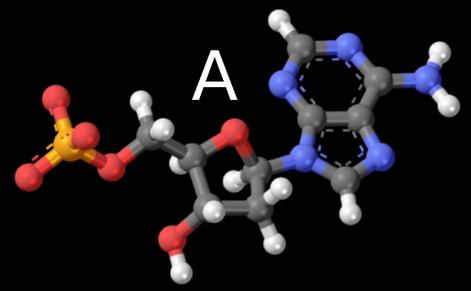
Mittelteil mit EDC kürzen
Water air mit pH+salt auf aktuellen STand bringe
fog PCR: auch lange Stränge zeigen und
die Sequenzierung
cCMP und cGMP images hatten einen Fehler

Emergence of Life in the Lab?

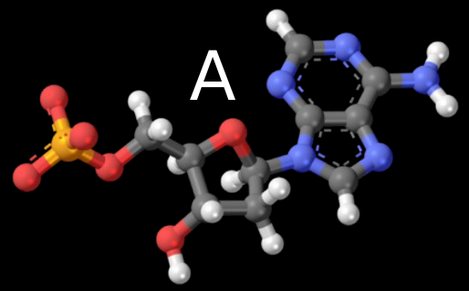
Microscale nonequilibria for the emergence of life

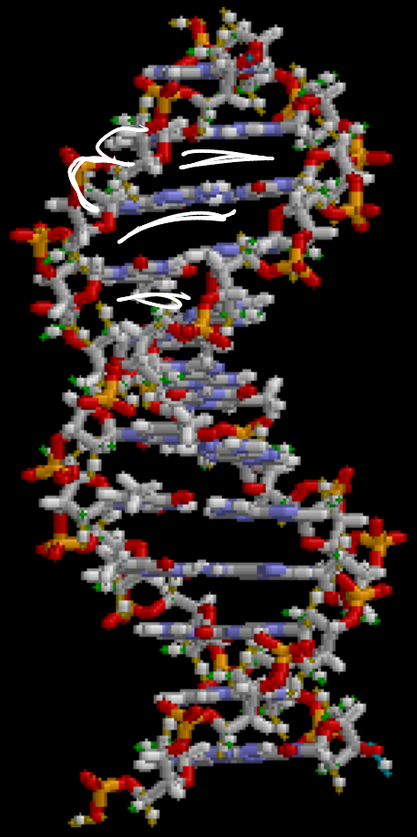
Dieter Braun
Biophysics, Center for NanoScience, LMU Munich

Emergence of Life



Emergence of Life





Sequence

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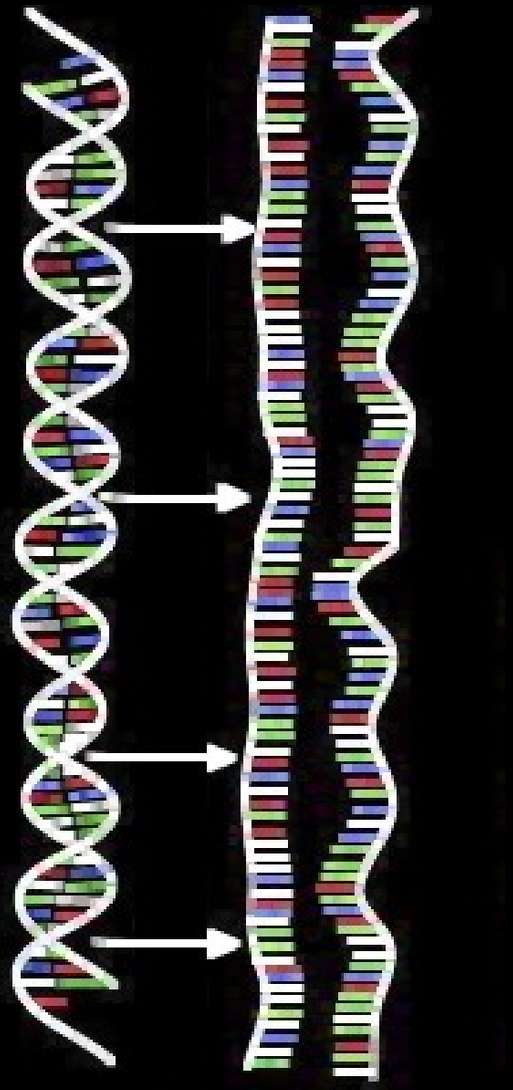
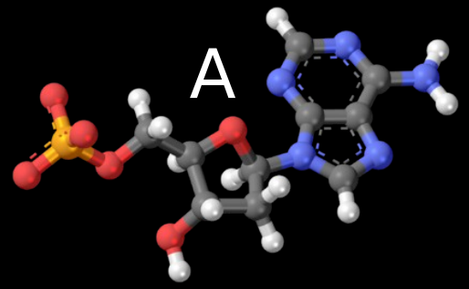
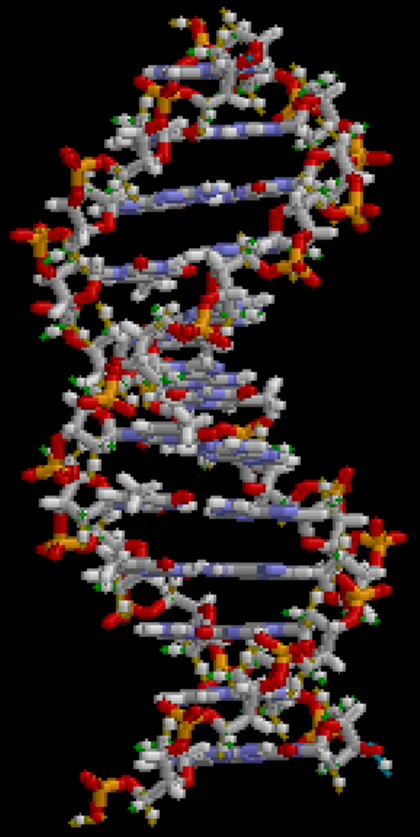
Emergence of Life







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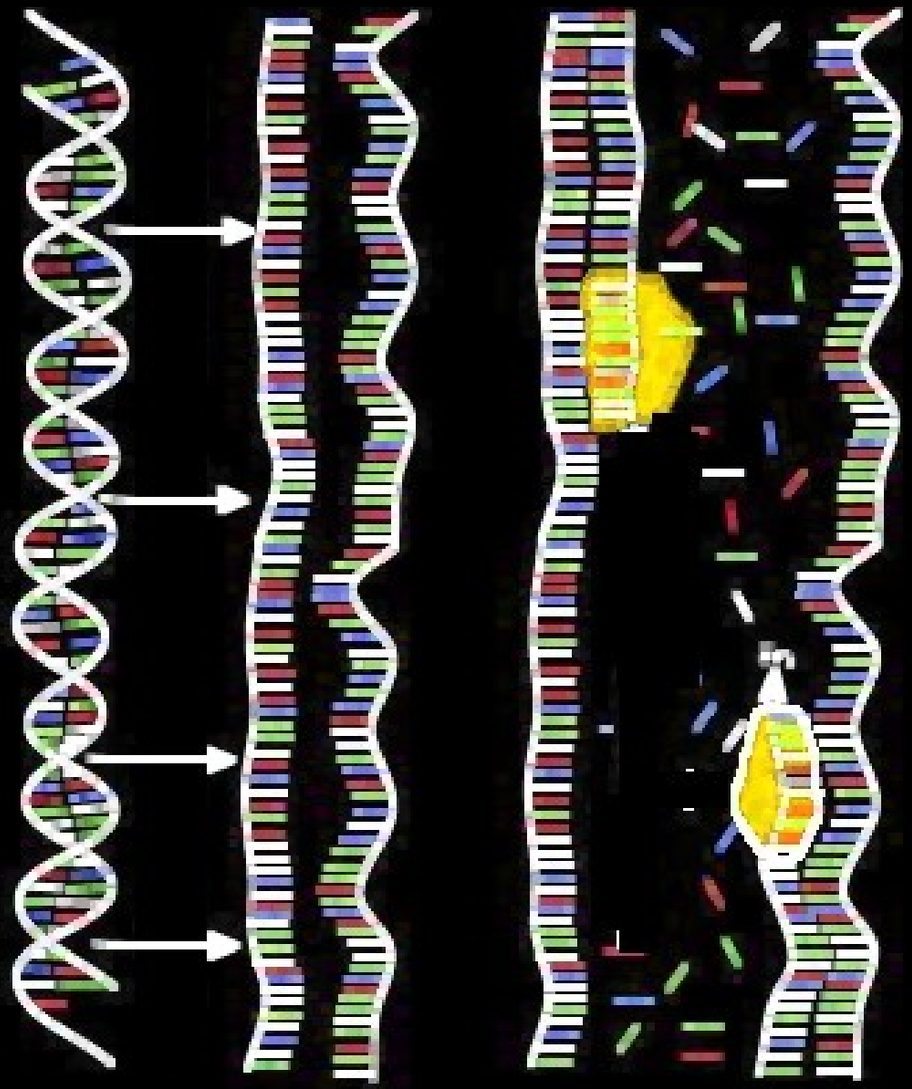
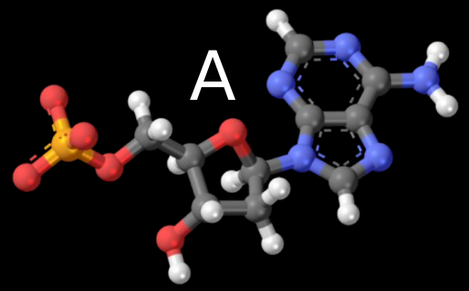
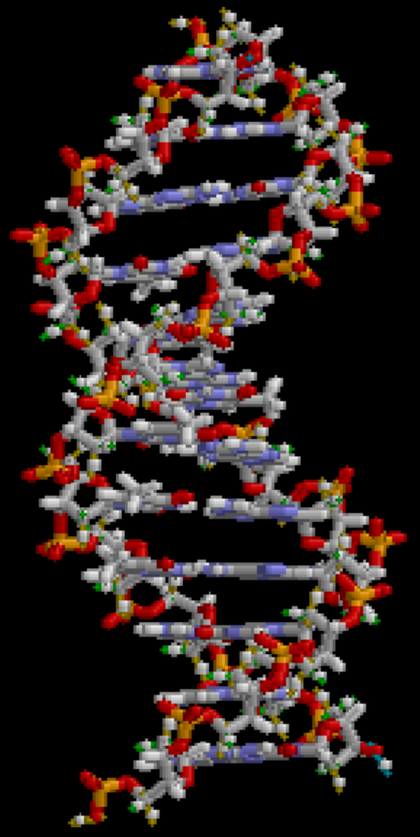
Emergence of Life







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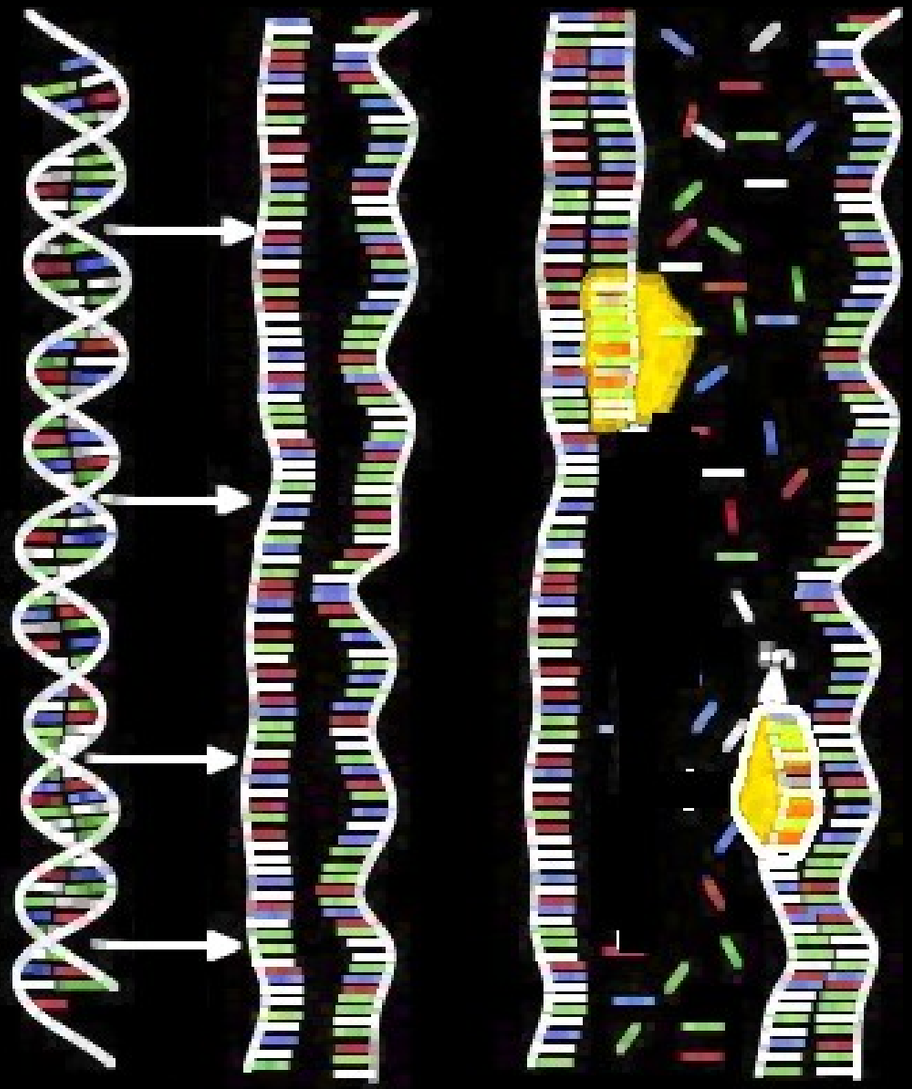
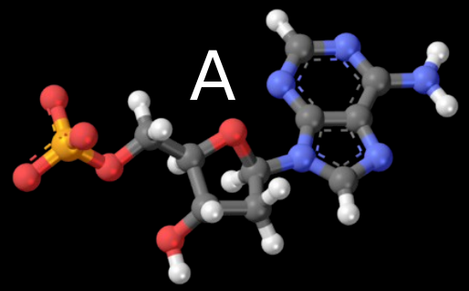
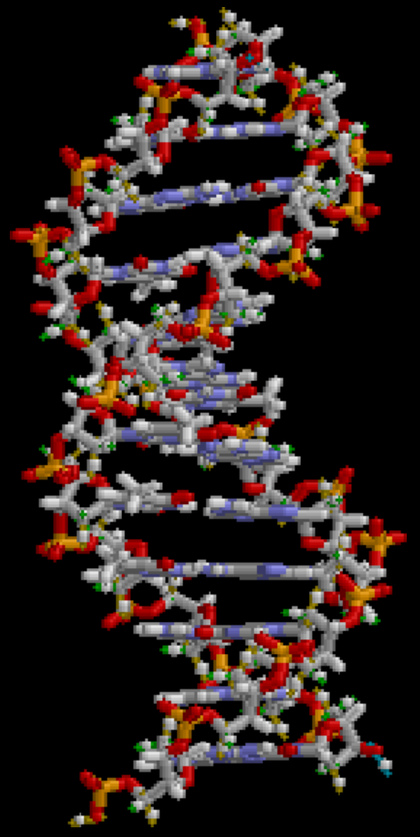
Emergence of Life







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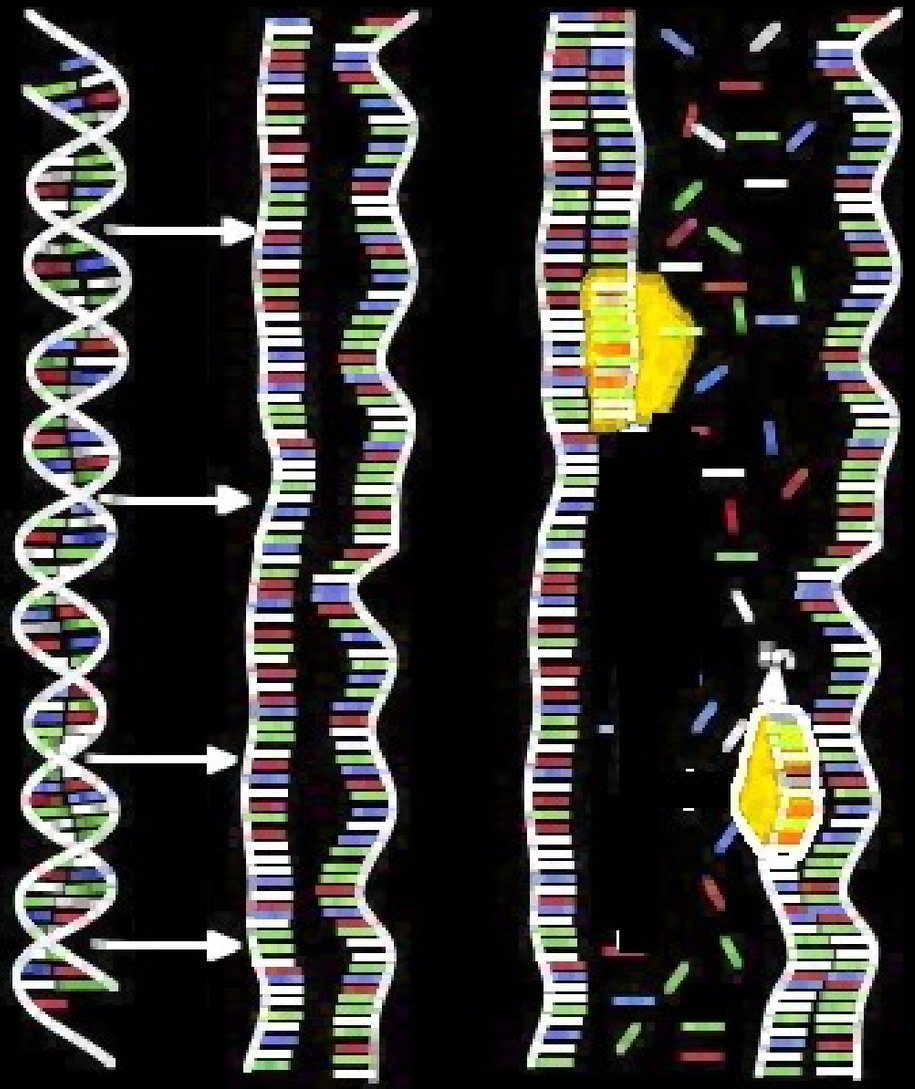
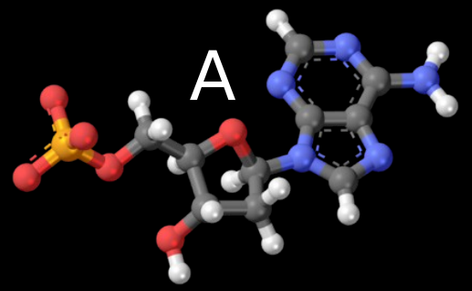
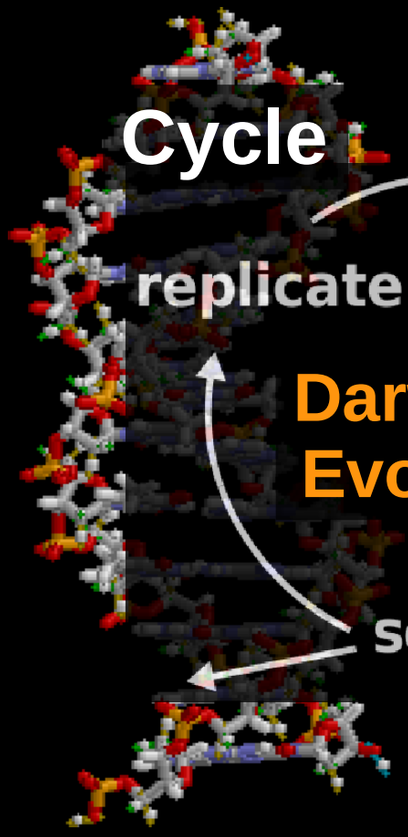
Emergence of Life







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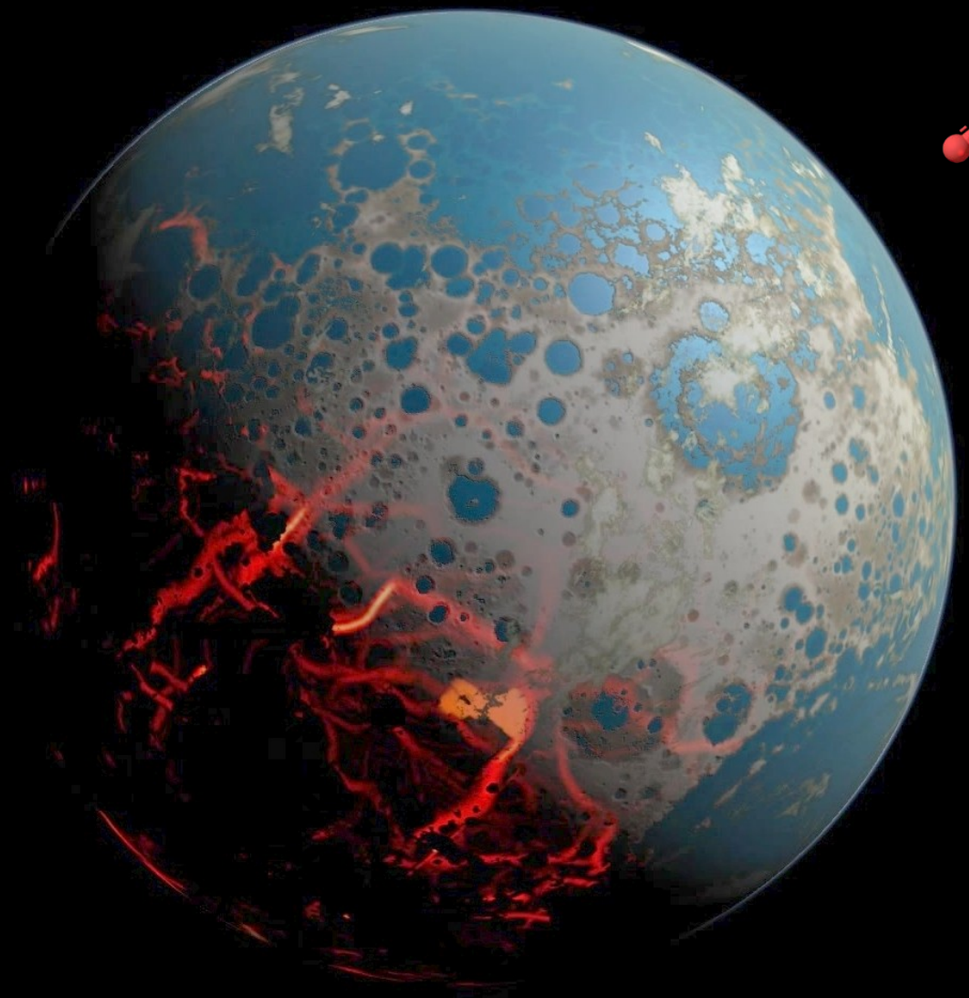
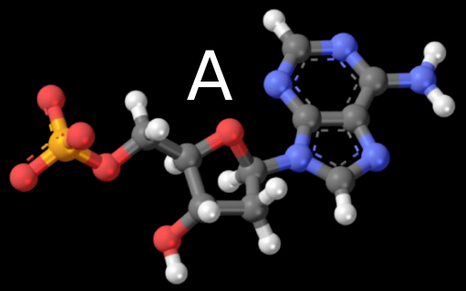
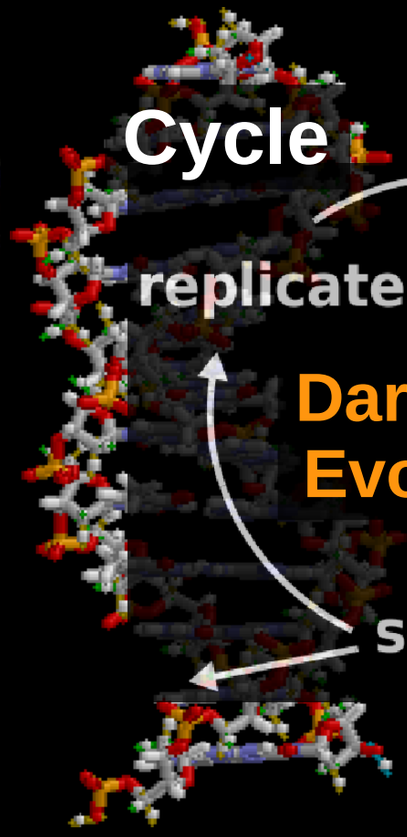
Emergence of Life







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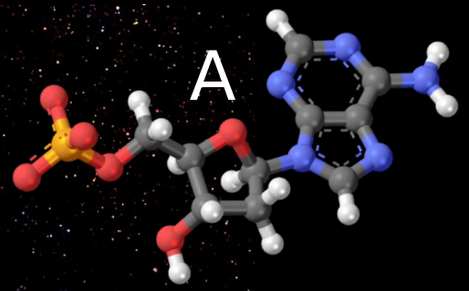
GACTACGCA

Emergence of Life

Moon forming impact



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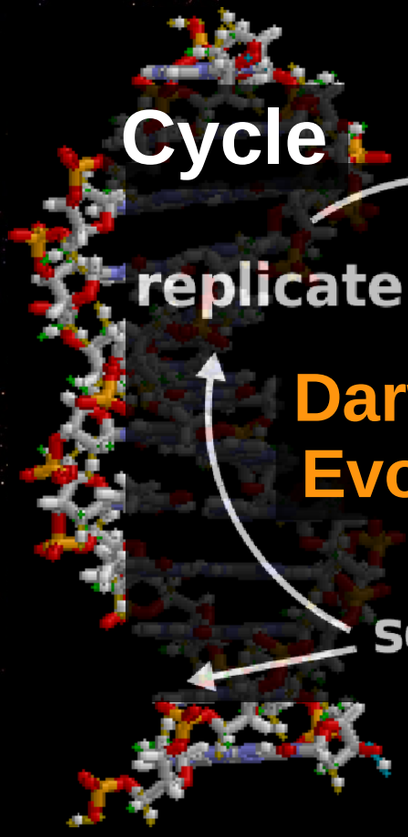
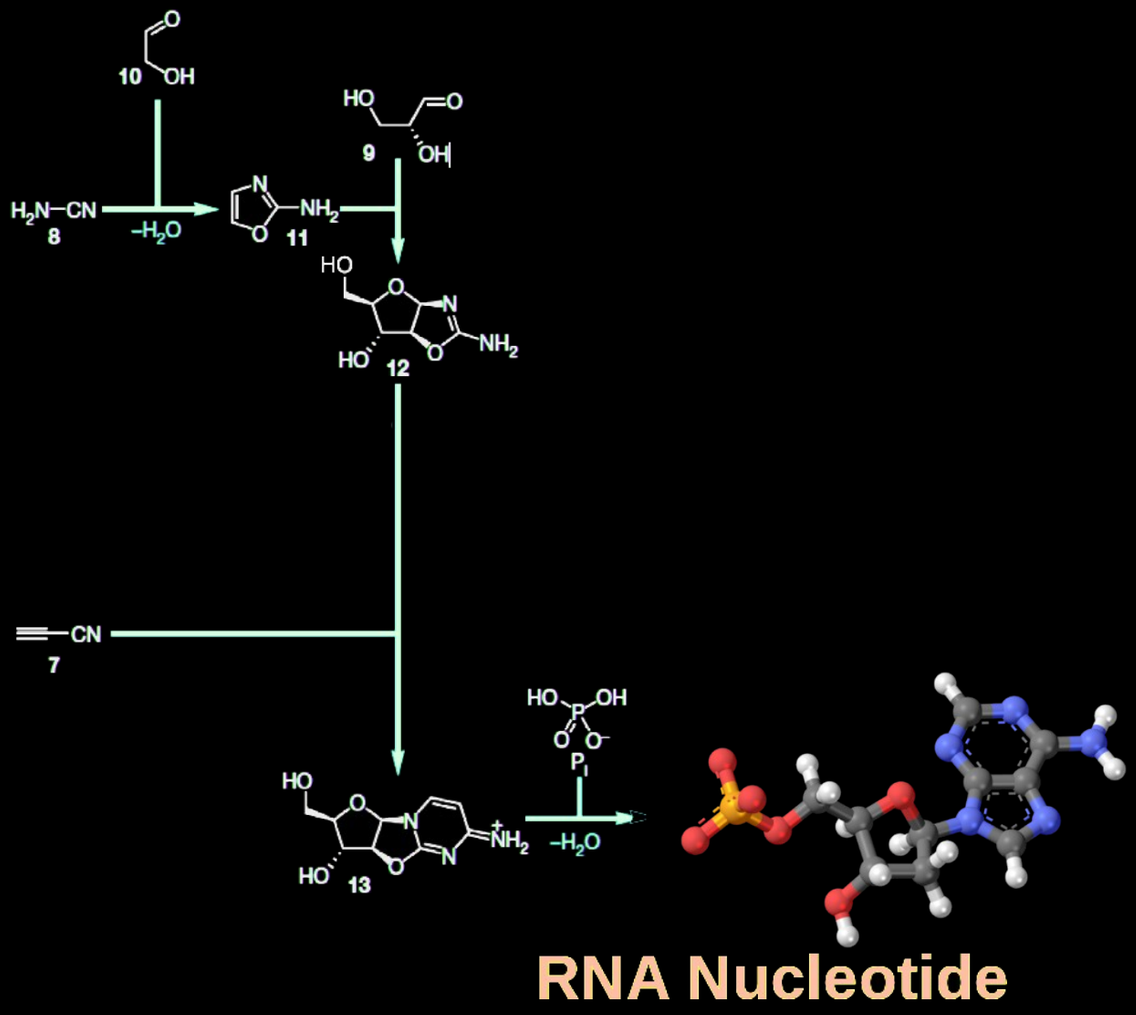


Chemical Space

Physical Space

Chemical Space

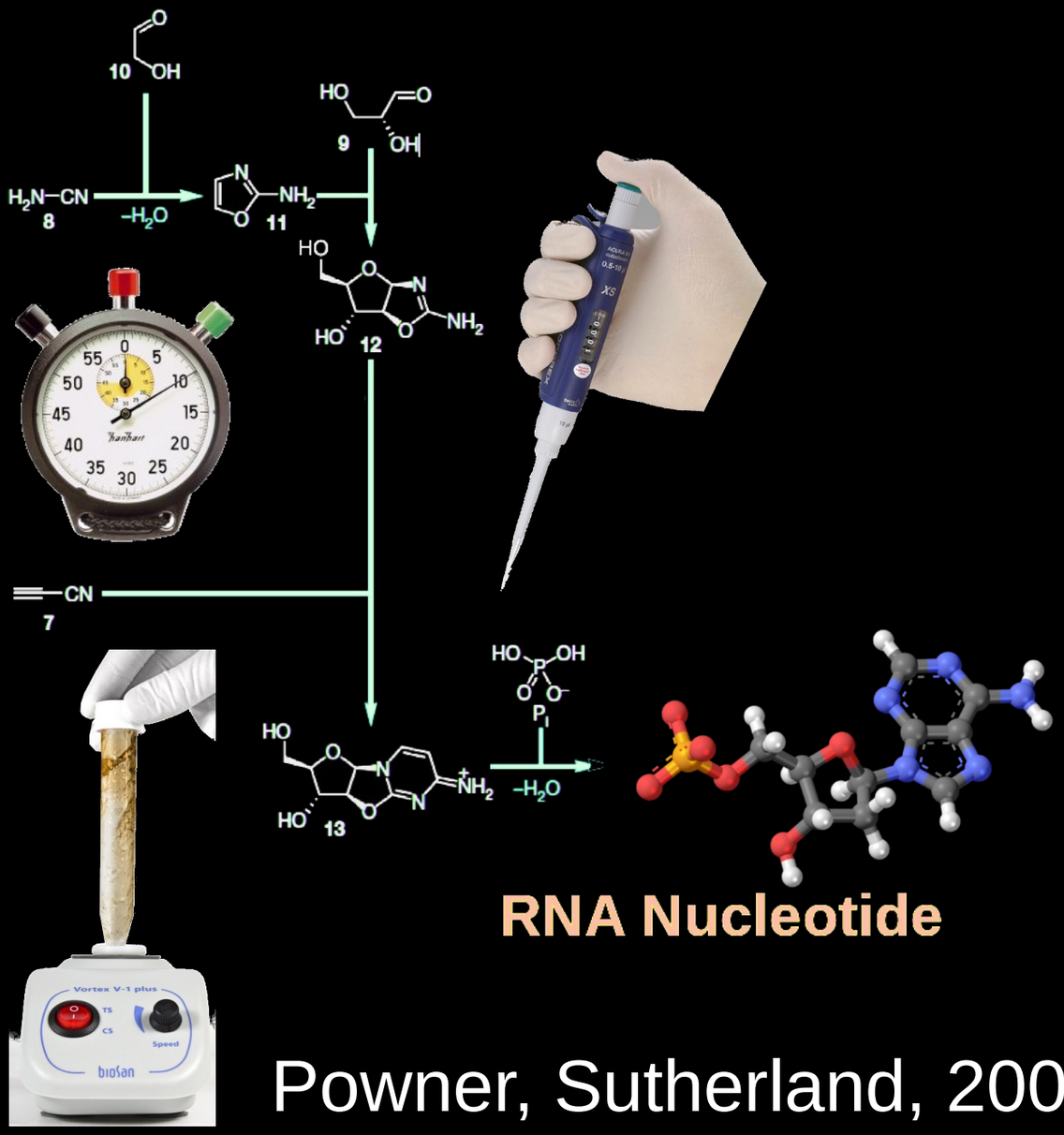
Physical Space



Powner, Sutherland, 2009

Chemical Space

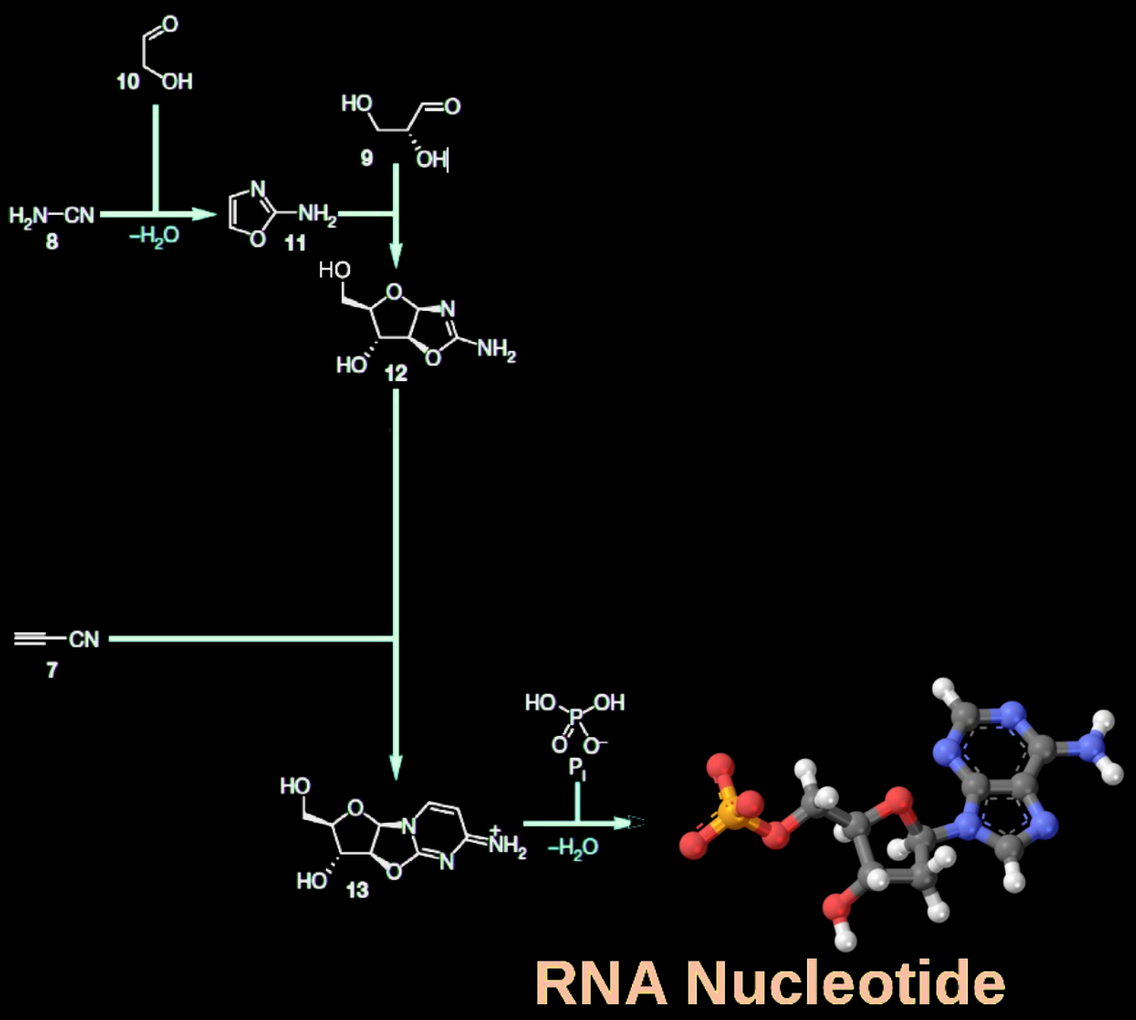
Physical Space

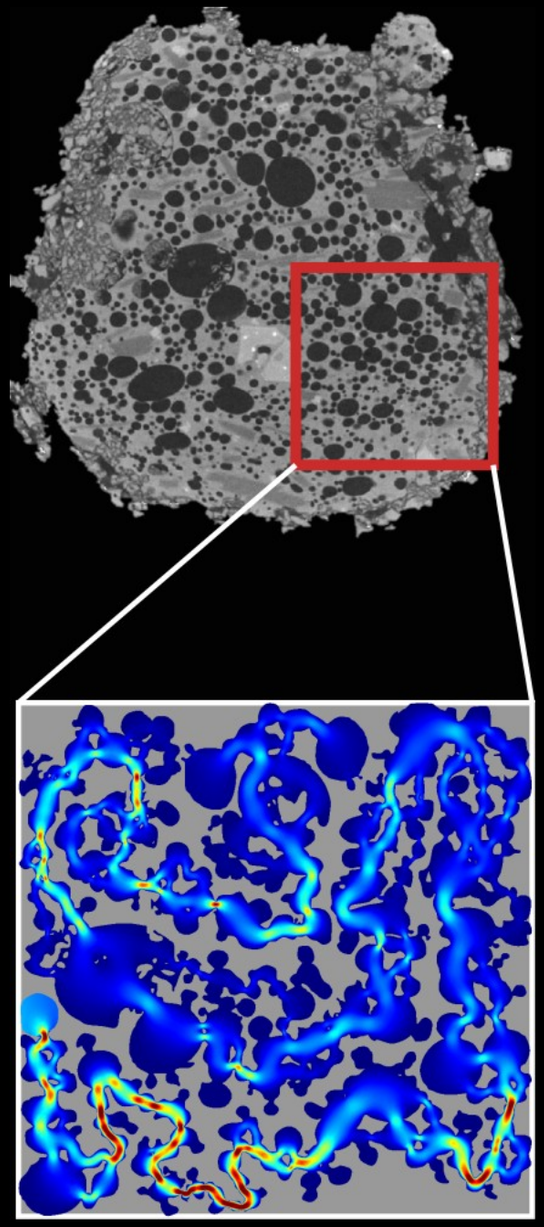


Powner, Sutherland, 2009

Chemical Space

Physical Space





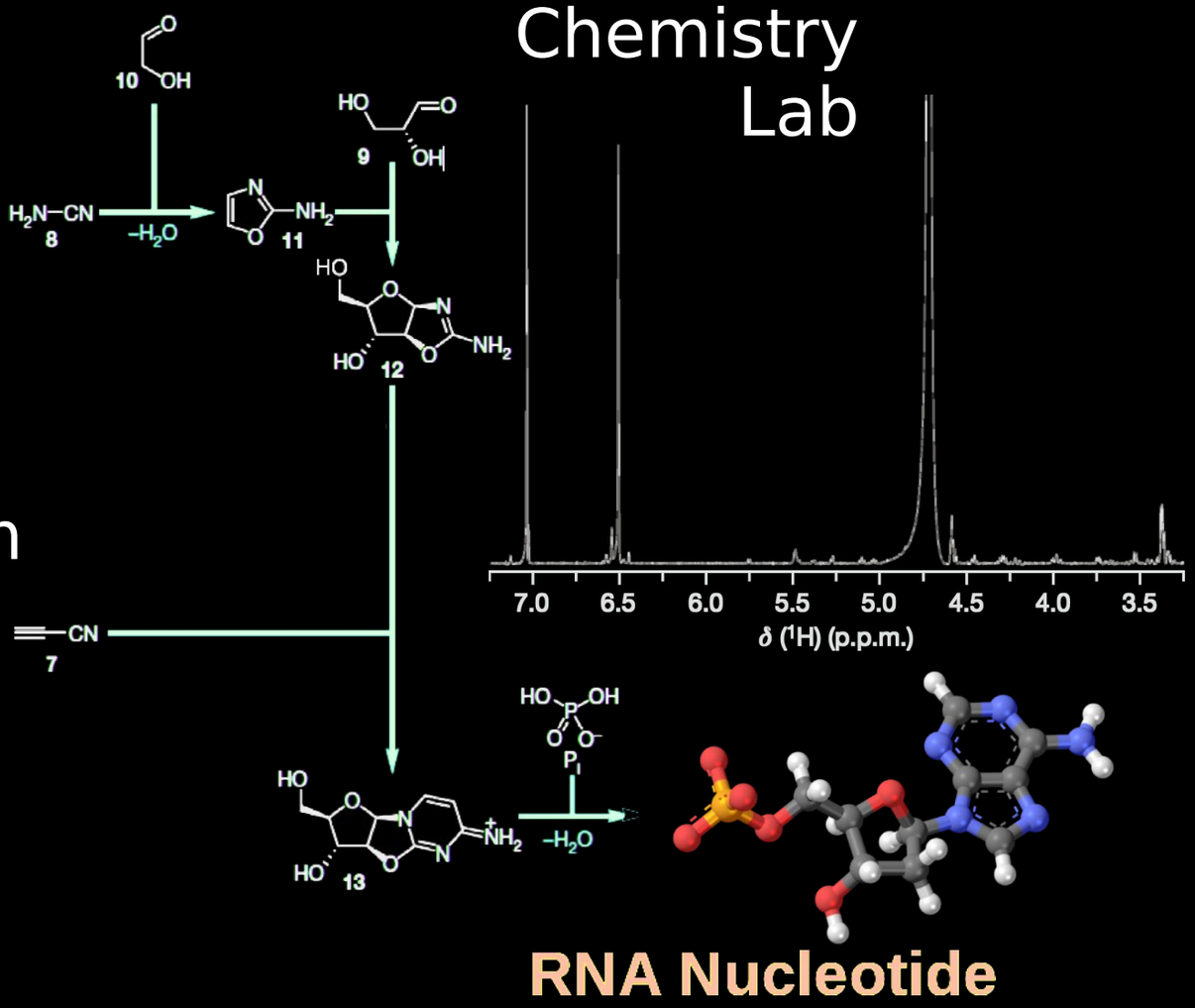
Powner, Sutherland, 2009

Chemical Space

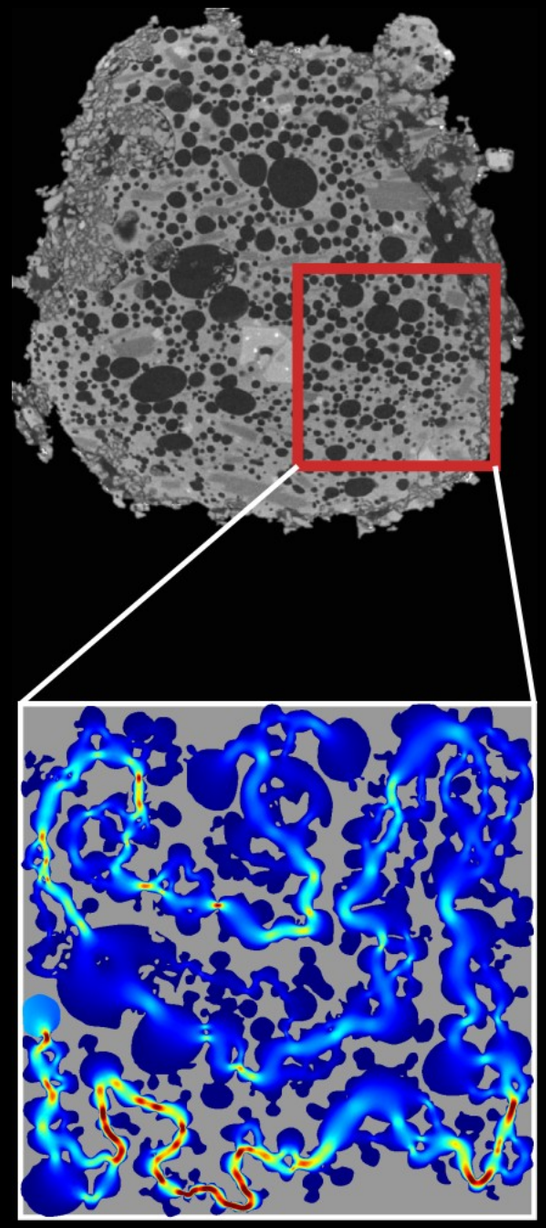
Physical Space

Chemistry Lab

NMR Spectrum



RNA Nucleotide

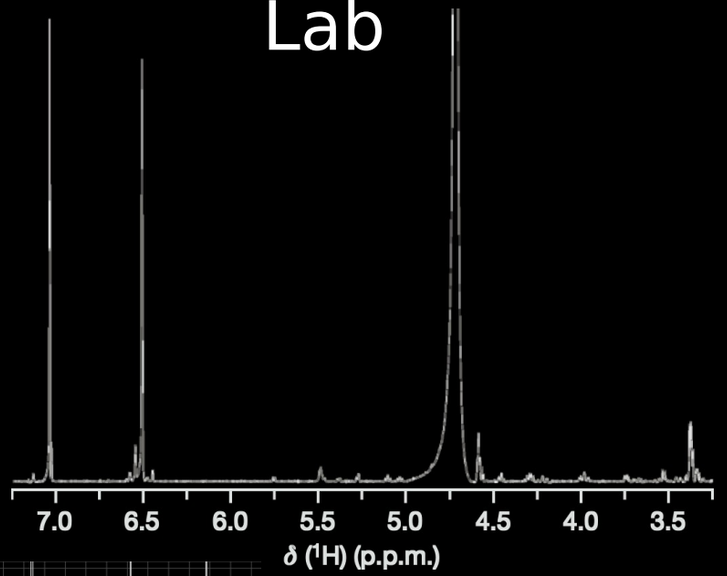


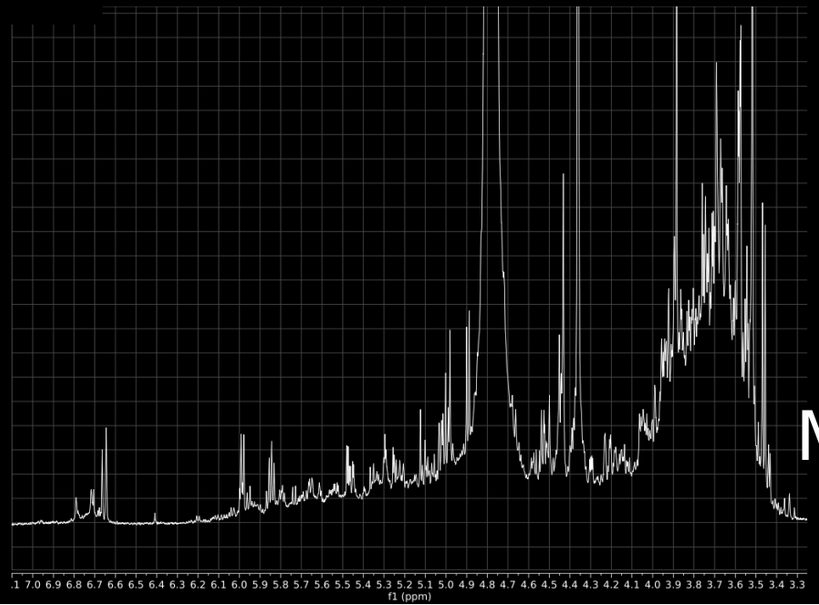
Chemical Space

Physical Space

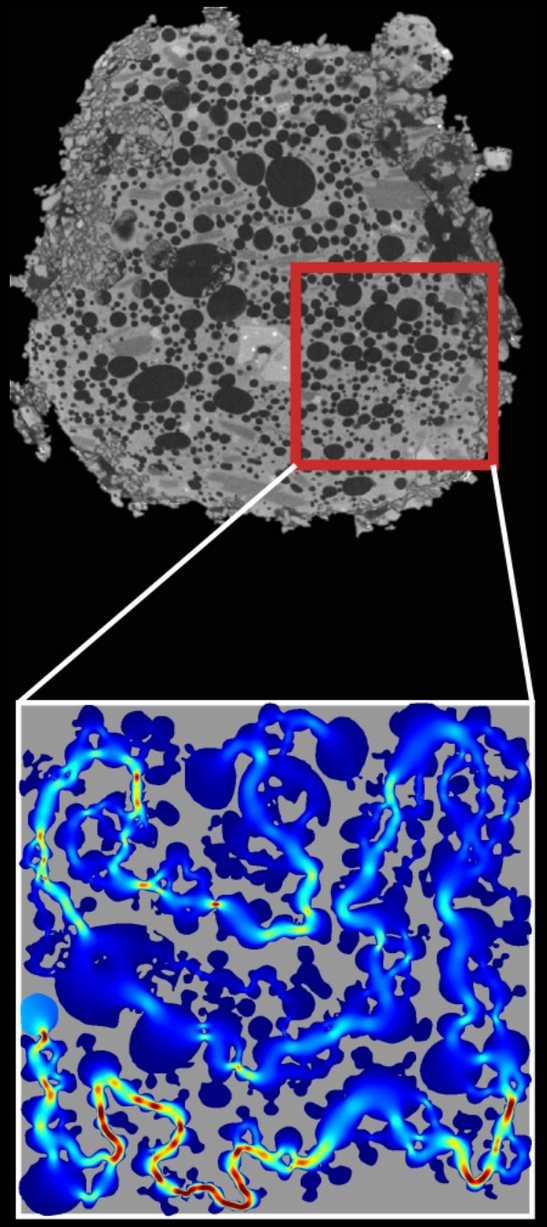
Chemistry Lab

NMR Spectrum

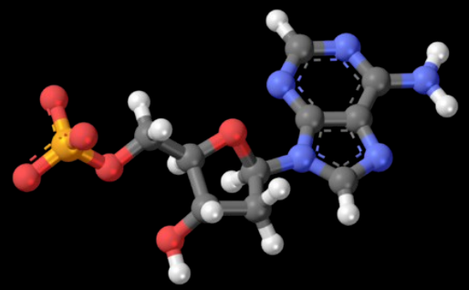




Microfluidics

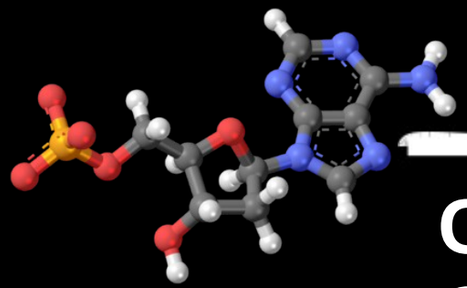


Life



Dead
Molecule

Life



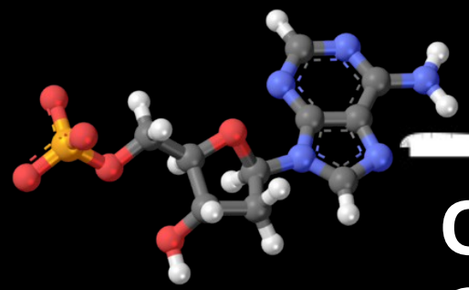
Dead
Molecule

Chemistry, Astronomy,
Geology, Biology

Time

Life

Nonequilibrium
Physics

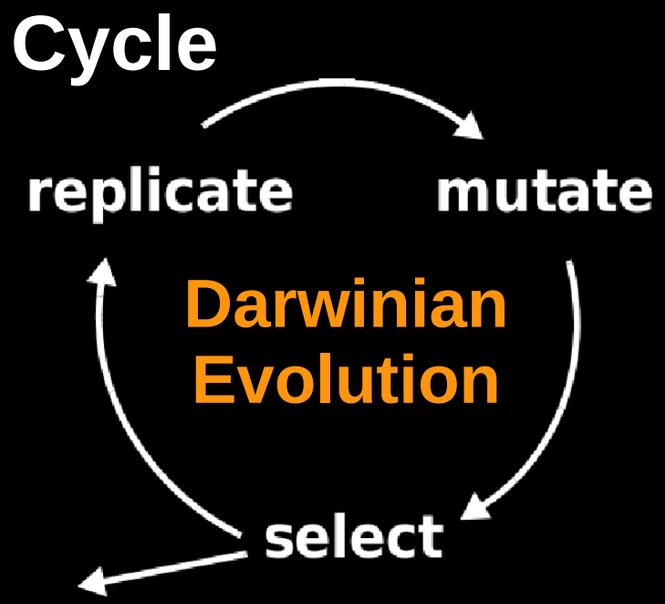


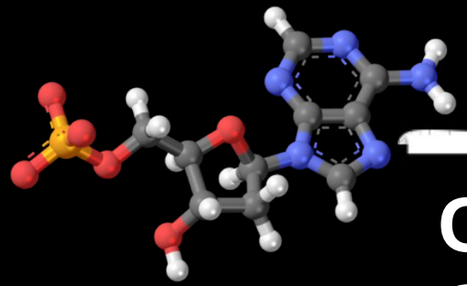
Chemistry, Astronomy,
Geology, Biology

Time

Dead
Molecule

Darwinian Evolution





Dead Molecule

Life

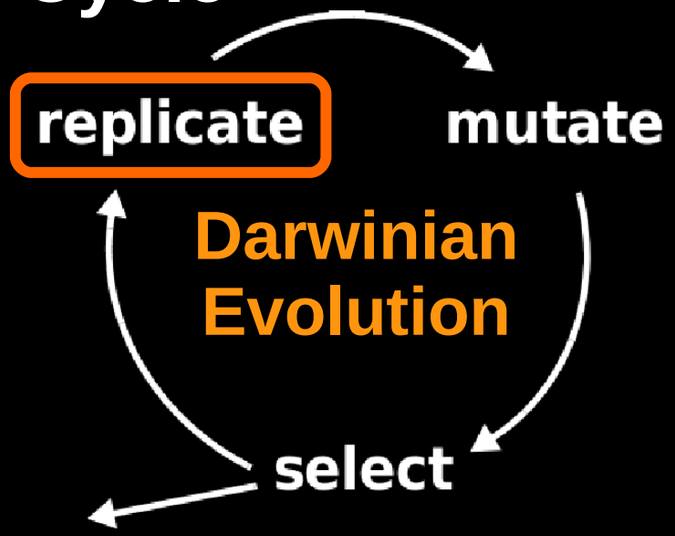
Nonequilibrium Physics

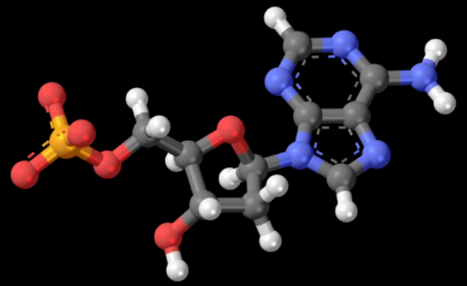
Chemistry, Astronomy, Geology, Biology

Time

Darwinian Evolution

Cycle



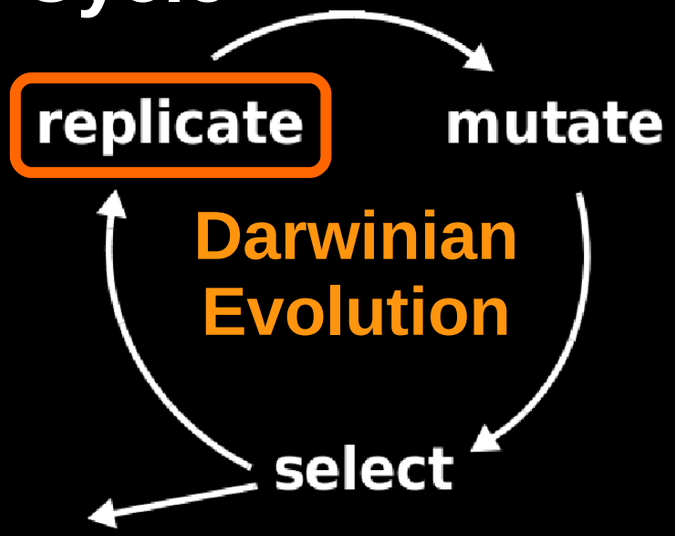


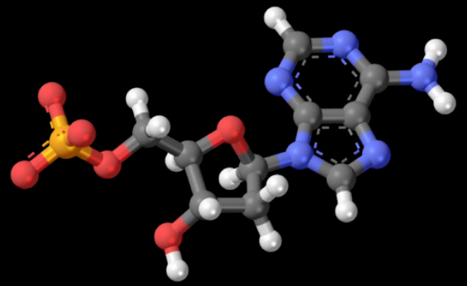
Dead Molecule

Replication with Proteins

Darwinian Evolution

Cycle





Dead Molecule

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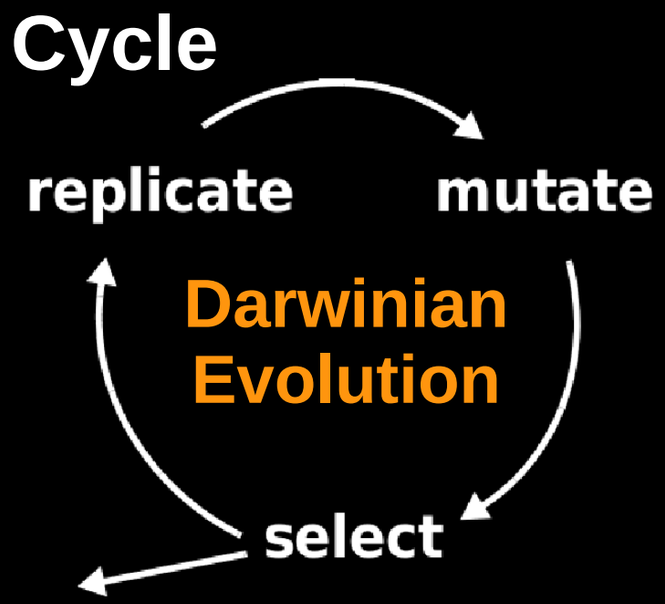
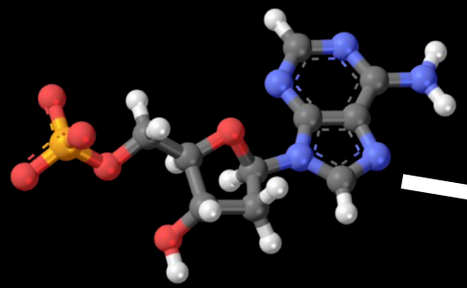
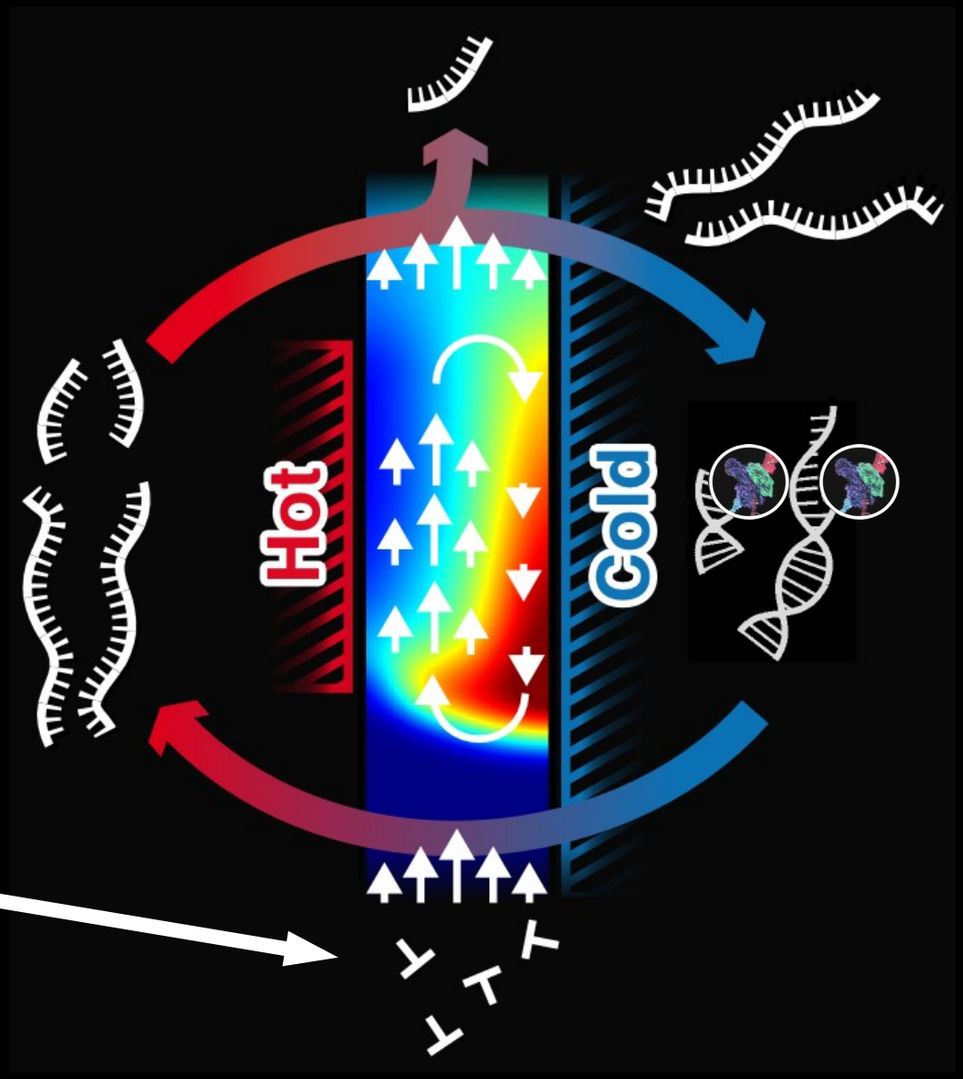


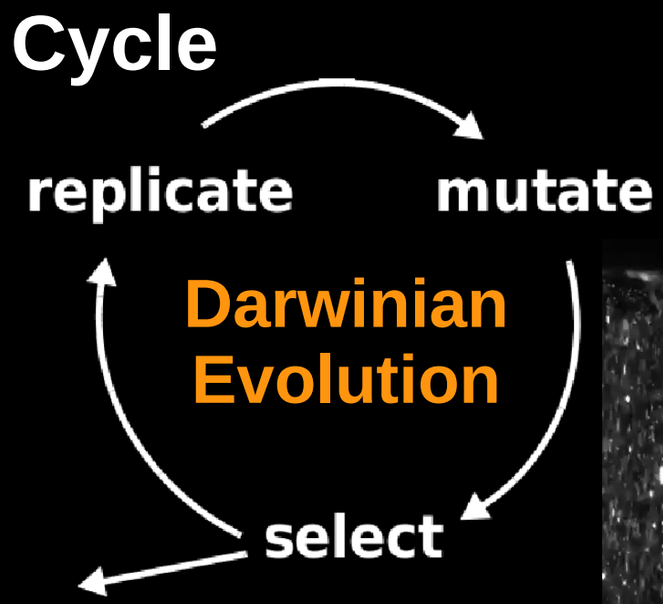


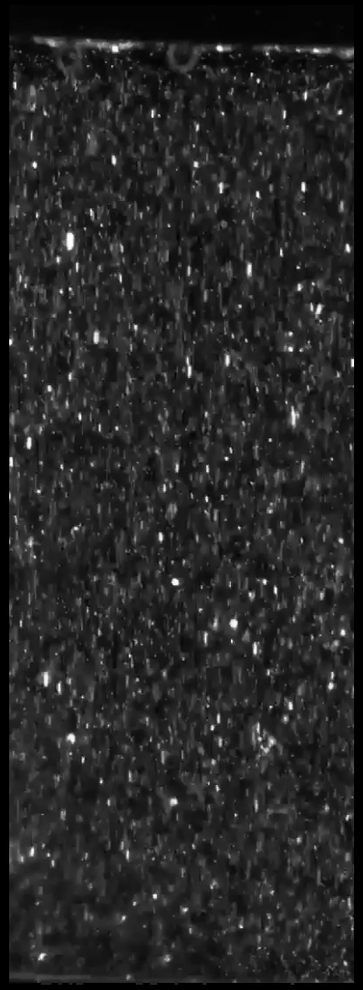
Dead
Molecule

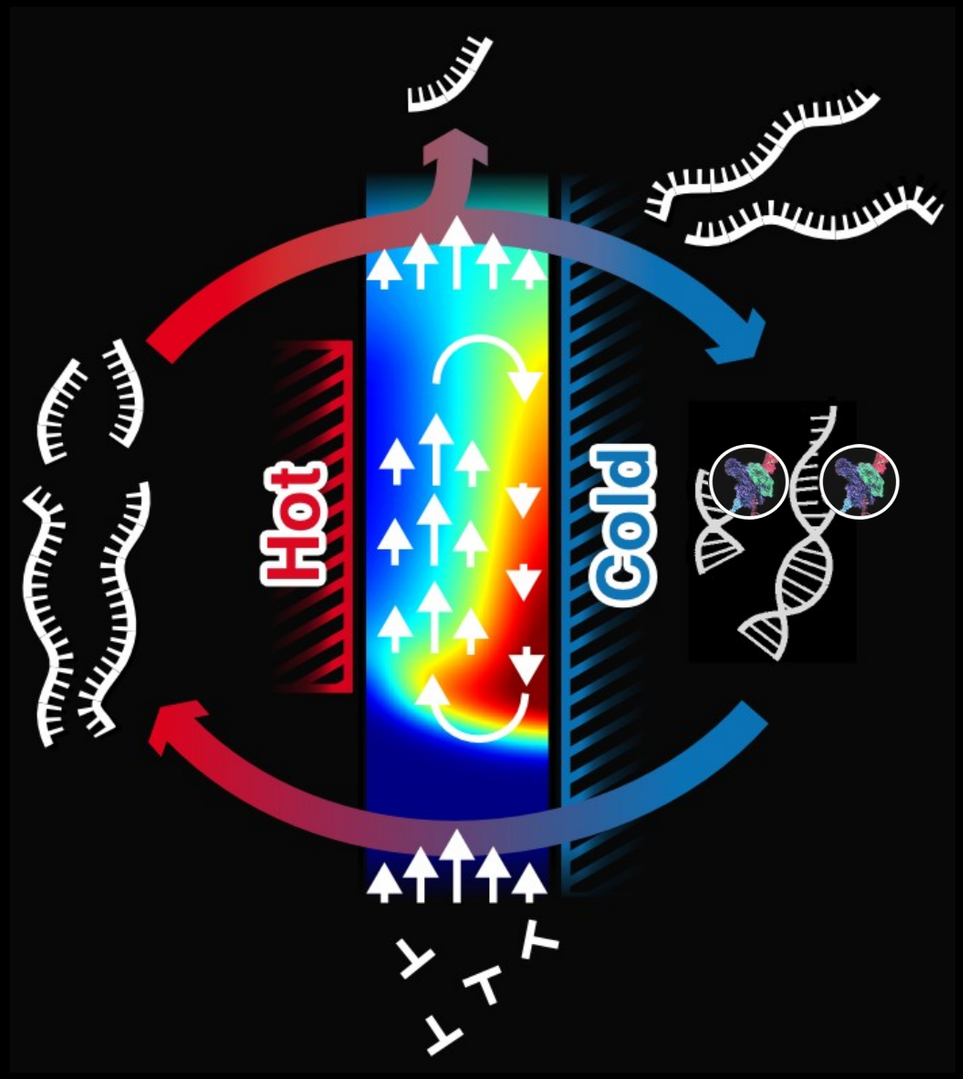


Nature Chemistry, 2015

Darwinian Evolution







Nature Chemistry, 2015

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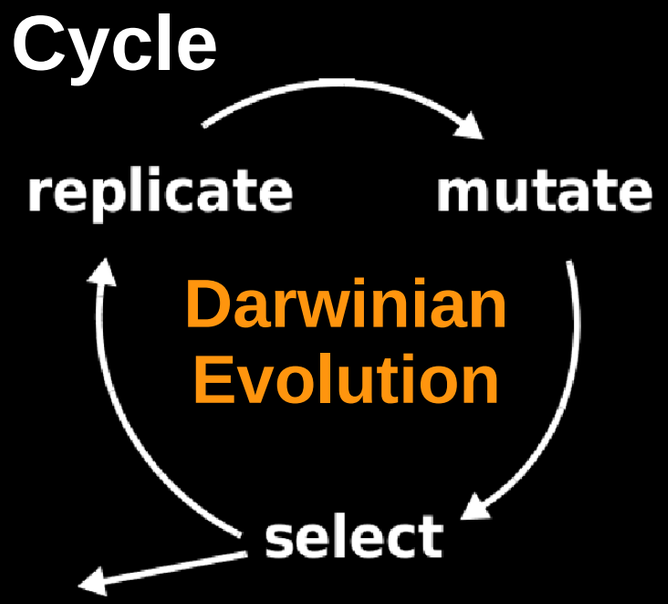
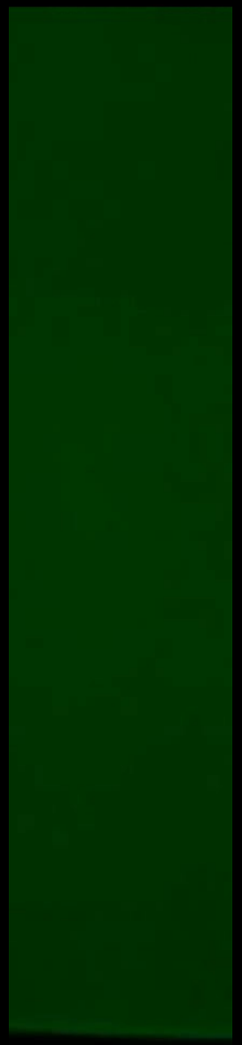
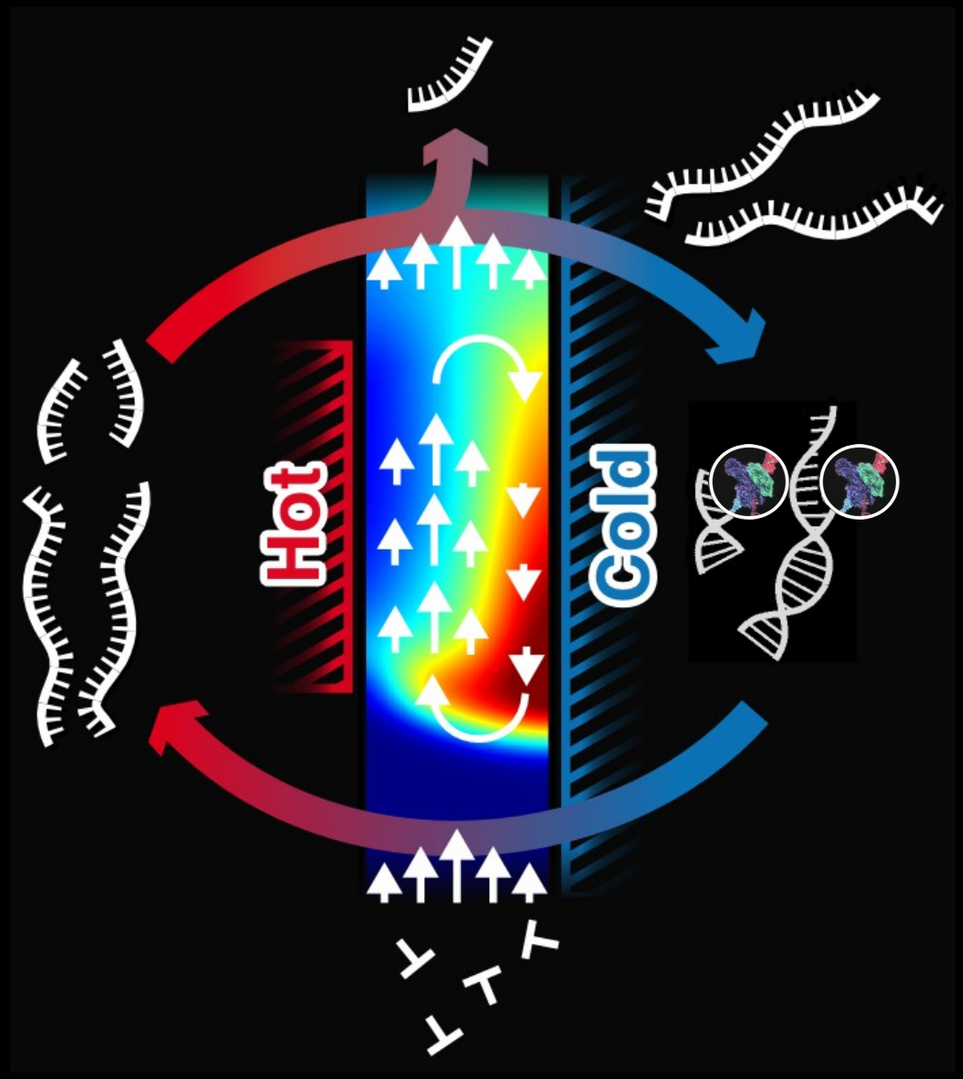


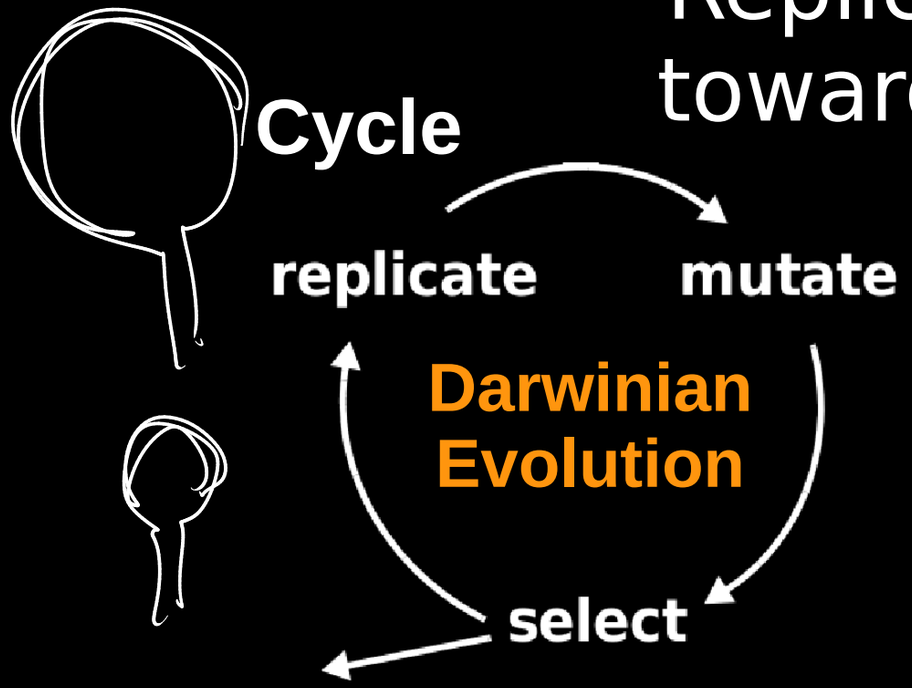


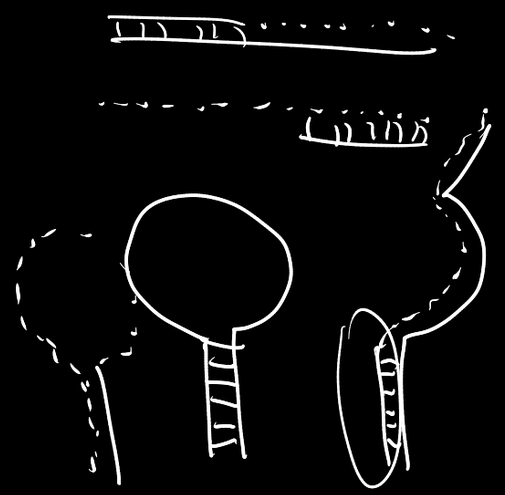


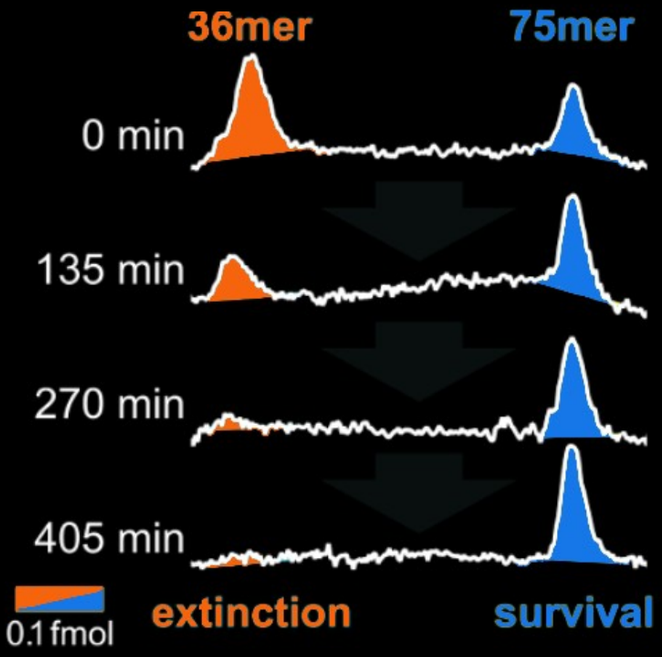
+Thermophoresis

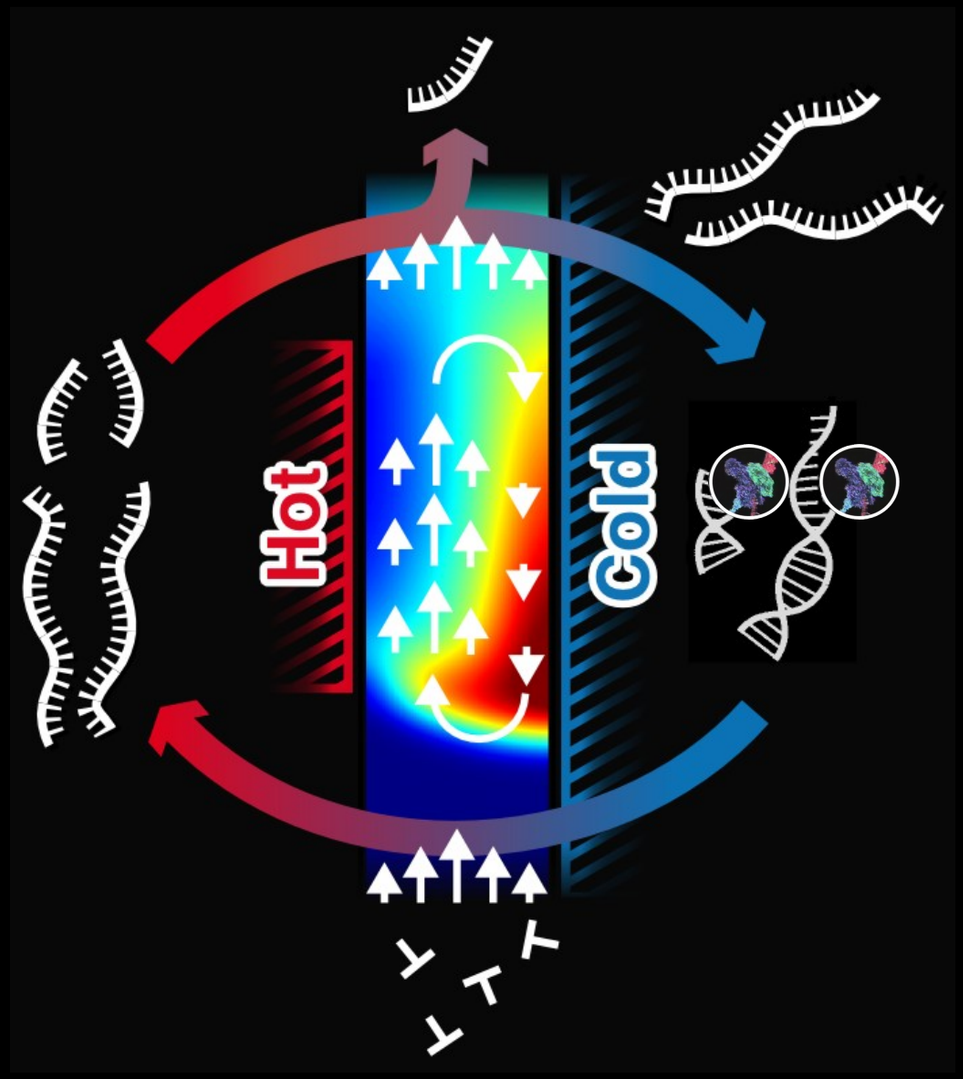
Nature Chemistry, 2015

Replication and Selection towards longer molecules



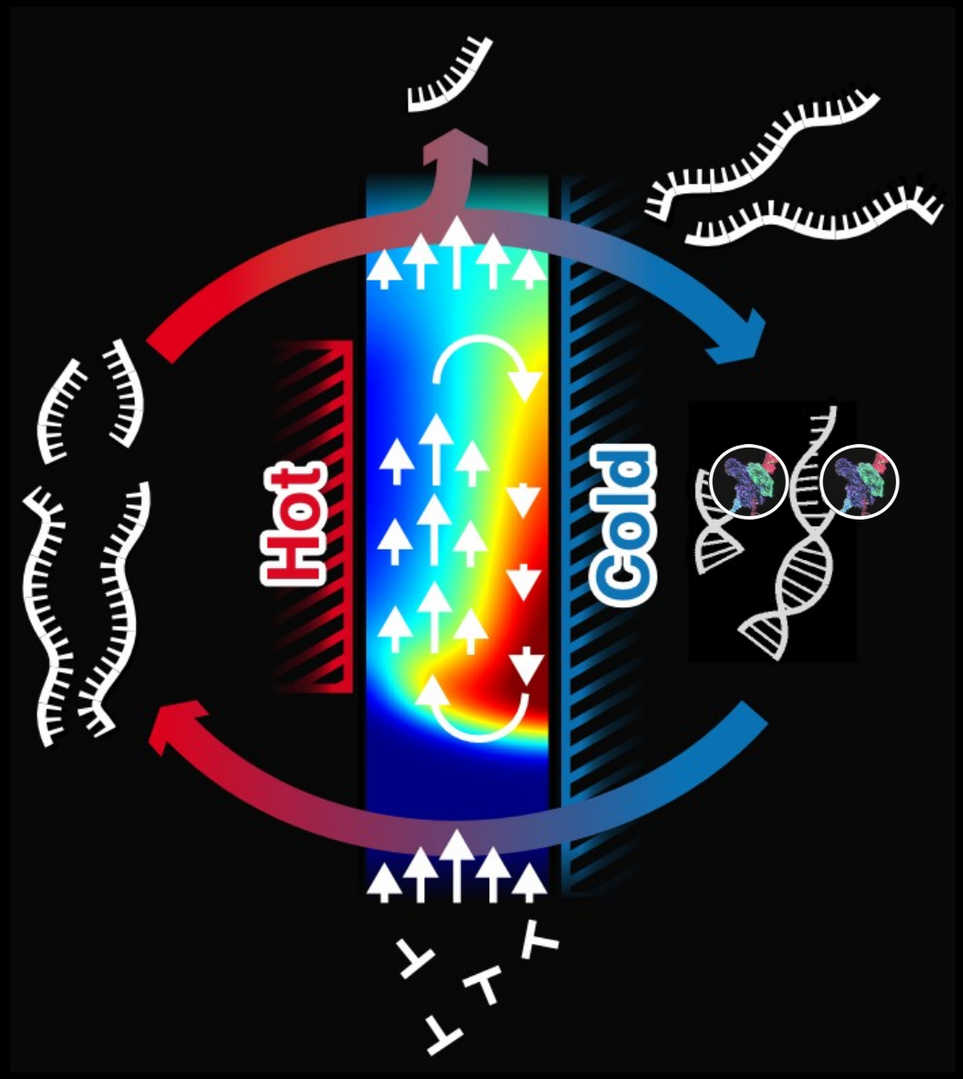






Nature Chemistry, 2015

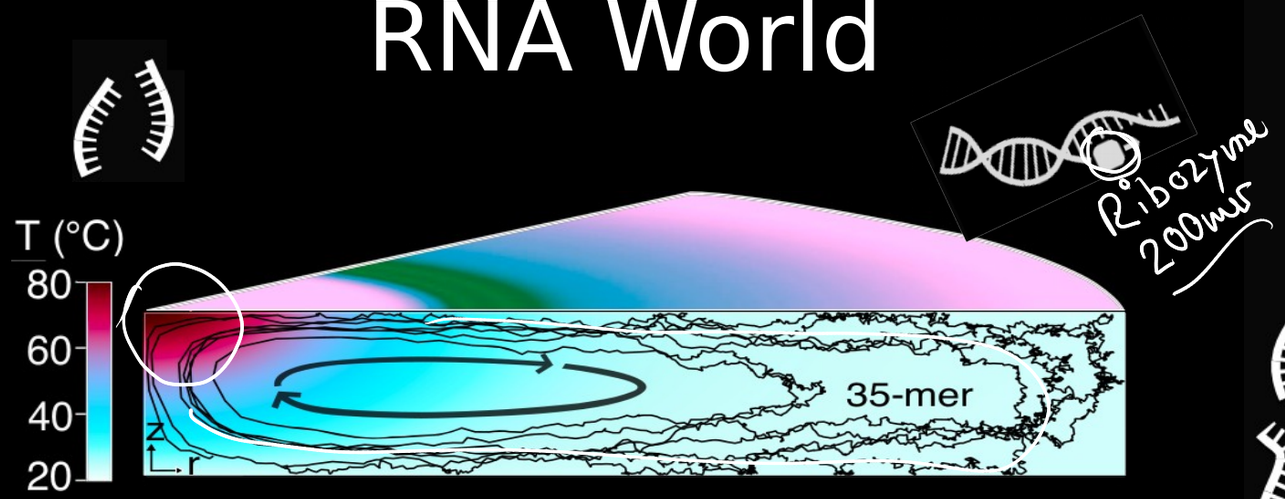
Molecular Evolution **before Proteins**

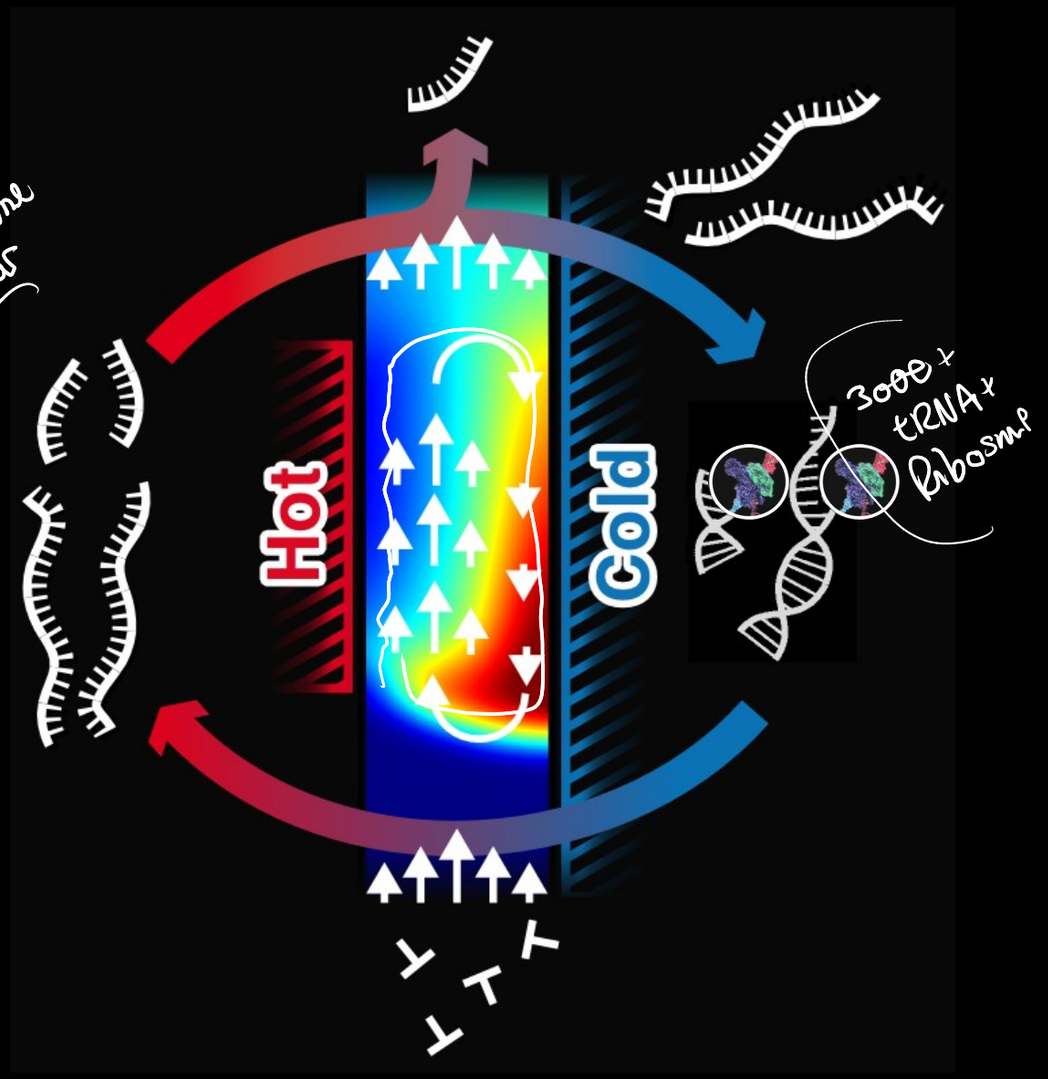


Nature Chemistry, 2015

Molecular Evolution **before Proteins**

RNA World



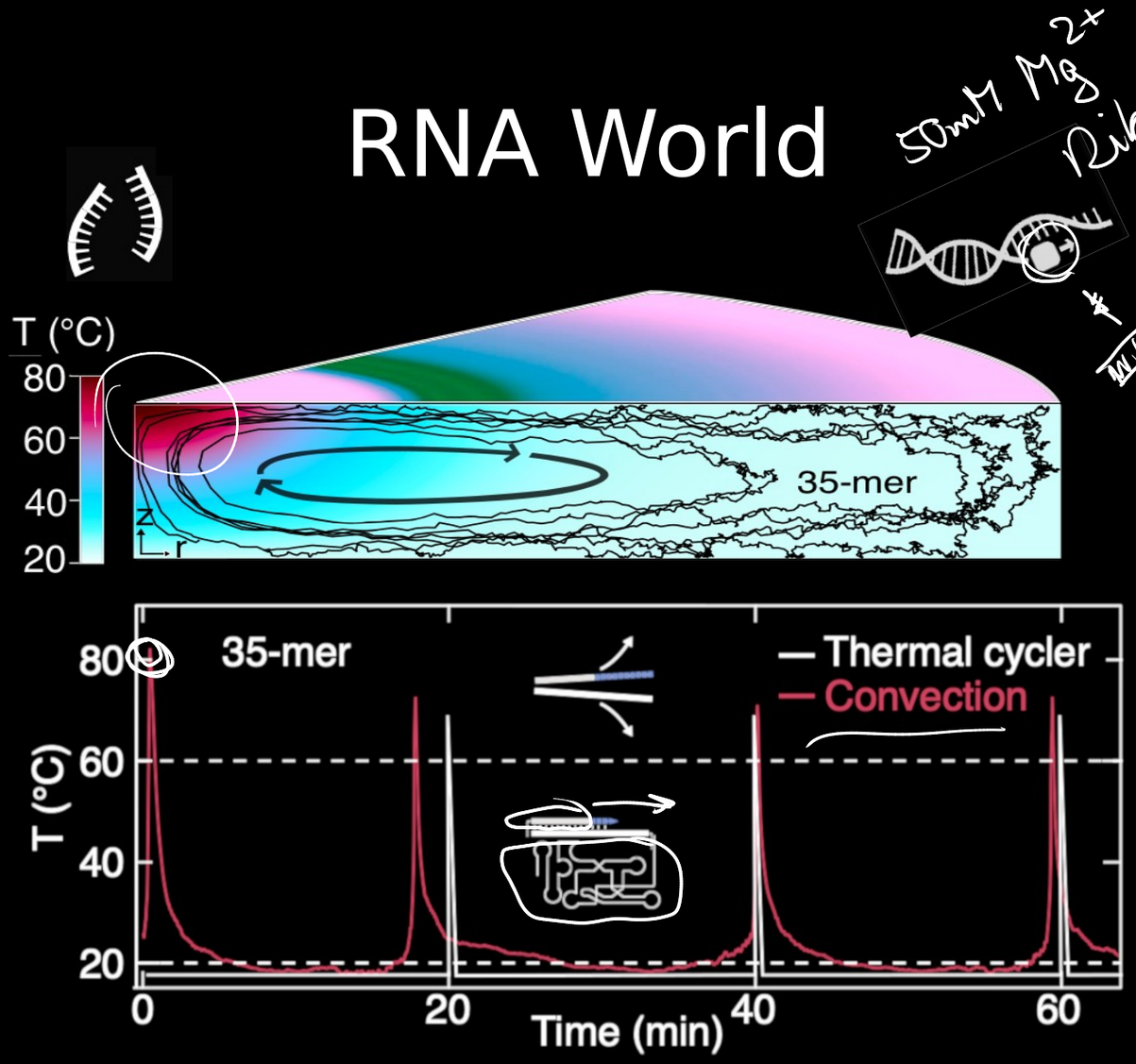


Physical Review Letters, 2020

Nature Chemistry, 2015

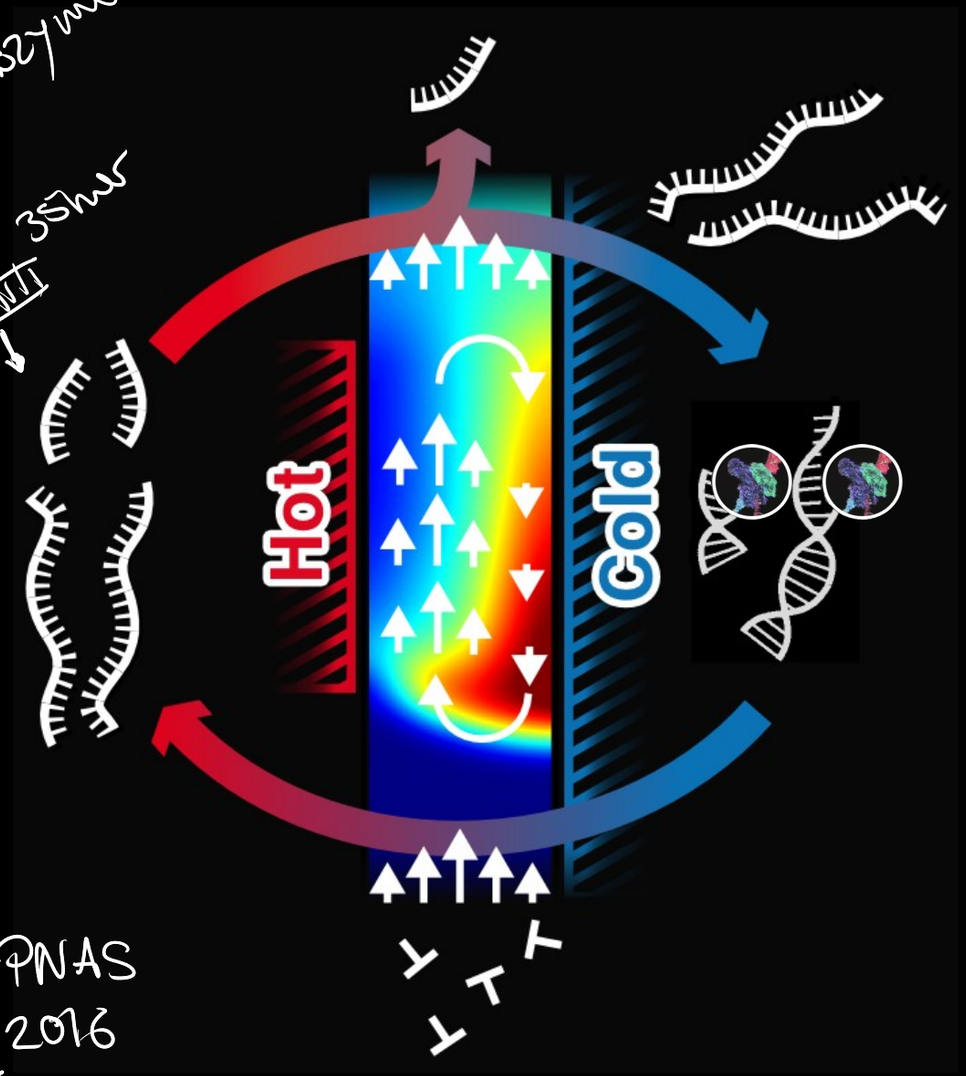
Molecular Evolution **before Proteins**

RNA World



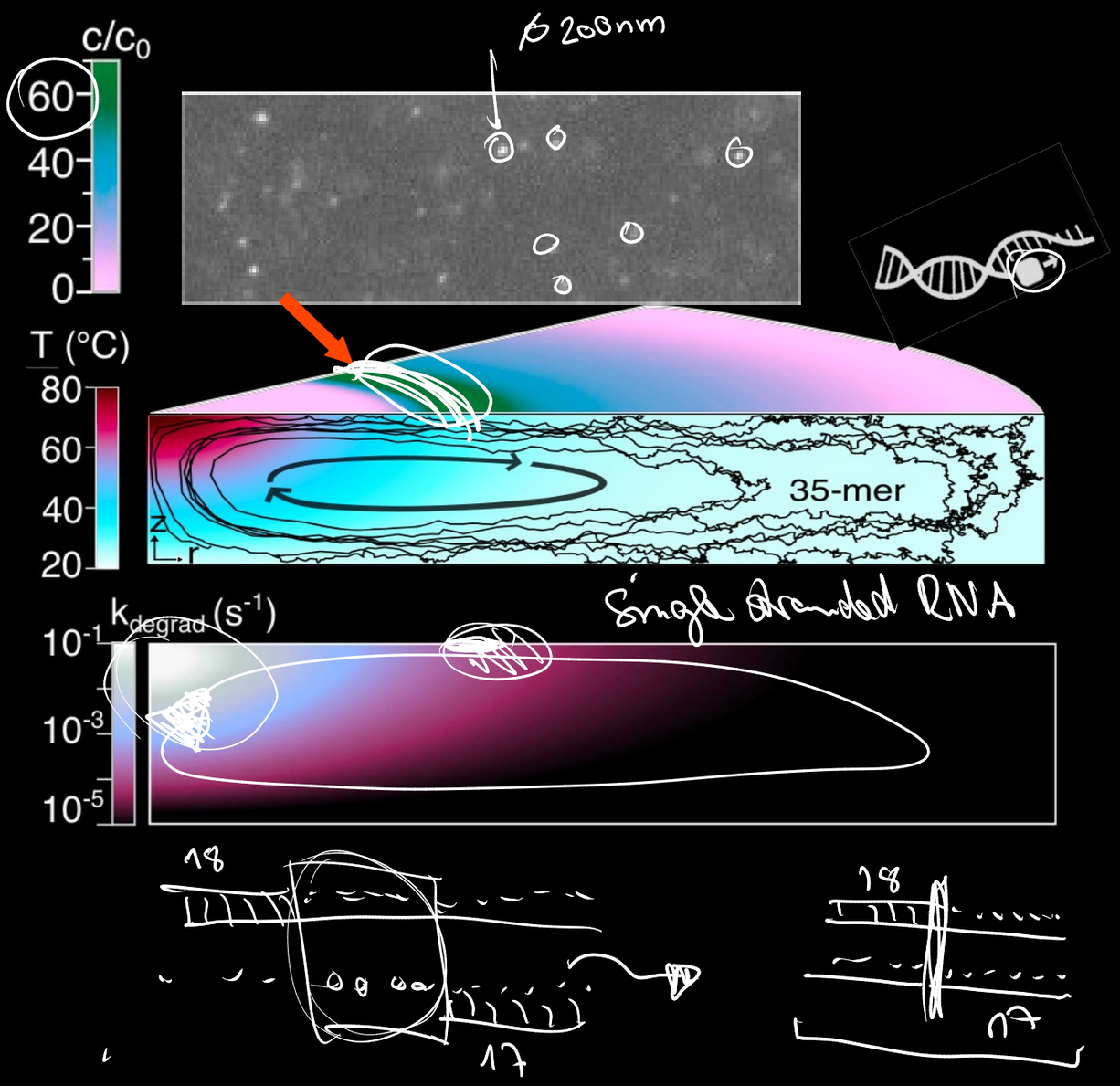
Physical Review Letters, 2020

PNAS 2016 Joyce

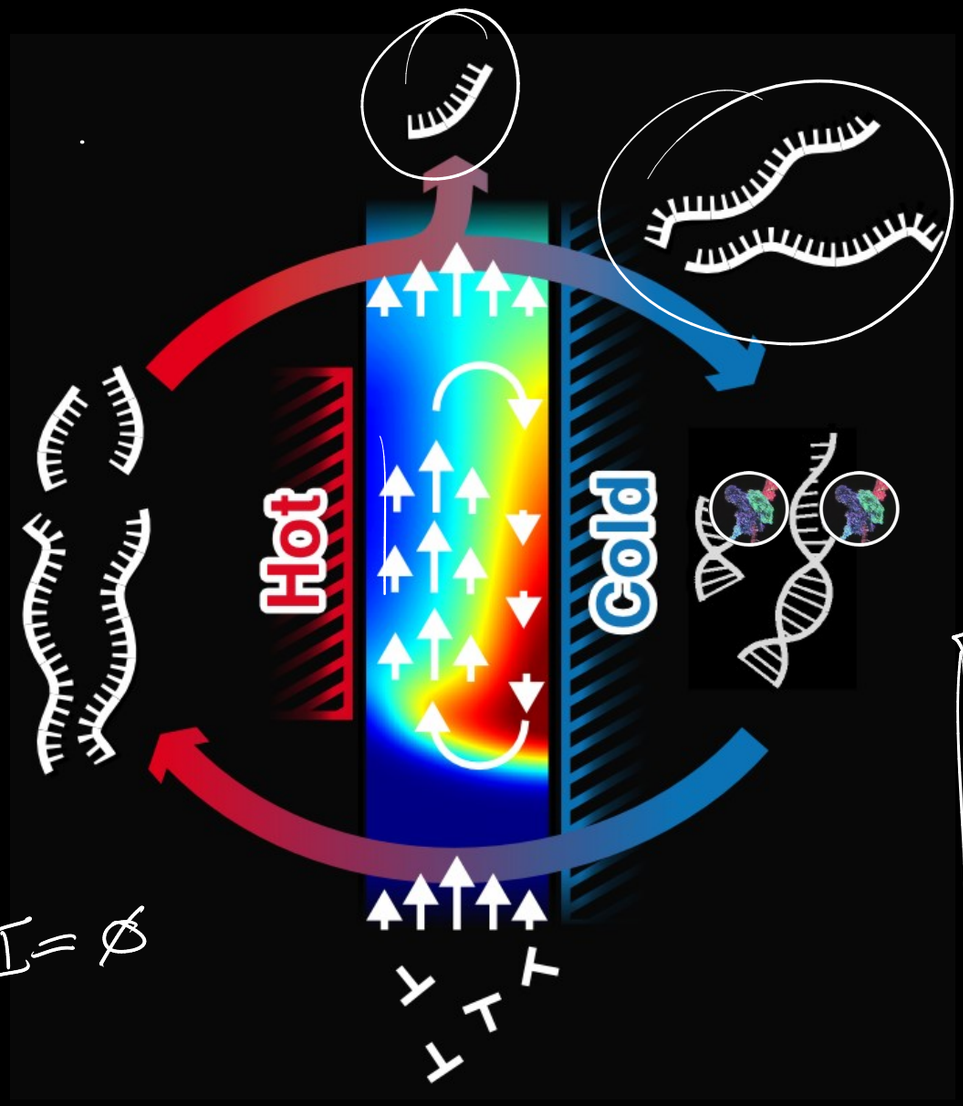


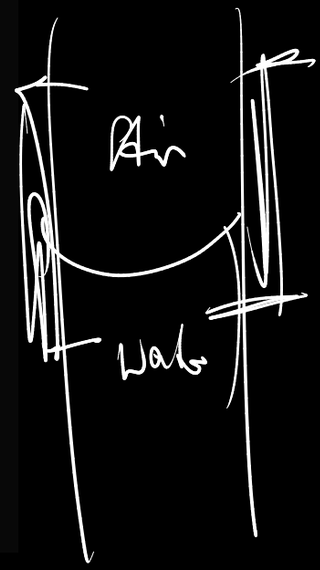
Nature Chemistry, 2015

Molecular Evolution **before Proteins**



Physical Review Letters, 2020

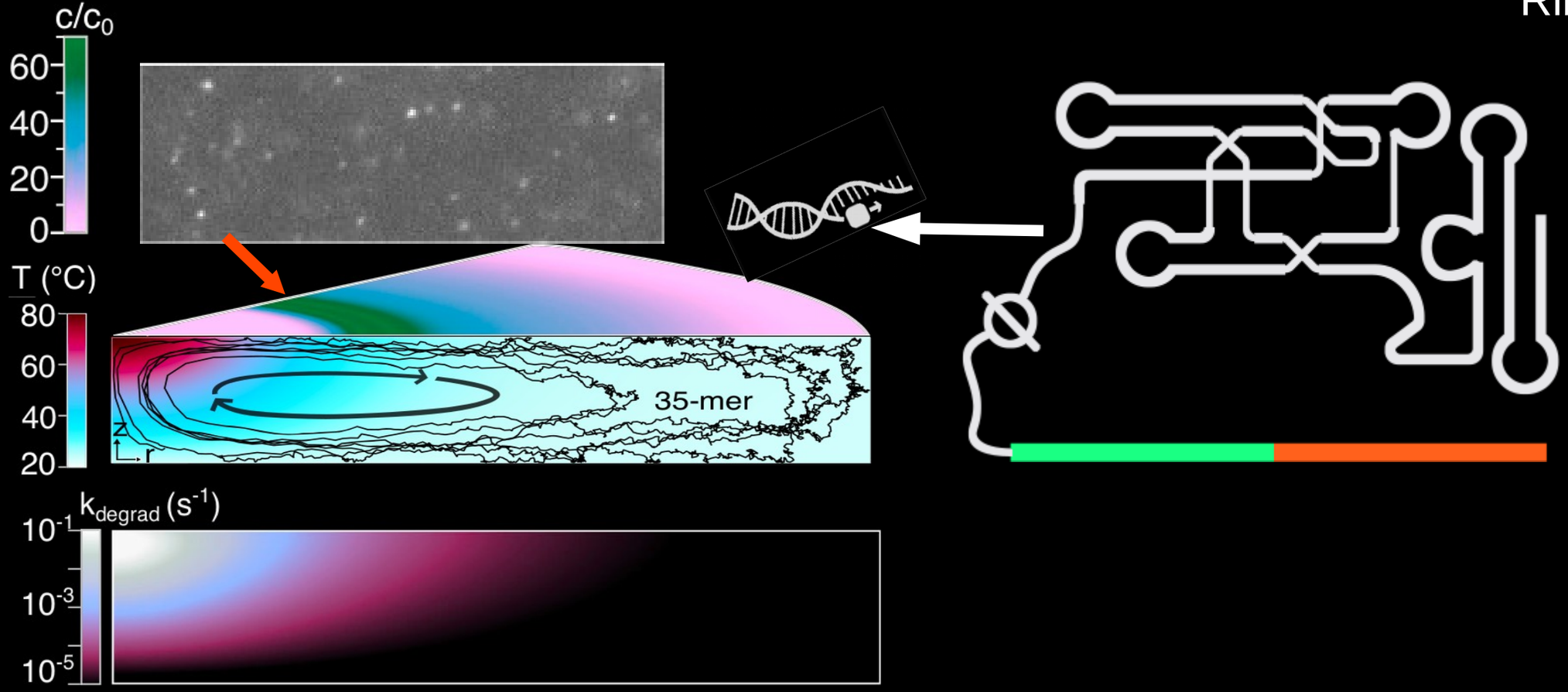




Nature Chemistry, 2015

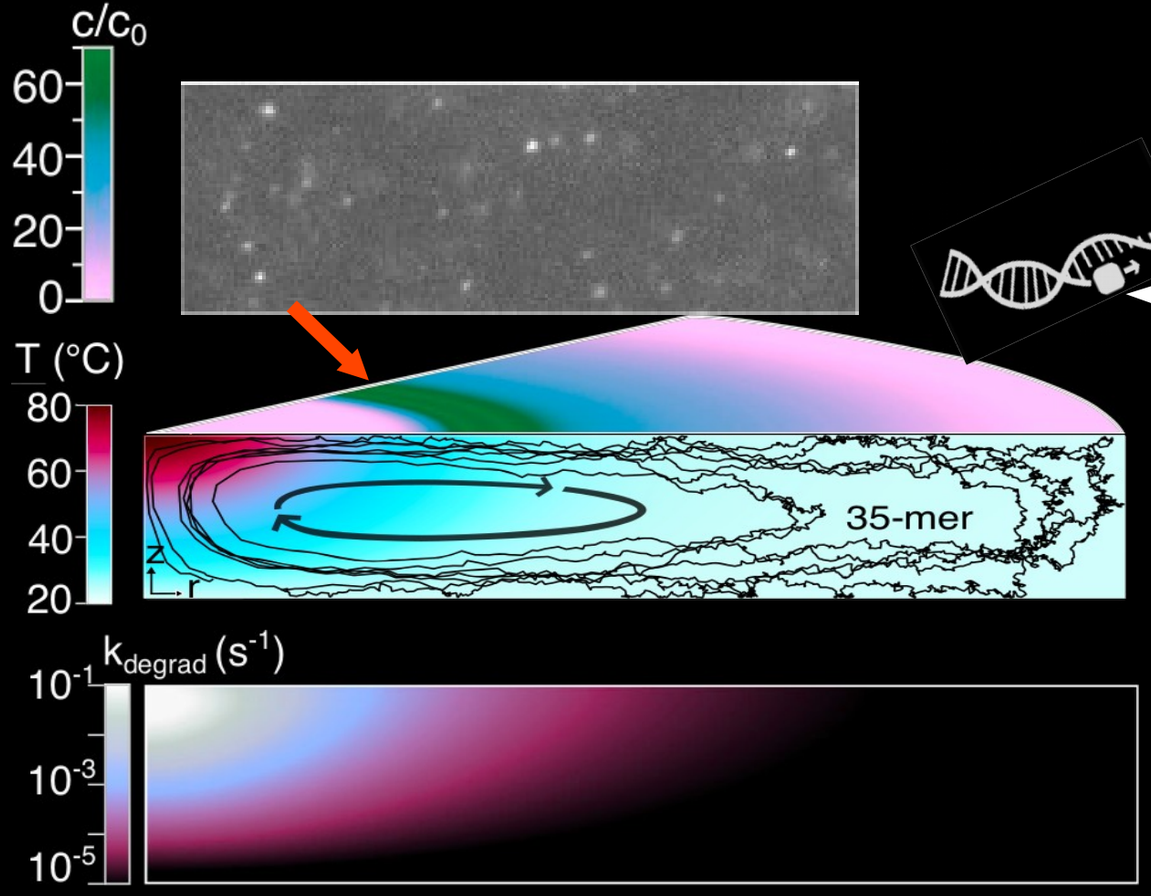
Molecular Evolution **before Proteins**

Ribozyme

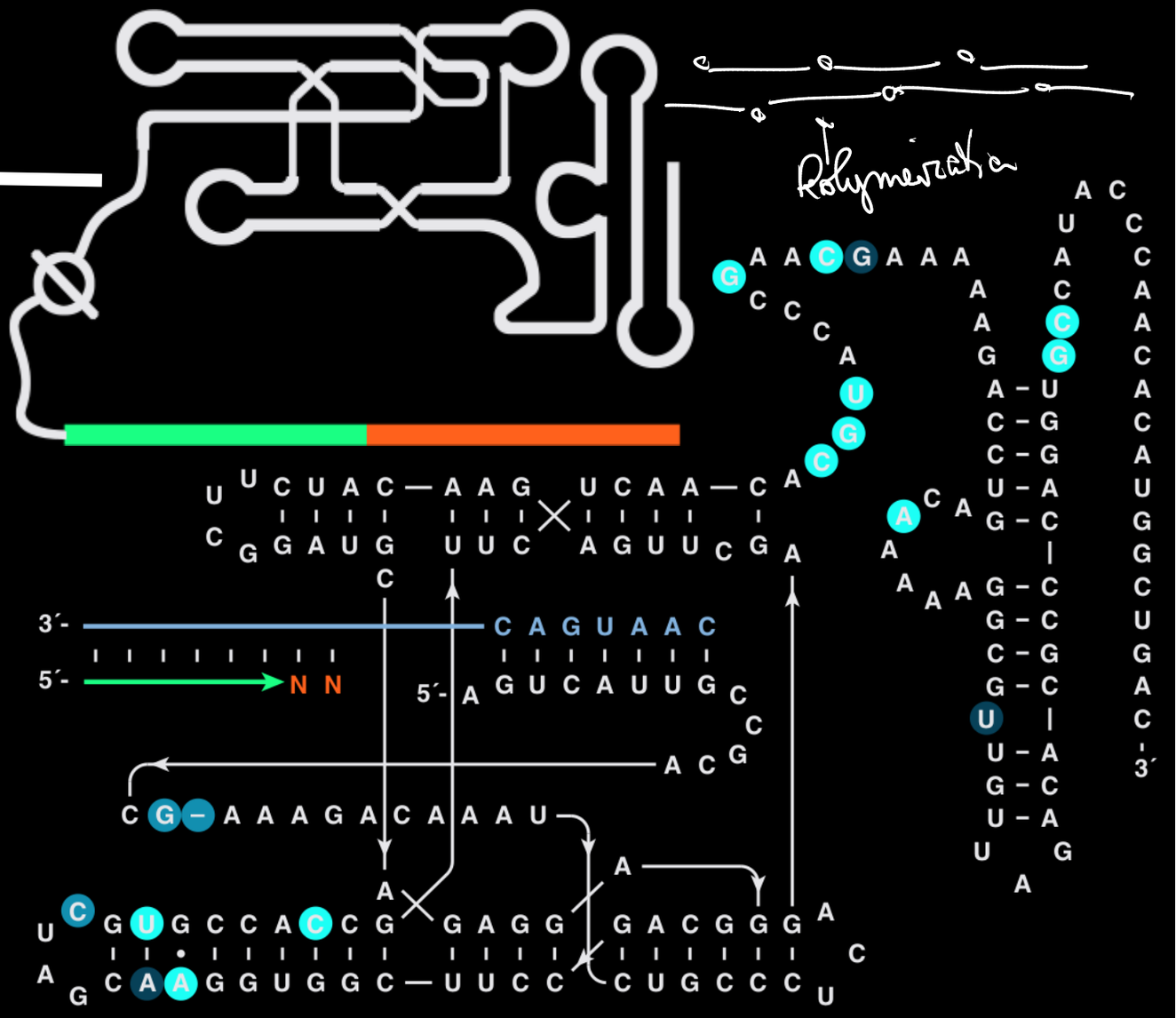


Physical Review Letters, 2020

Molecular Evolution **before Proteins**



Ribozyme



Physical Review Letters, 2020

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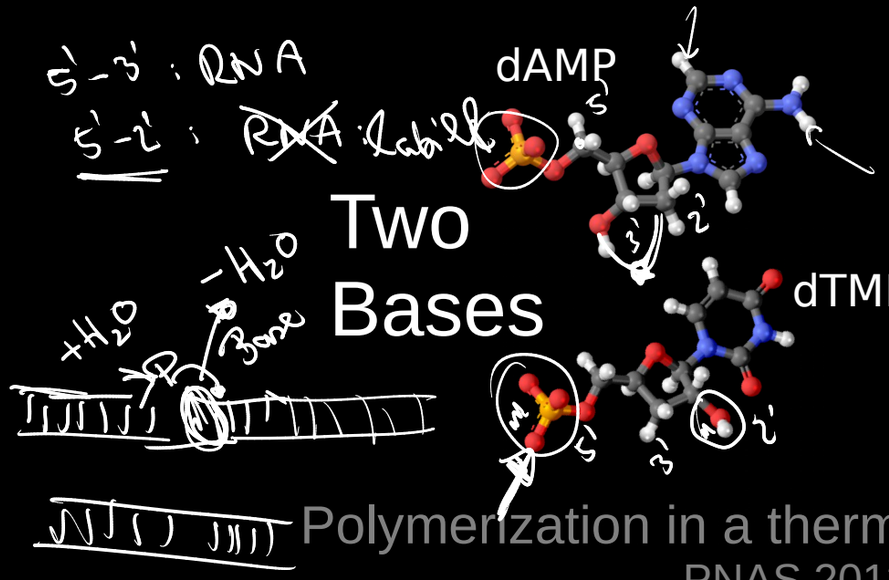

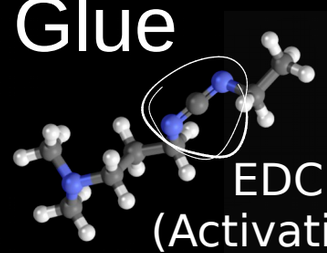

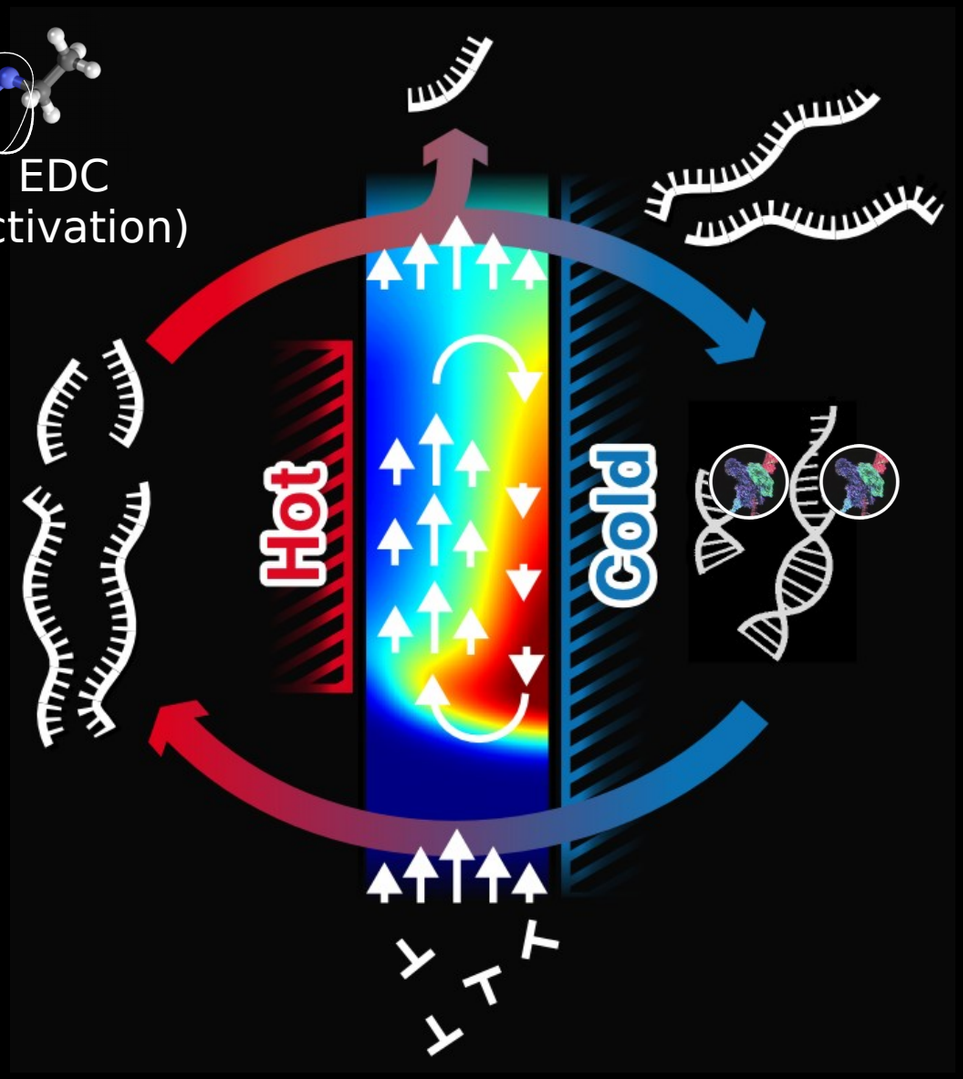

Polymerization in a thermal trap
PNAS 2013, PCCP 2016

Replication by connecting
long strands of DNA
Chemical Science 2019

Symmetry breaking of sequences
PRL 2017, PRX 2019

Gelation of DNA
Angewandte 2016

Effects at water-gas interface
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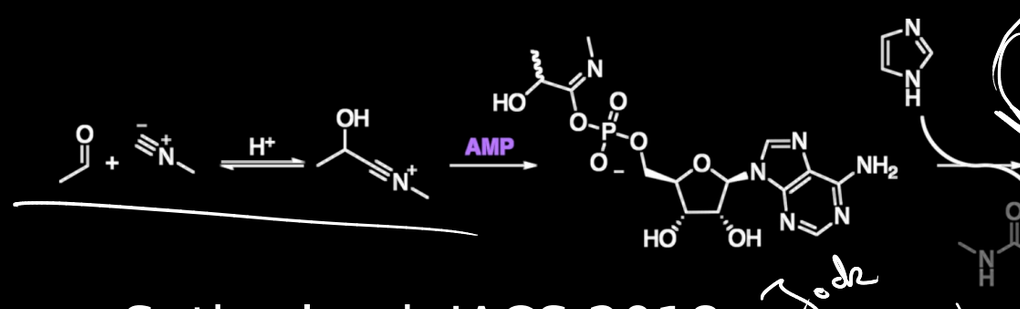
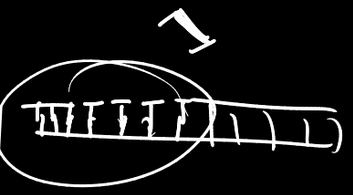


Sutherland, JACS 2018



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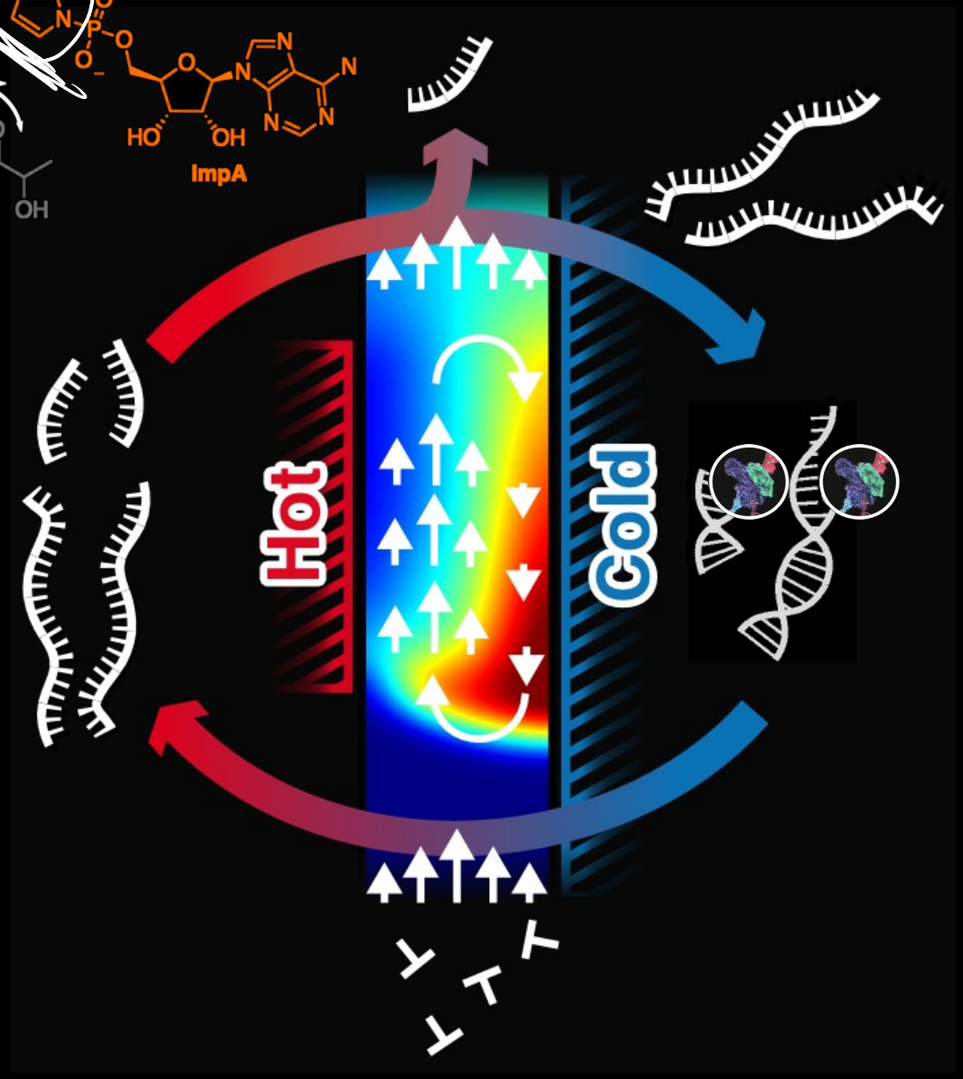

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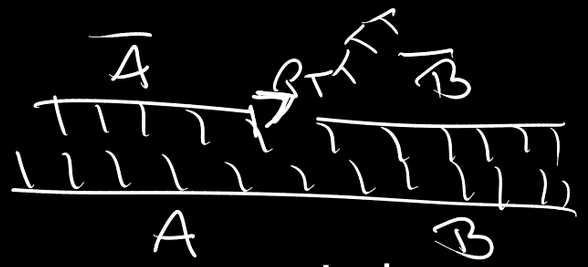
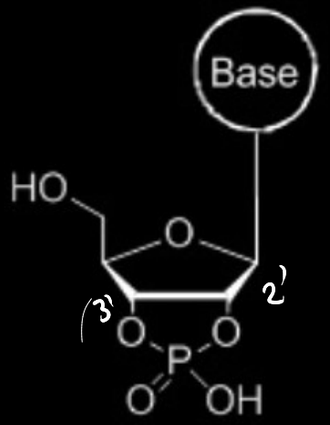


Lohrmann, Orgel, 1973



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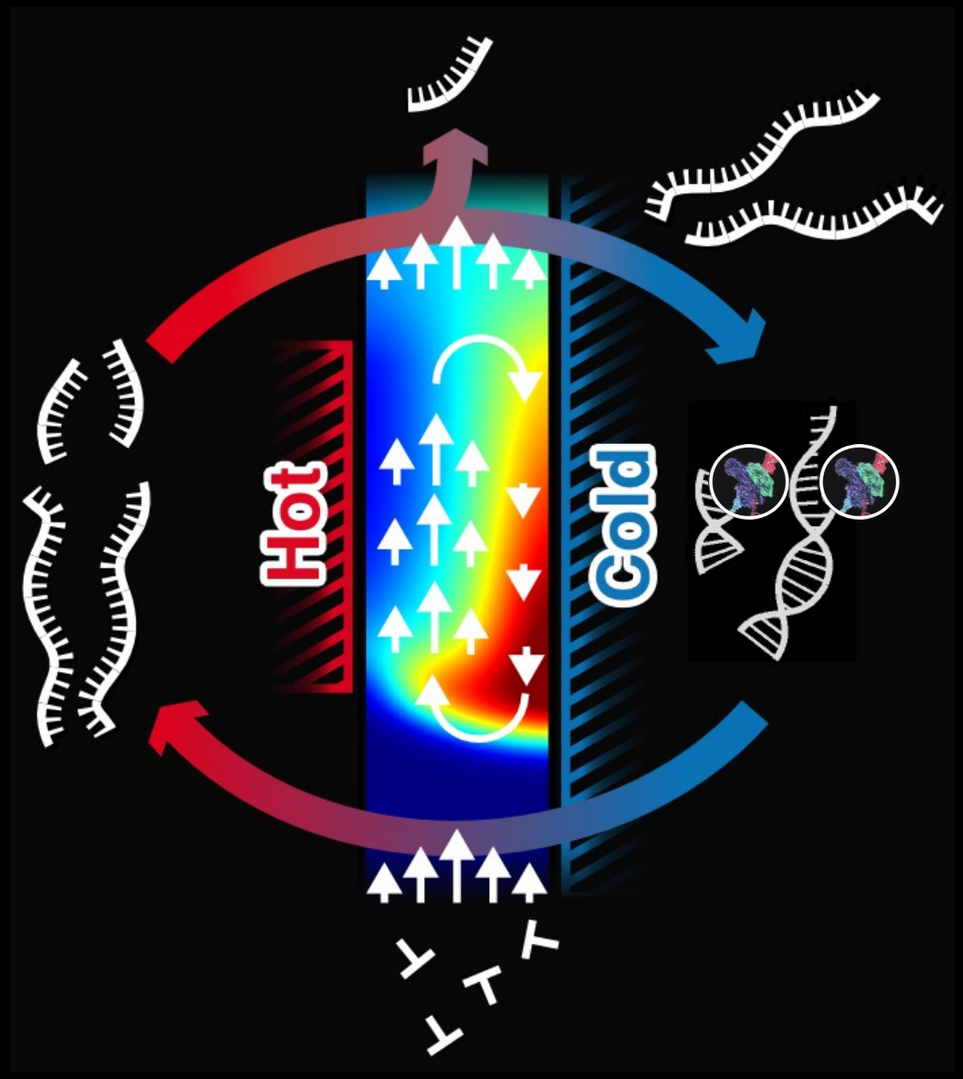

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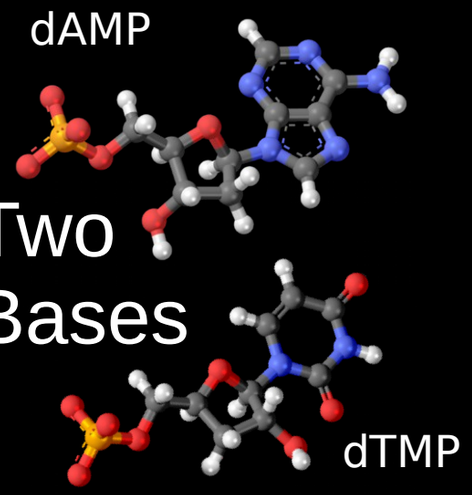
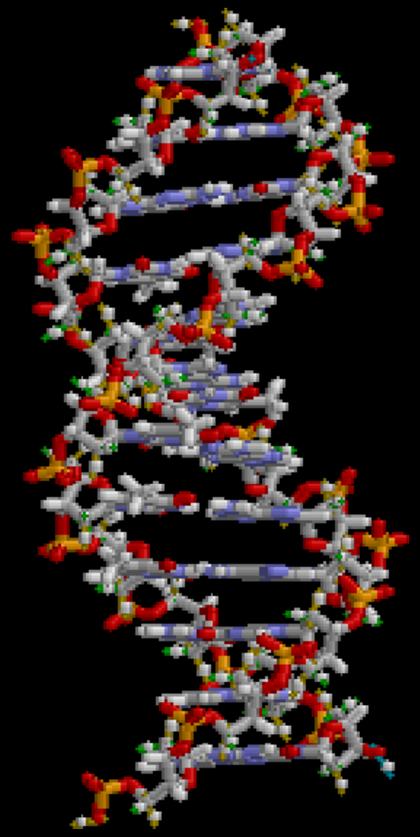
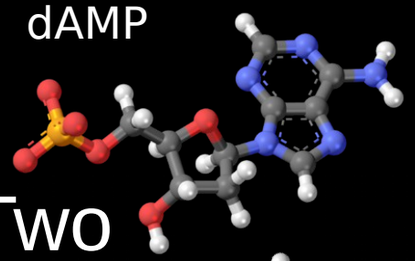


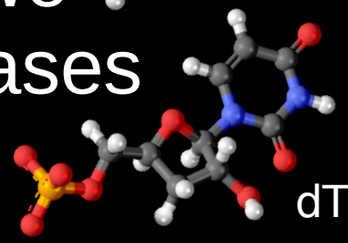


Polymerization in a thermal trap

dAMP

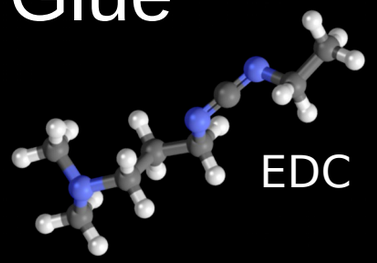


Two Bases



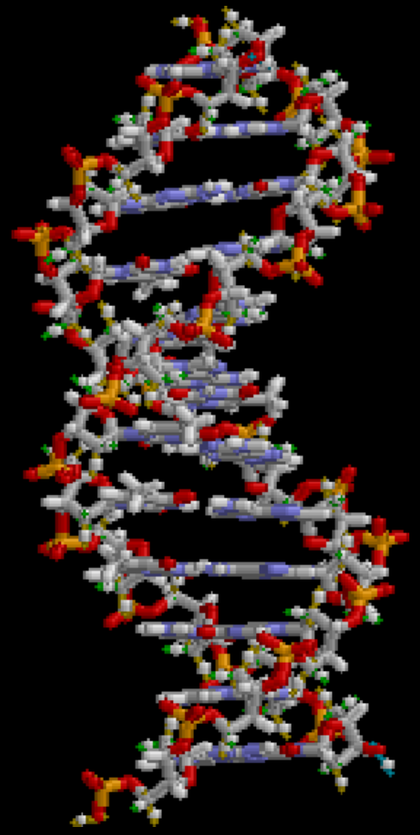
dTMP

Glue



EDC

at high concentrations



Polymerization in a thermal trap

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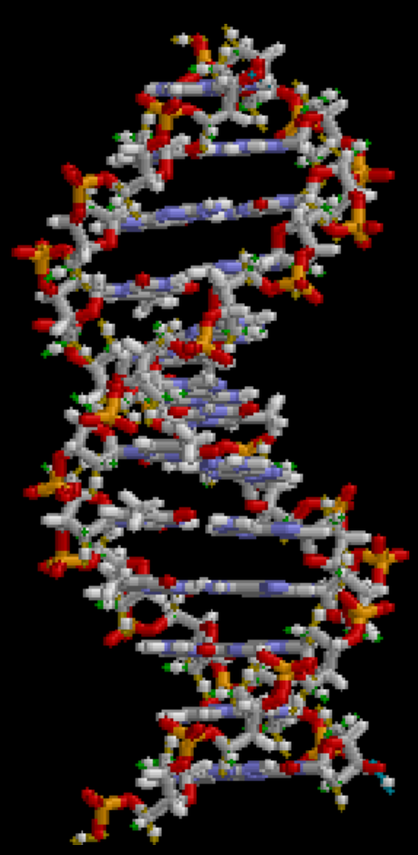

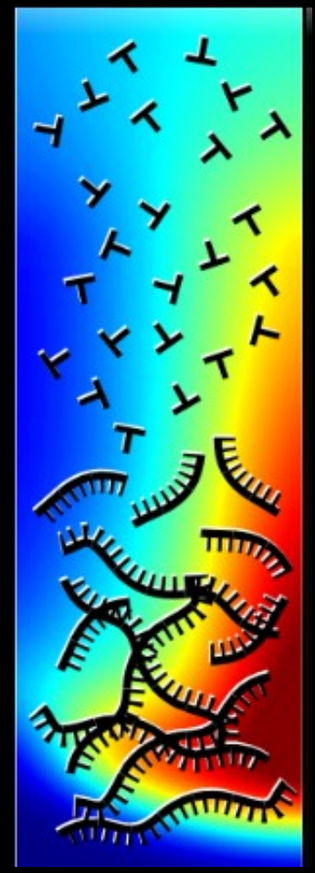

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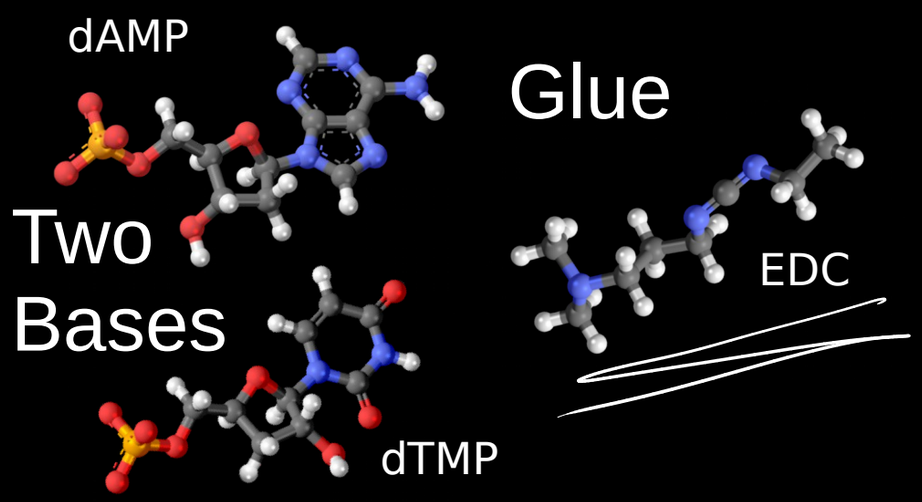
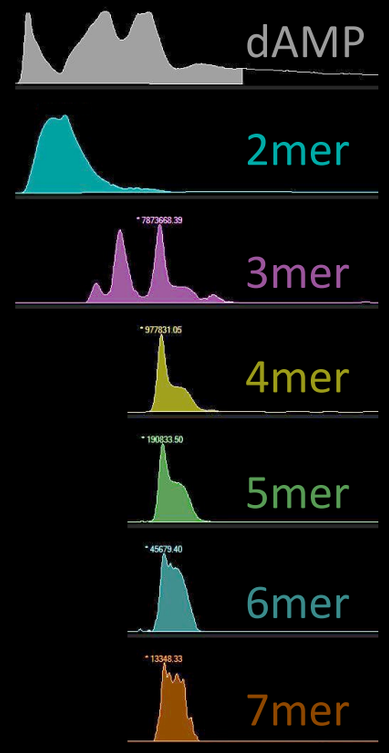
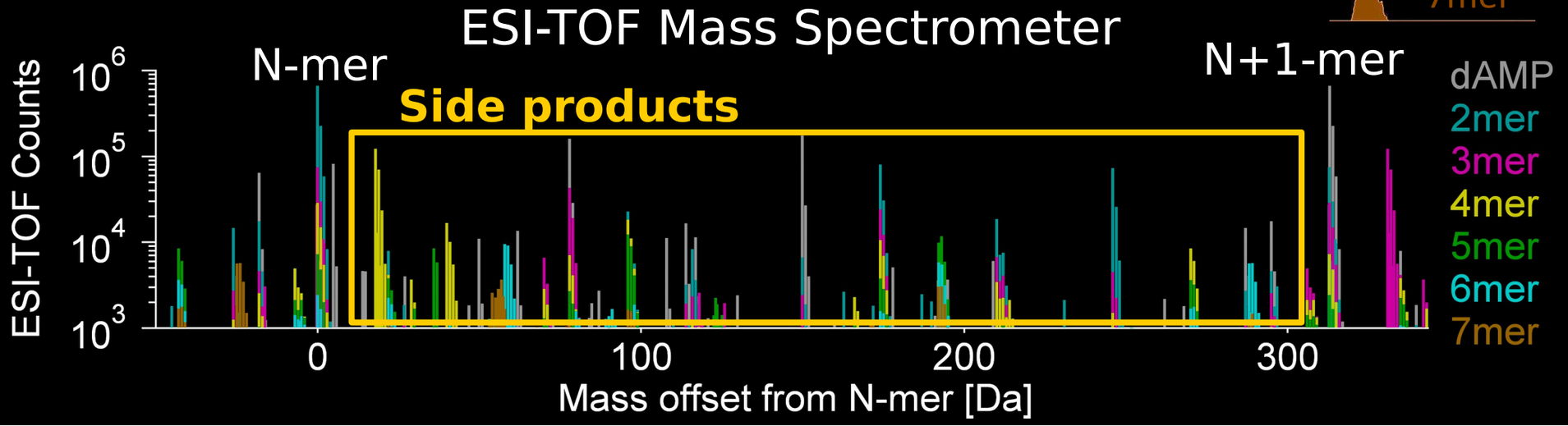
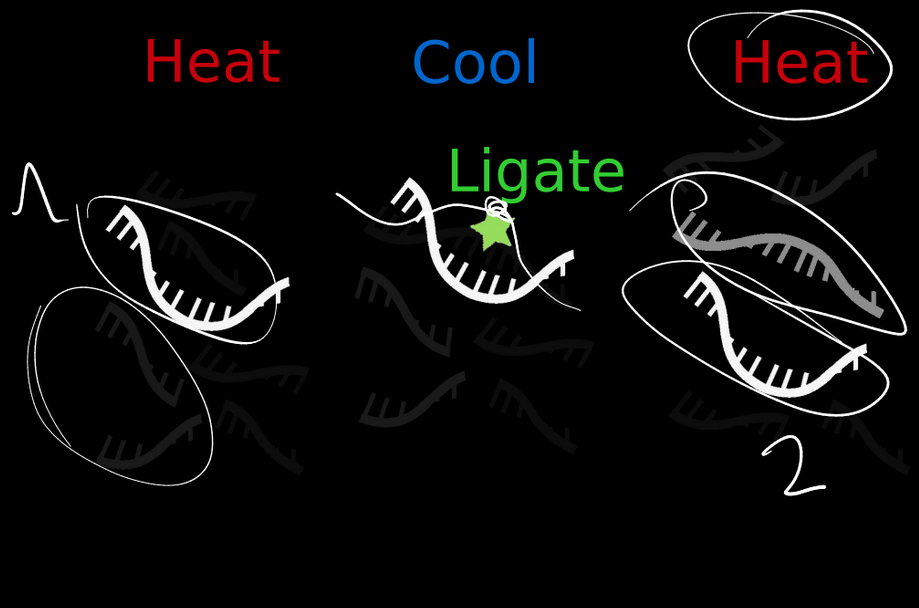


at high concentrations





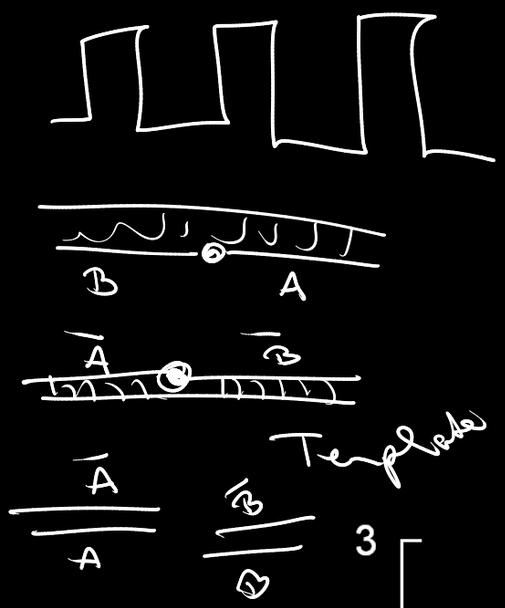
Ligation Chain Reaction with EDC

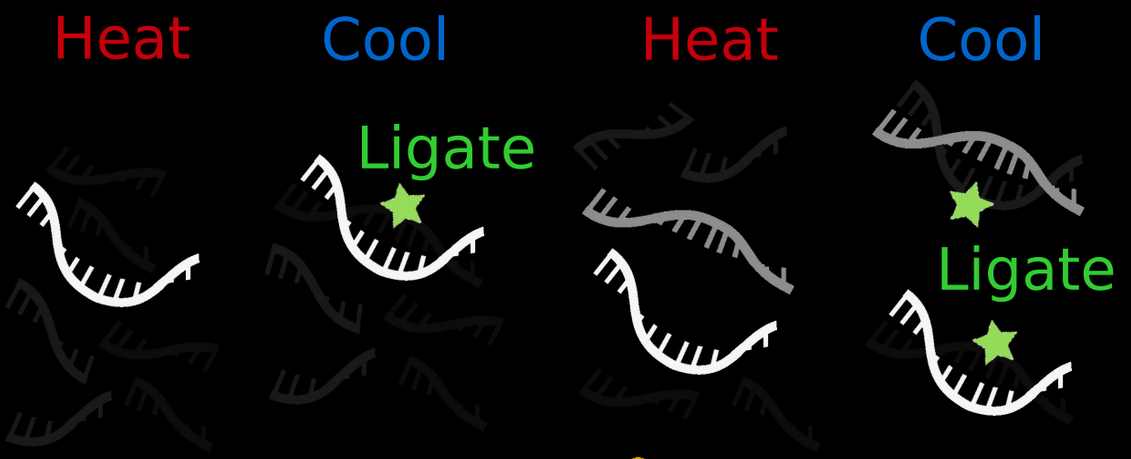


Exponential Replication

Chemical Science 2019

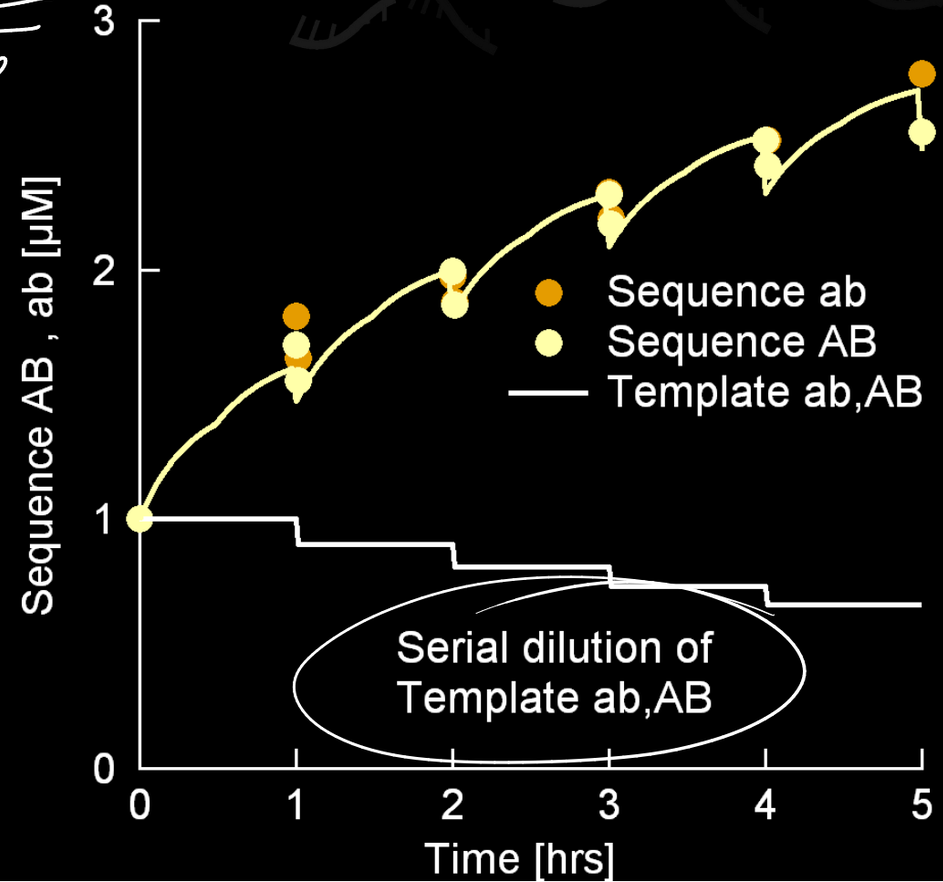
Ligation Chain Reaction with EDC



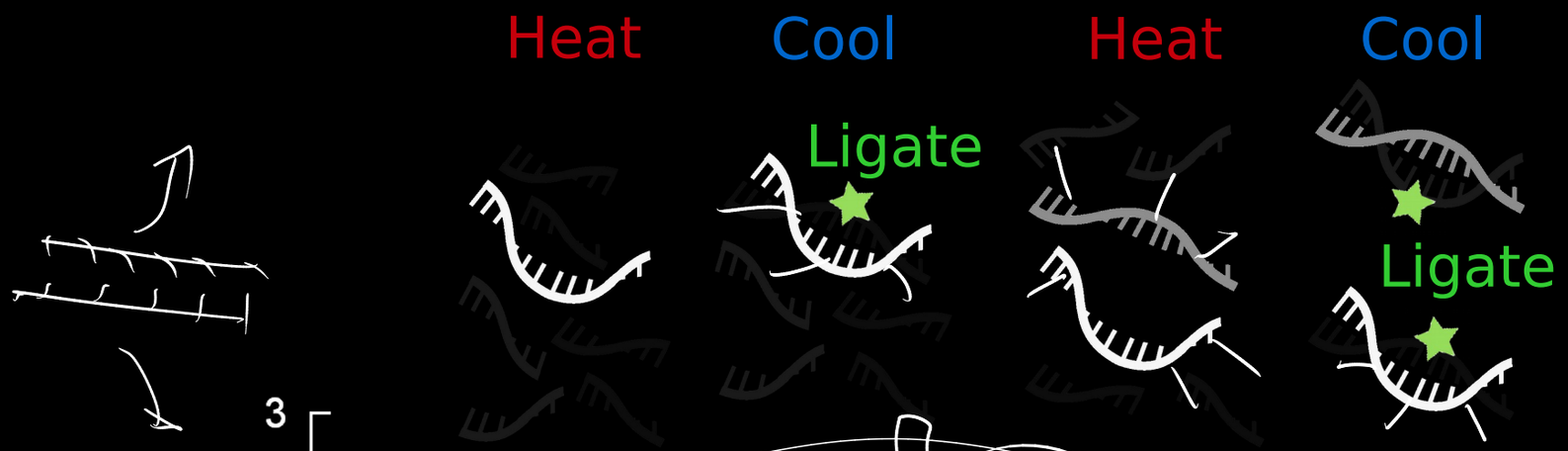


Exponential Replication

Chemical Science 2019



Ligation Chain Reaction with EDC



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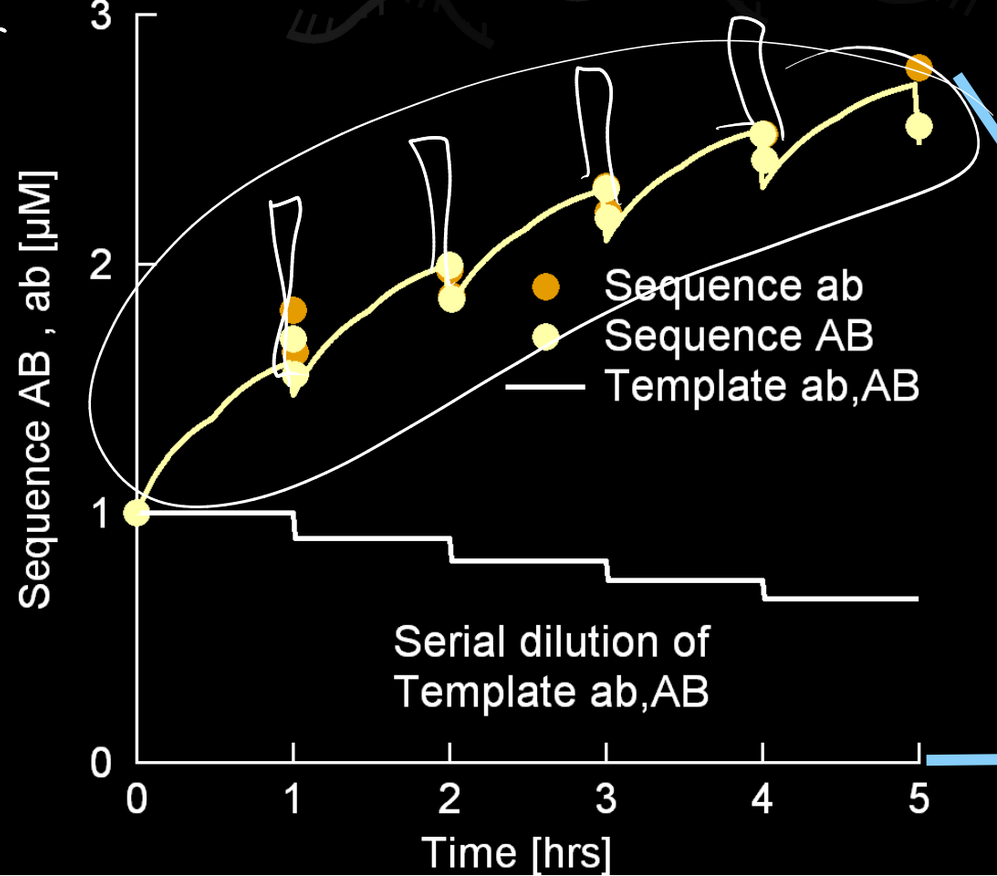
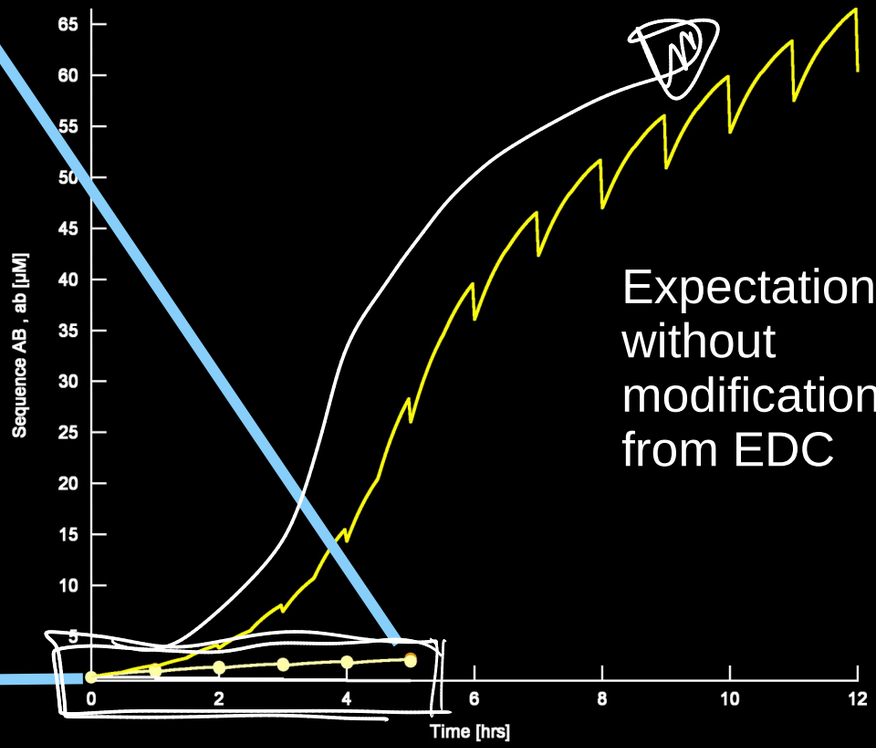
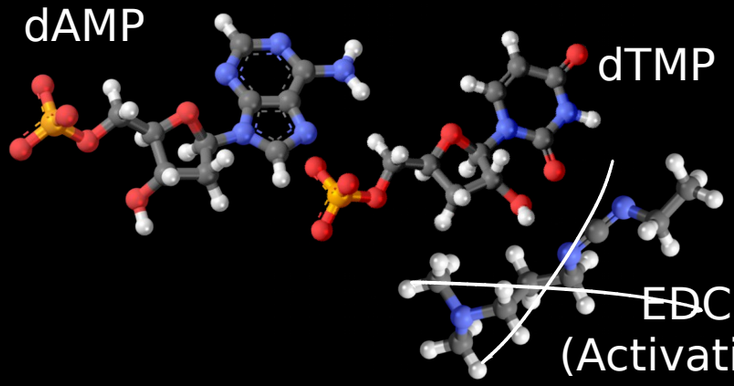


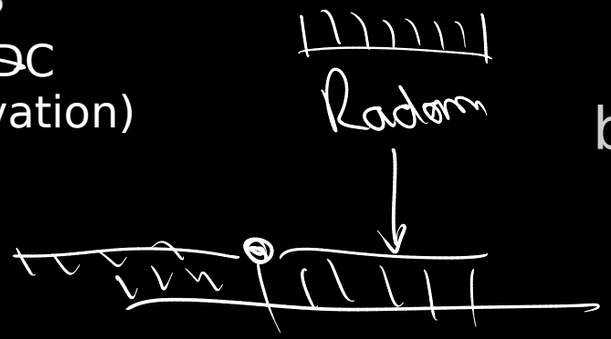


Expectation without modification from EDC

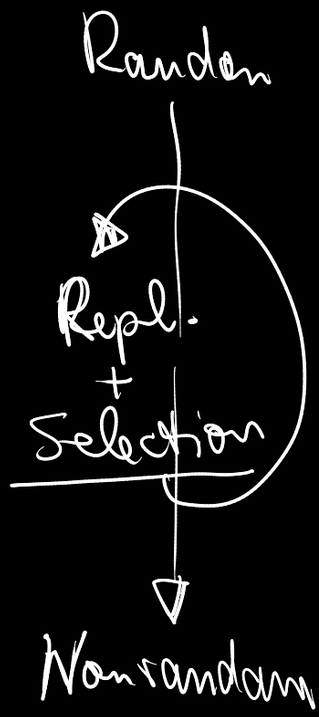


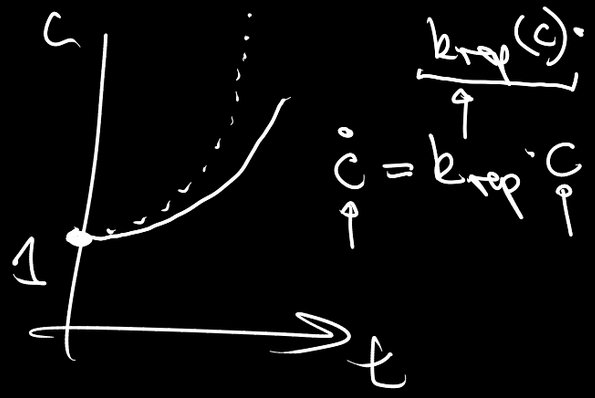
Nucleotides

Polymerization
to random sequences



Replication
base-wise, by ligation
by hydrogelation, by
mechano-selection



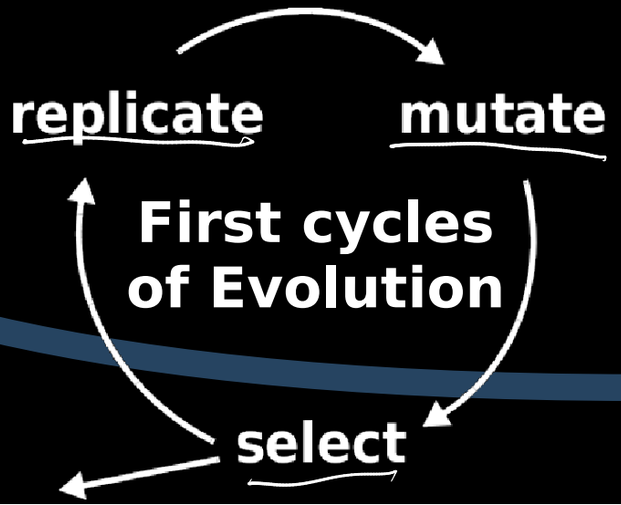


Symmetry breaking
by nonlinear sequence
cooperation mechanisms

concentration-dependent replication.

Selection
for function* between
purified phenotypes

*of surviving hydrolysis, boost replication by c↑

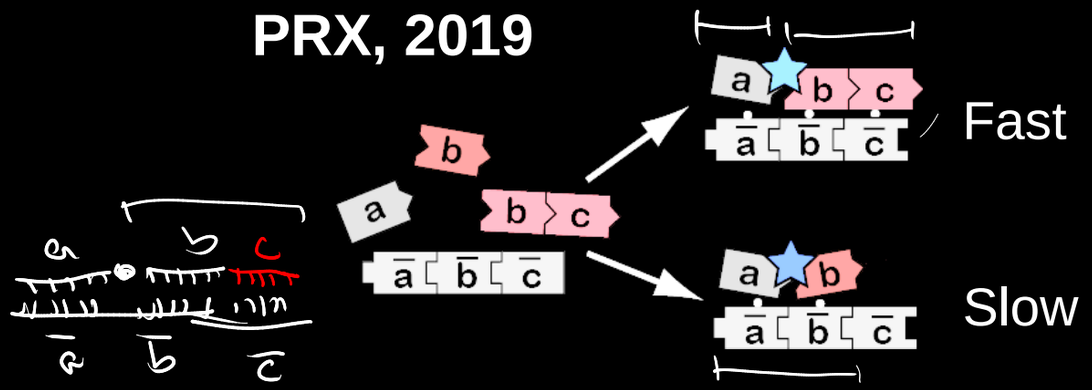


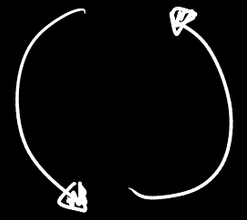
Life

Symmetry breaking in Replication

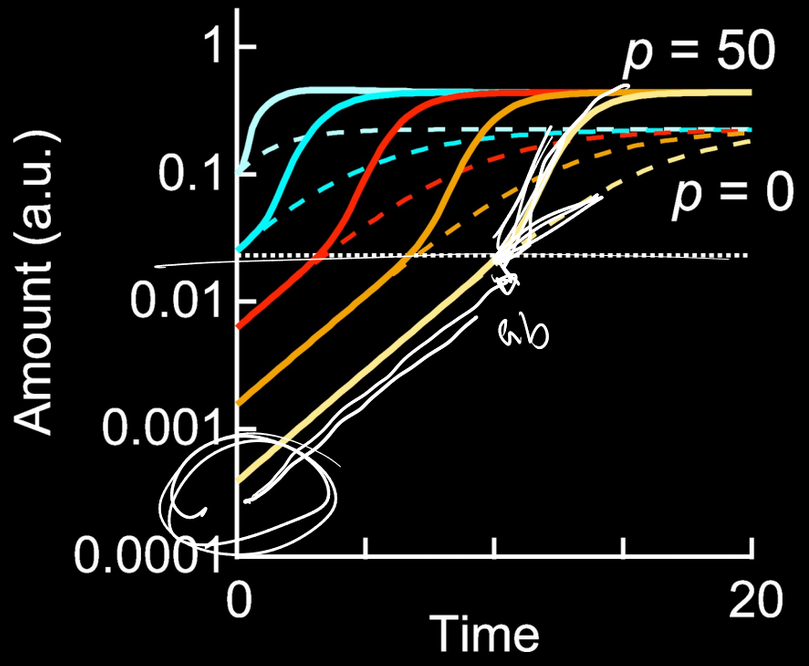
Sequence self-selection in Ligation

PRX, 2019

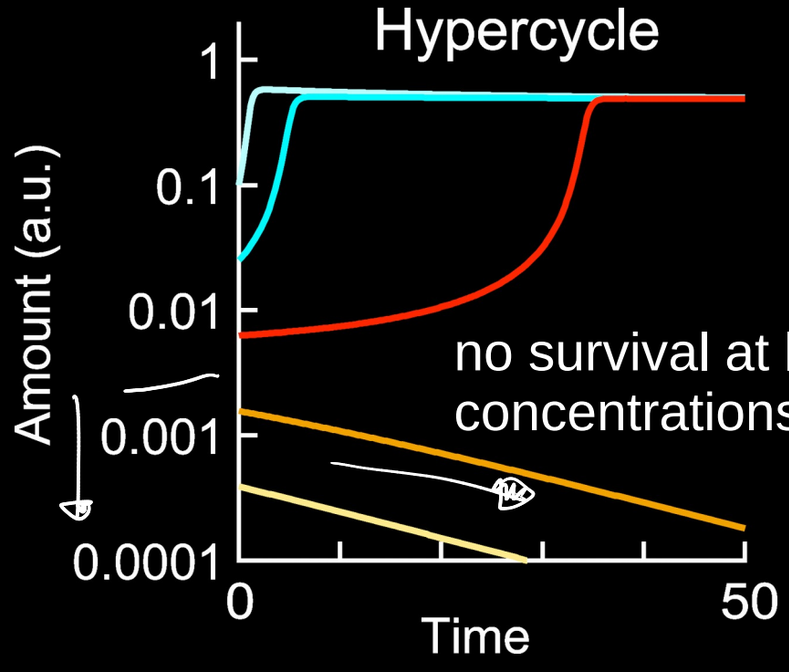




Cooperative cascade



Hypercycle



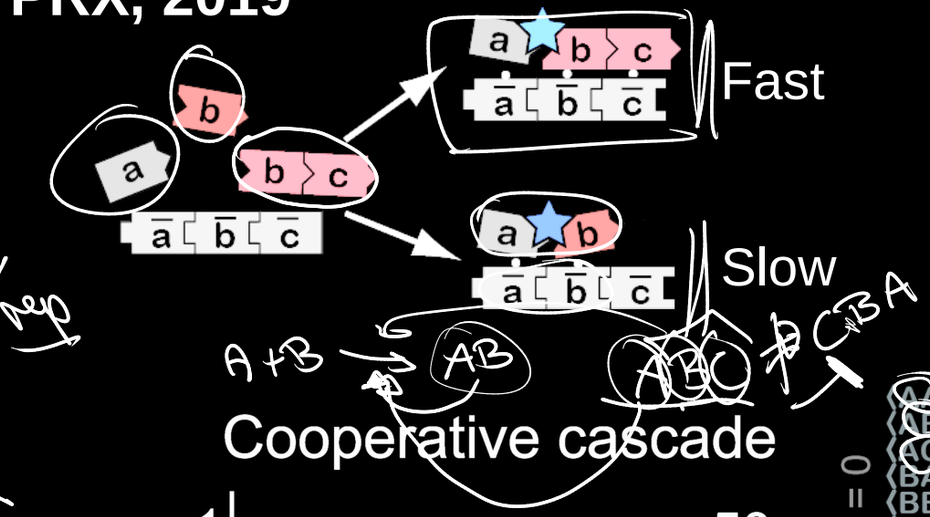
$\dot{C} = k_{rep} \cdot C^{1+\alpha}$

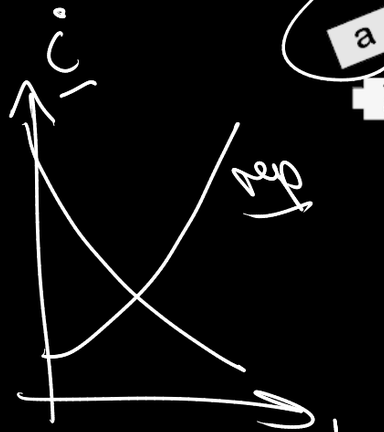
$\alpha > 0$

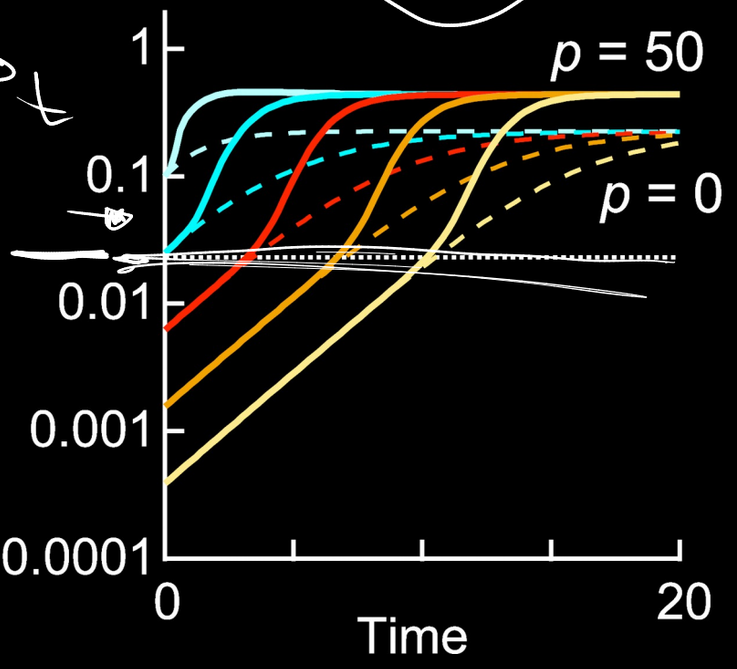
Symmetry breaking in Replication

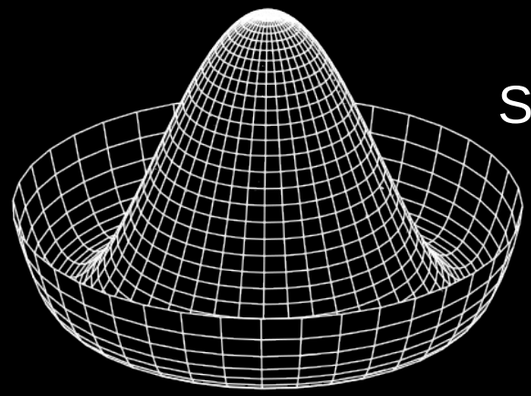
Sequence self-selection in Ligation

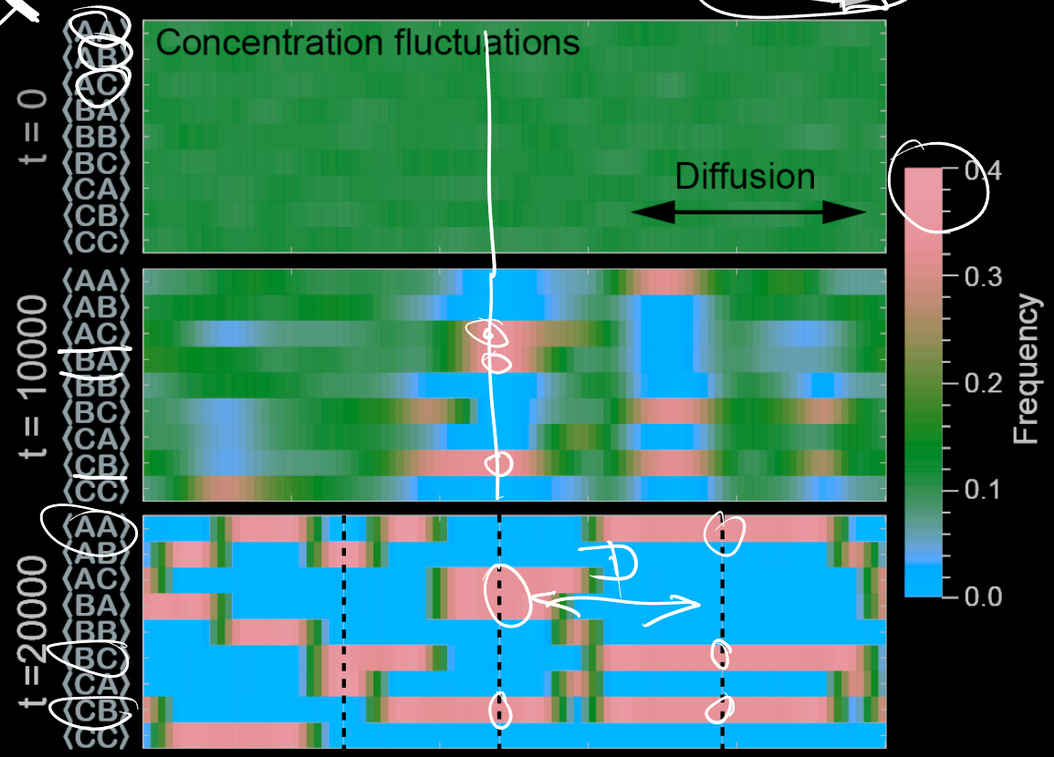
PRX, 2019











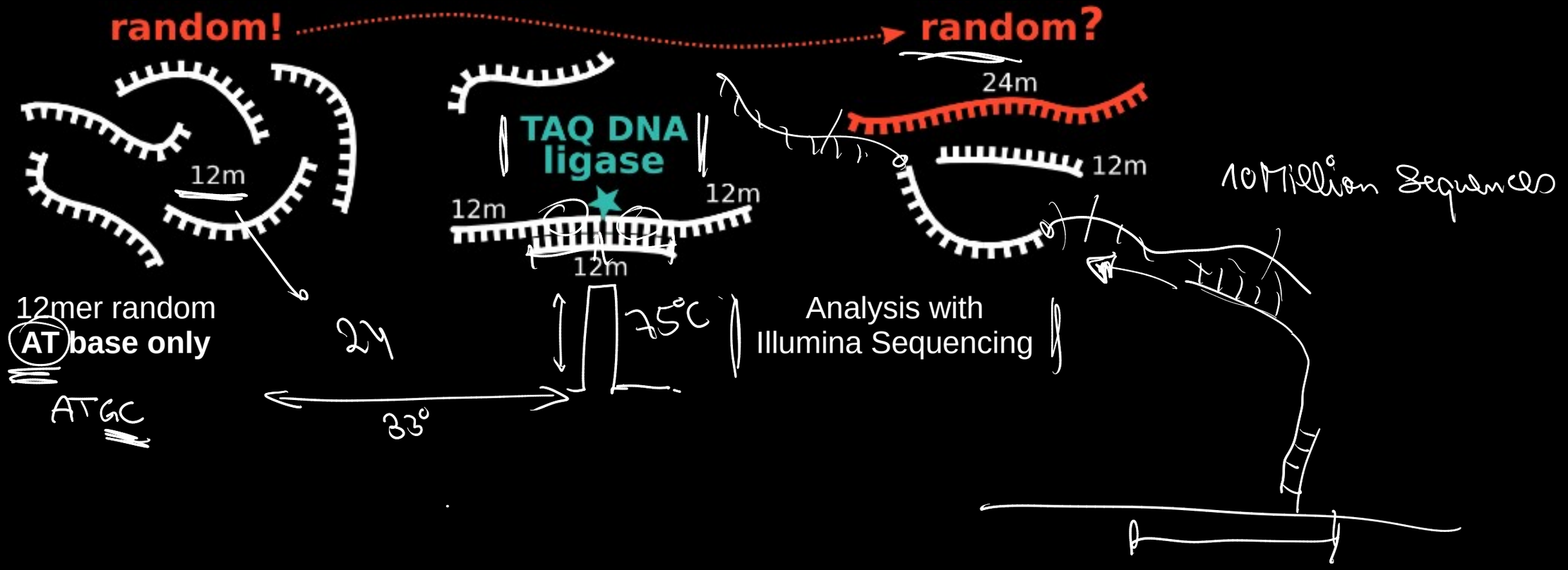
...CBACBA...

...AAAAA...

...CBCB...

Replication dynamics in sequence space

From Random to Non-random Sequences



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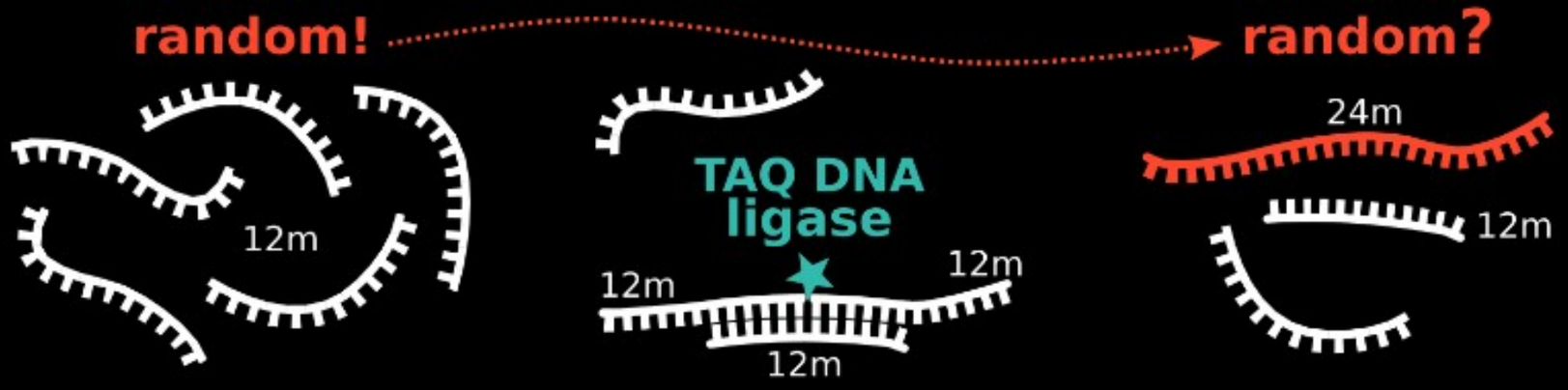
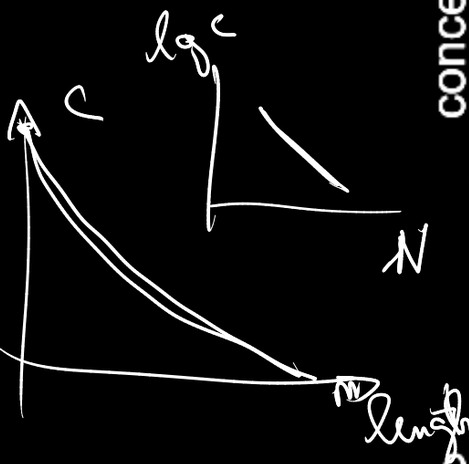
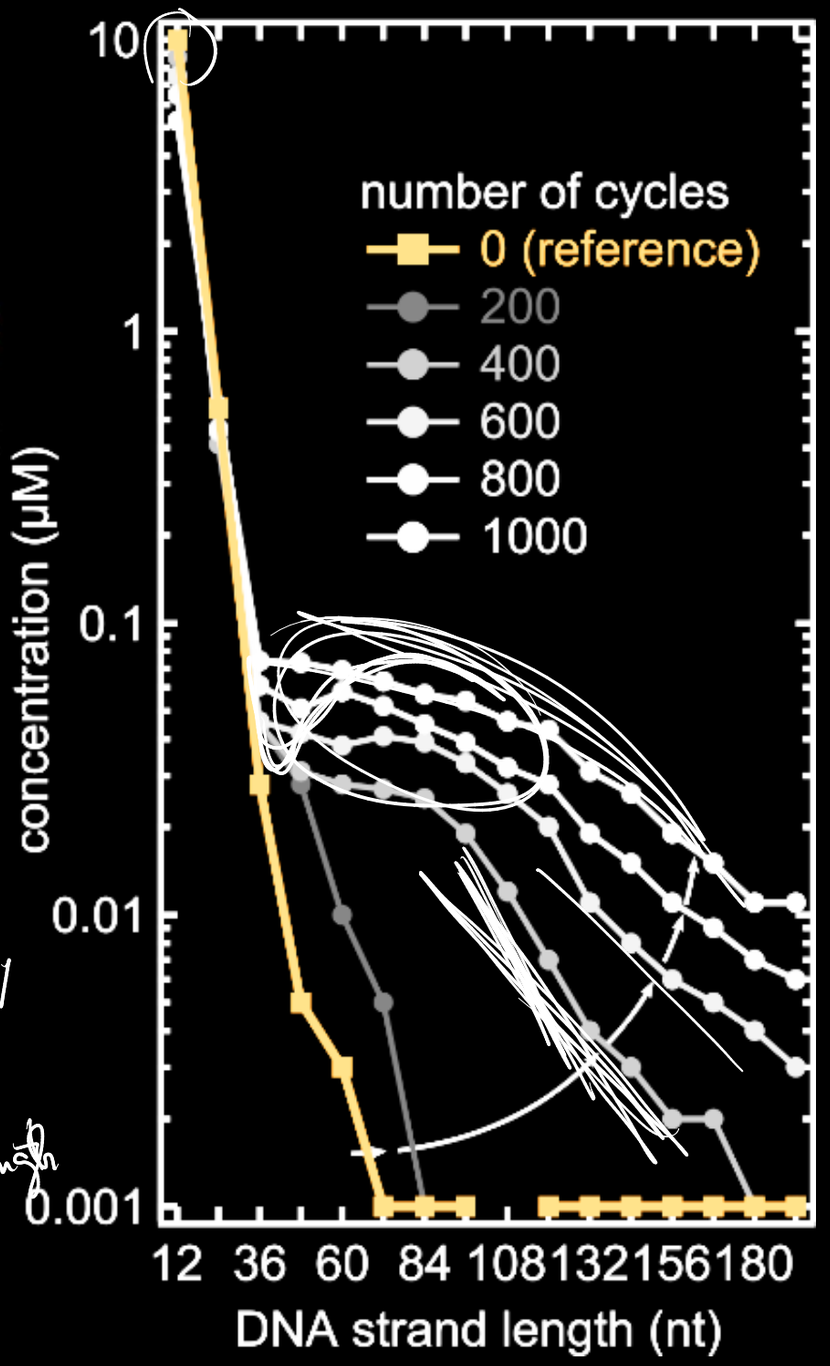


12mer random
AT base only

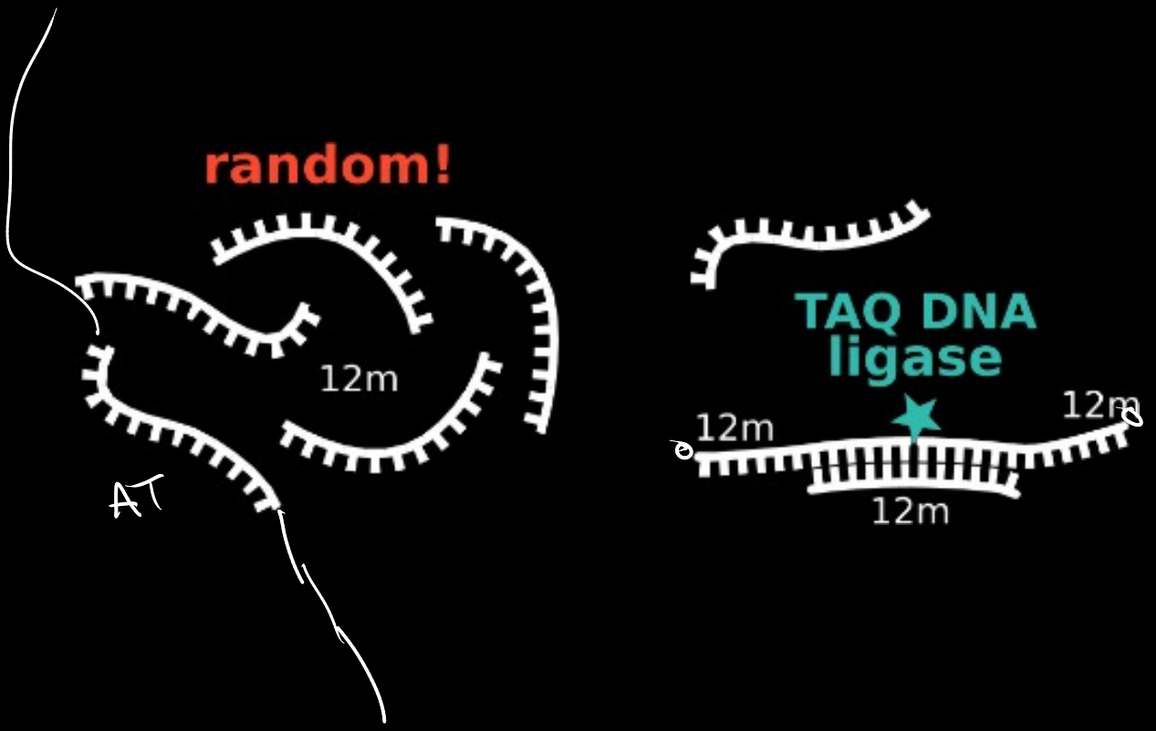
Analysis with
Illumina Sequencing



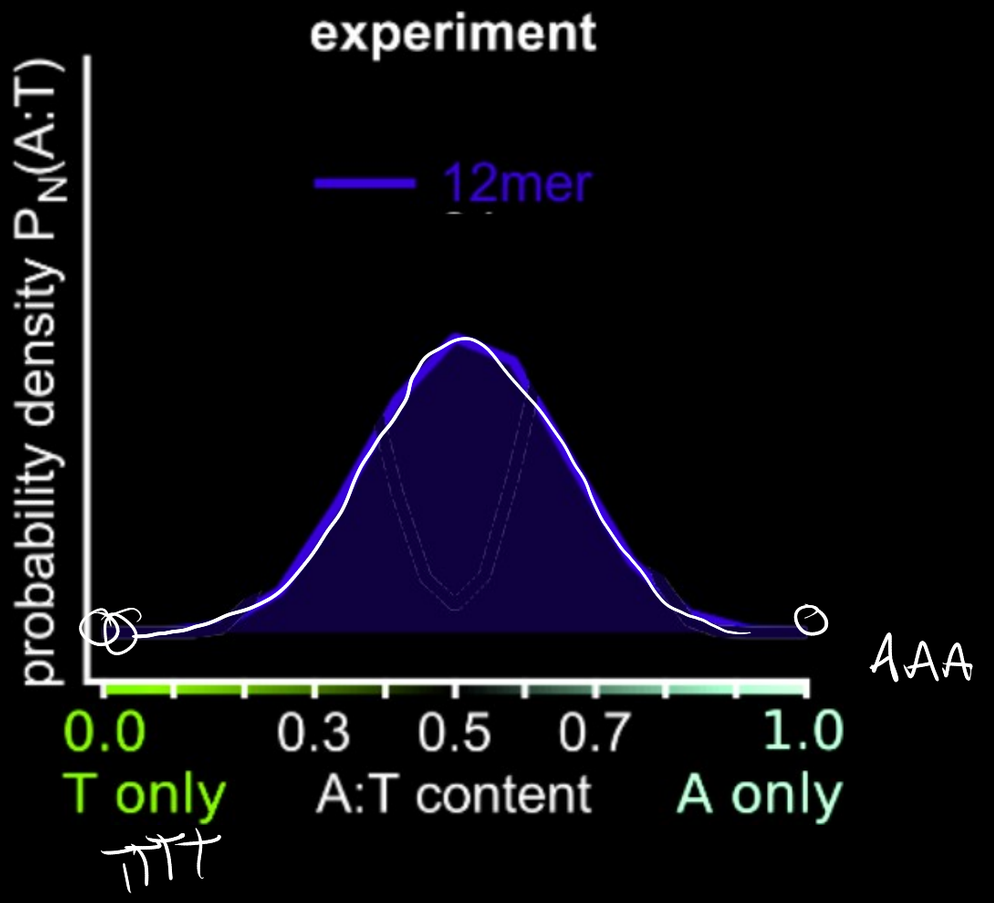


PNAS, under revision

Replication dynamics in sequence space

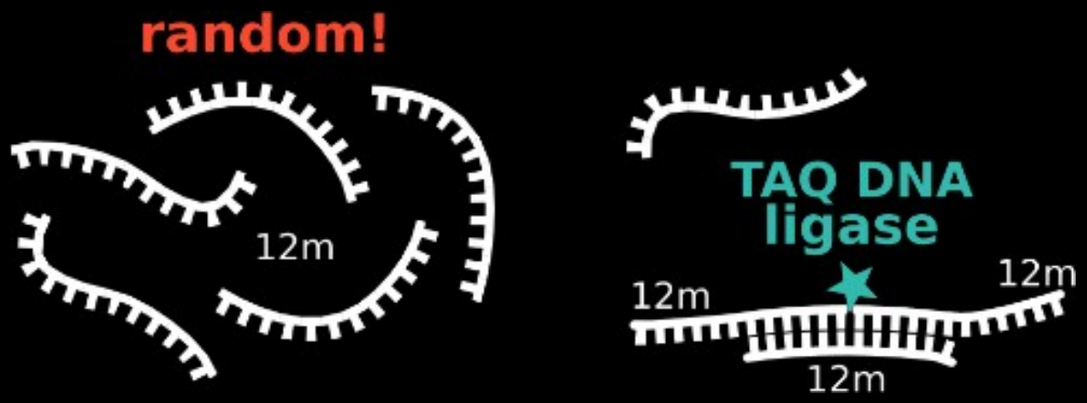


Replication avoids hairpins by evolving complementary pools



PNAS, under revision

Dynamics in sequence space



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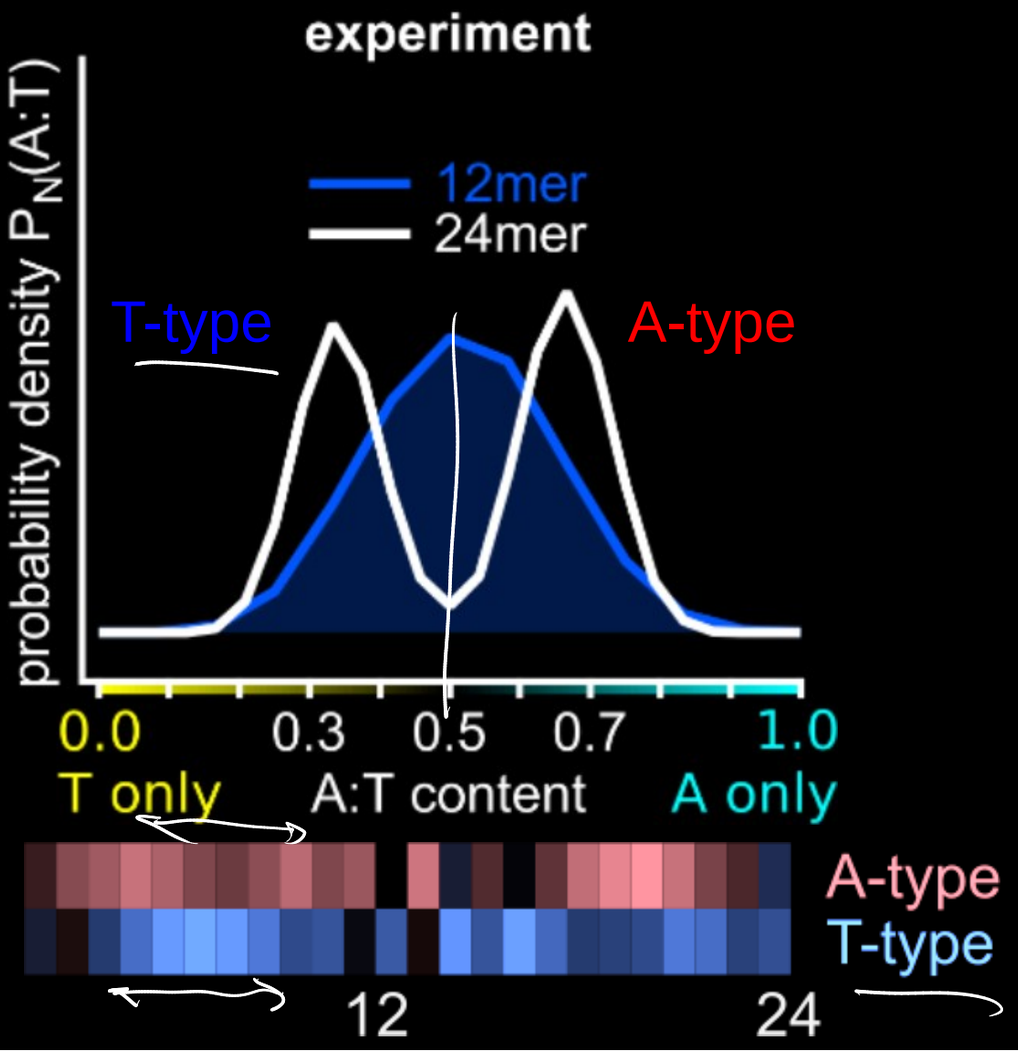
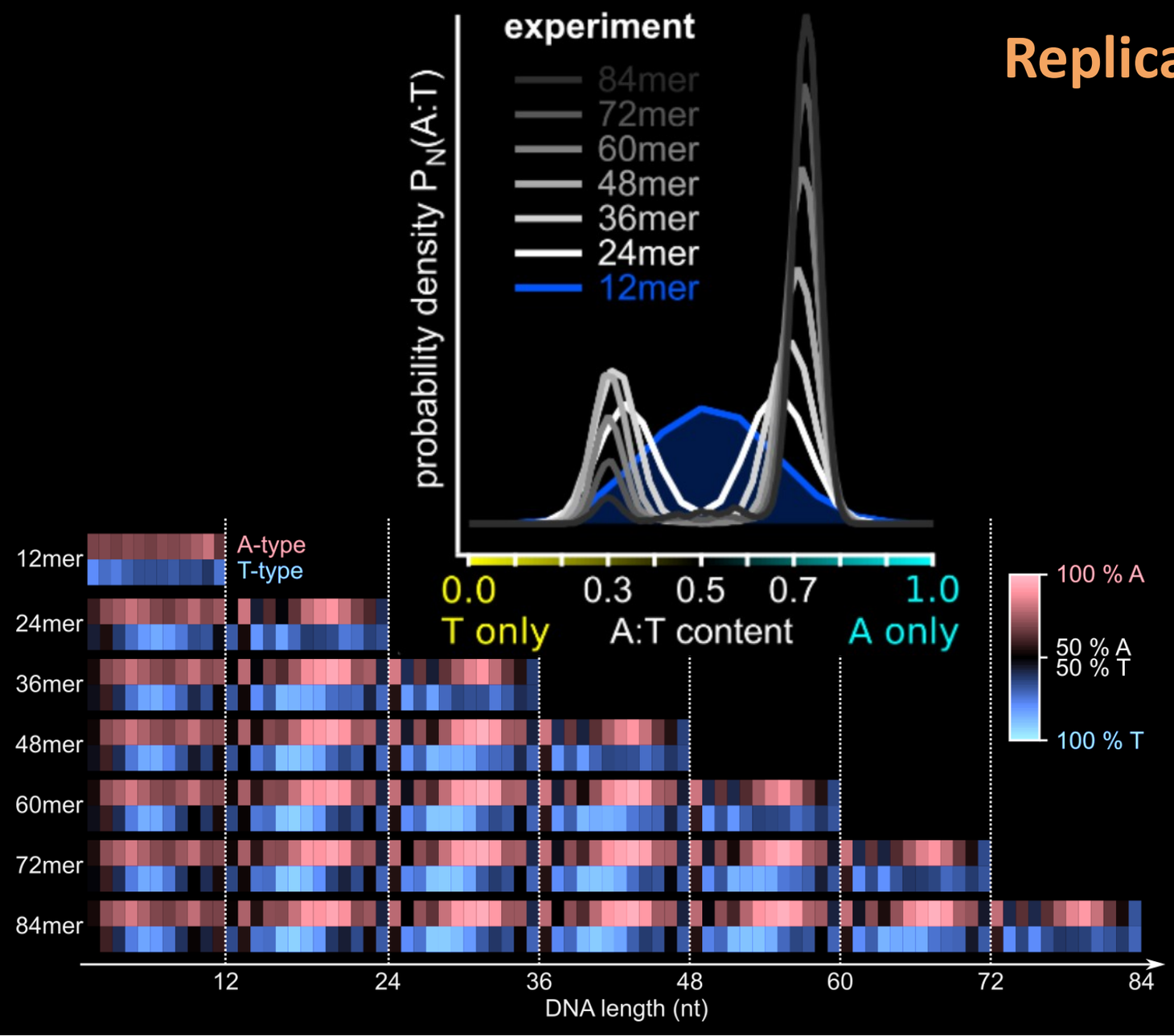
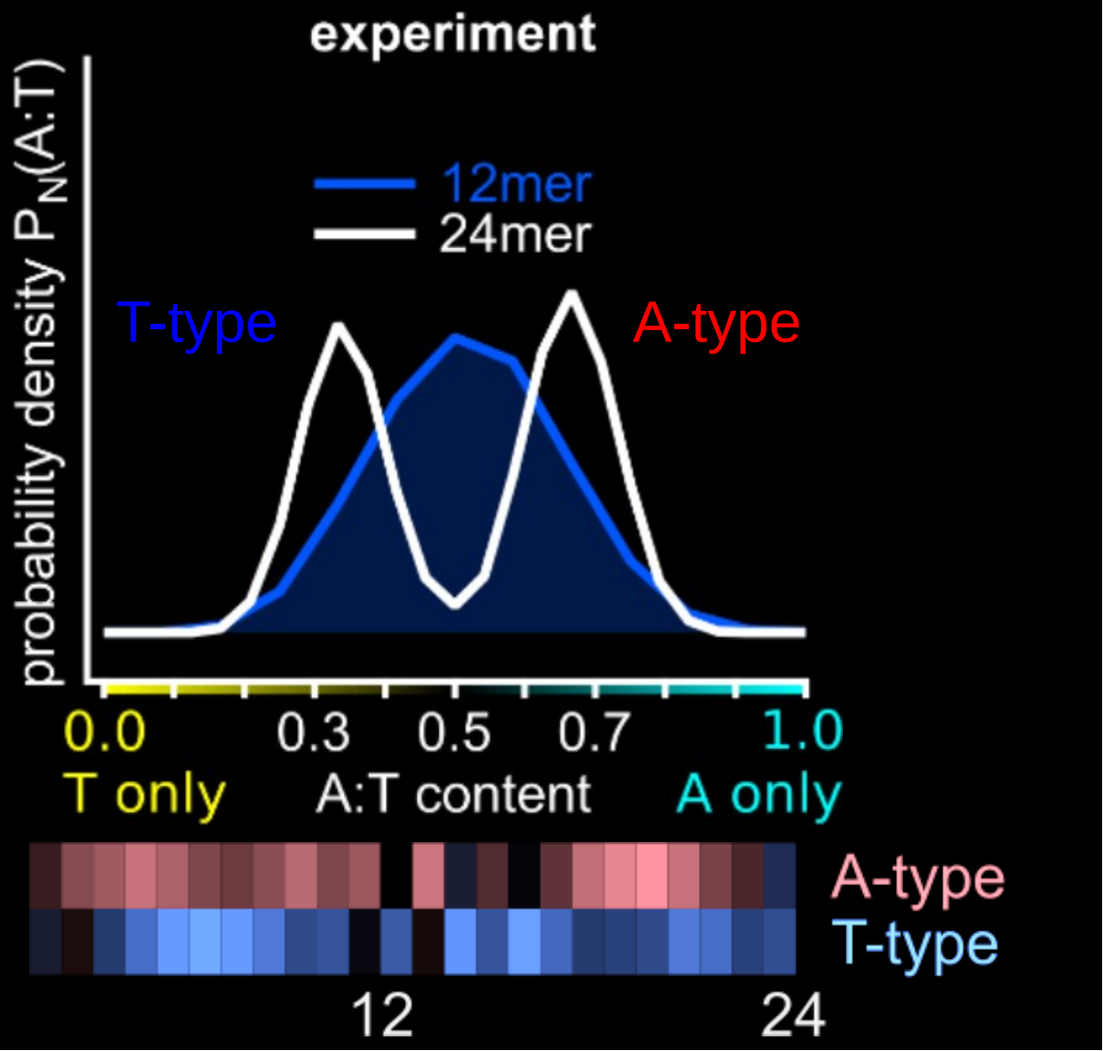


PNAS, under revision

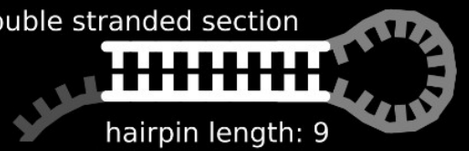
Dynamics in sequence space

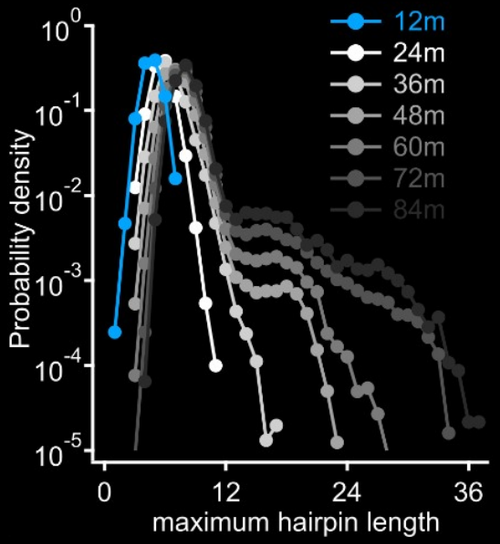
Replication avoids hairpins by evolving complementary pools

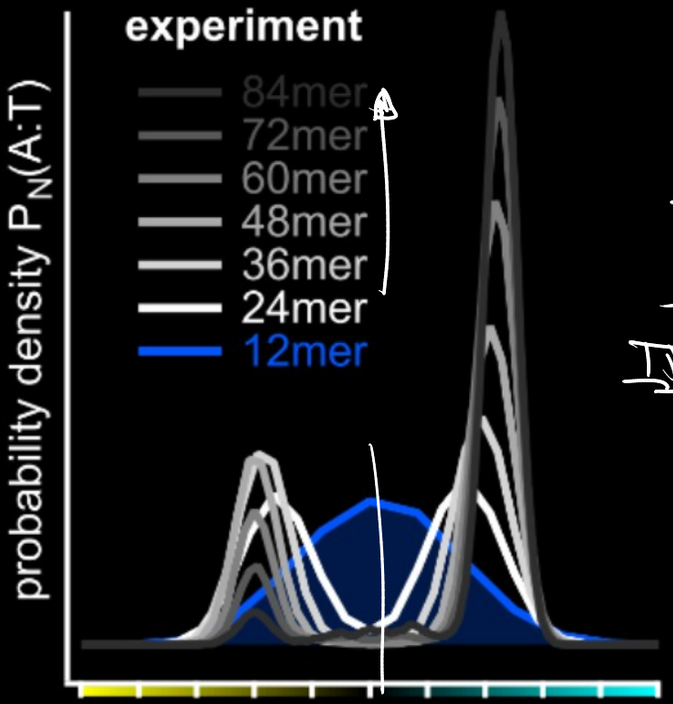


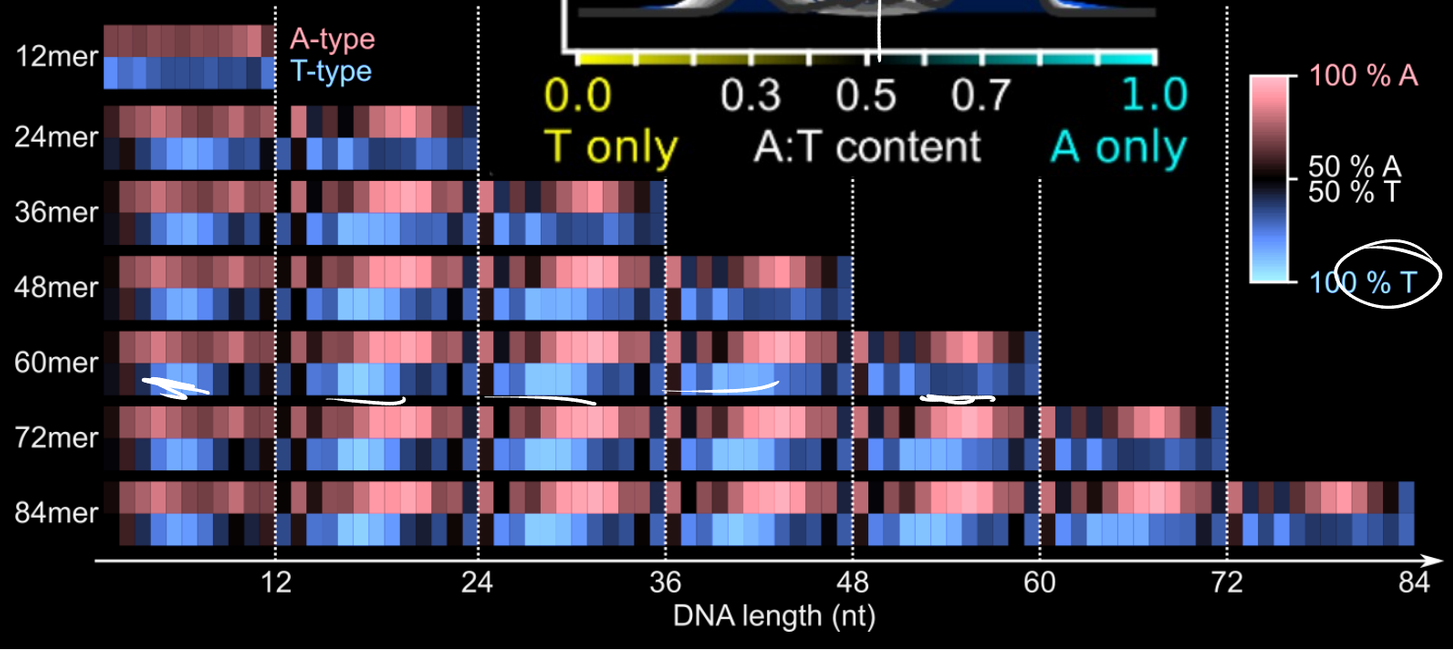


Dynamics in sequence space

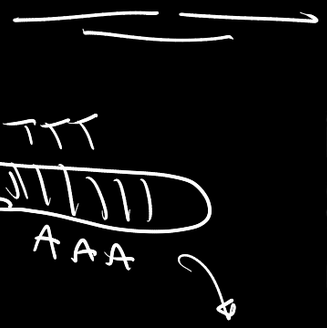


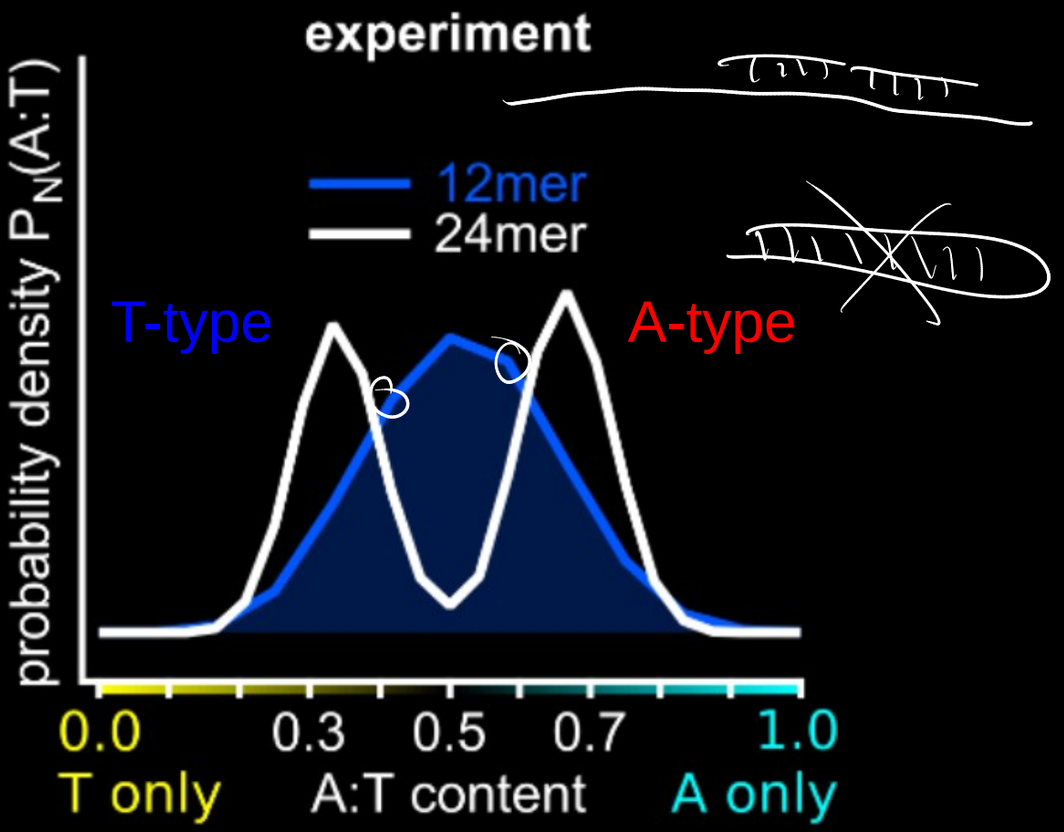






Replication avoids hairpins by evolving complementary pools

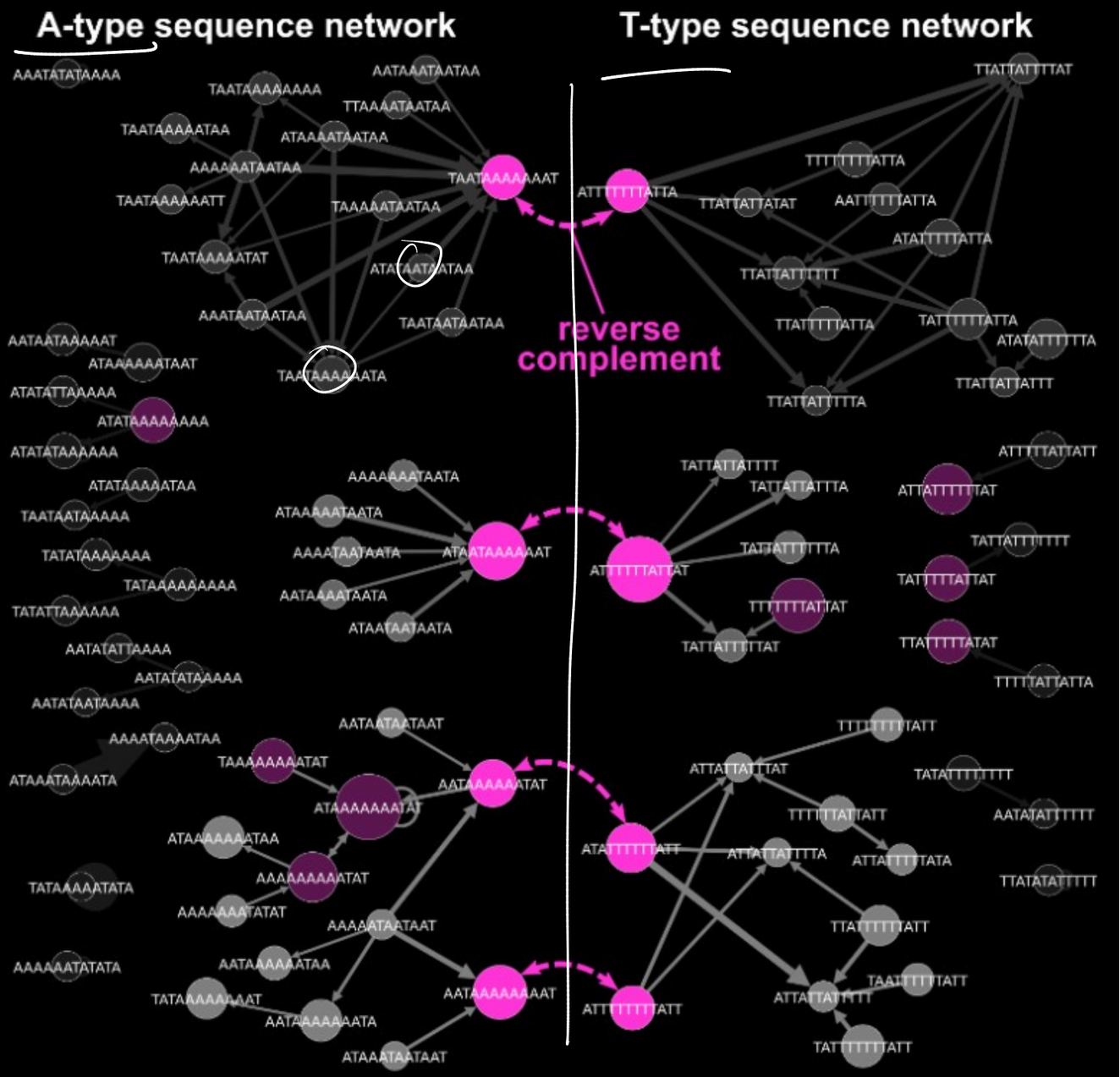




Dynamics in sequence space

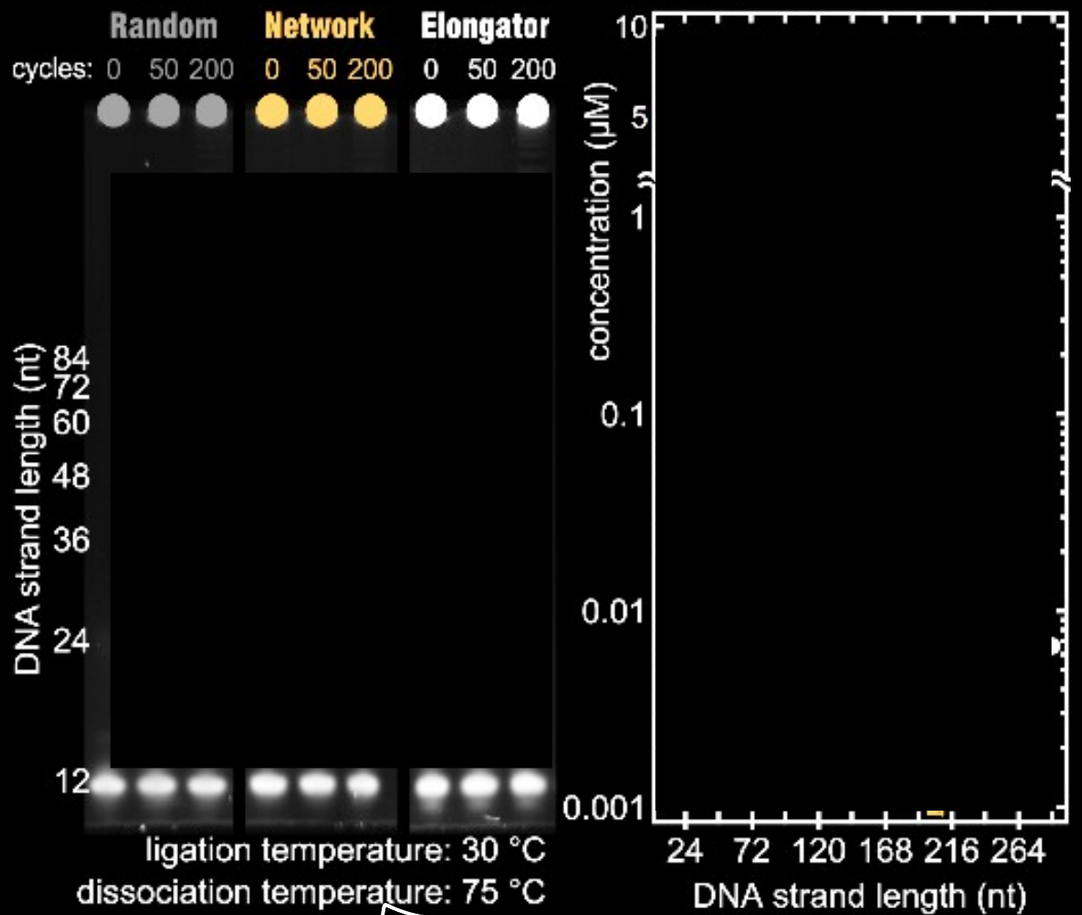
Replication amplifies patterns at the ligation site

Replication avoids hairpins by evolving complementary pools

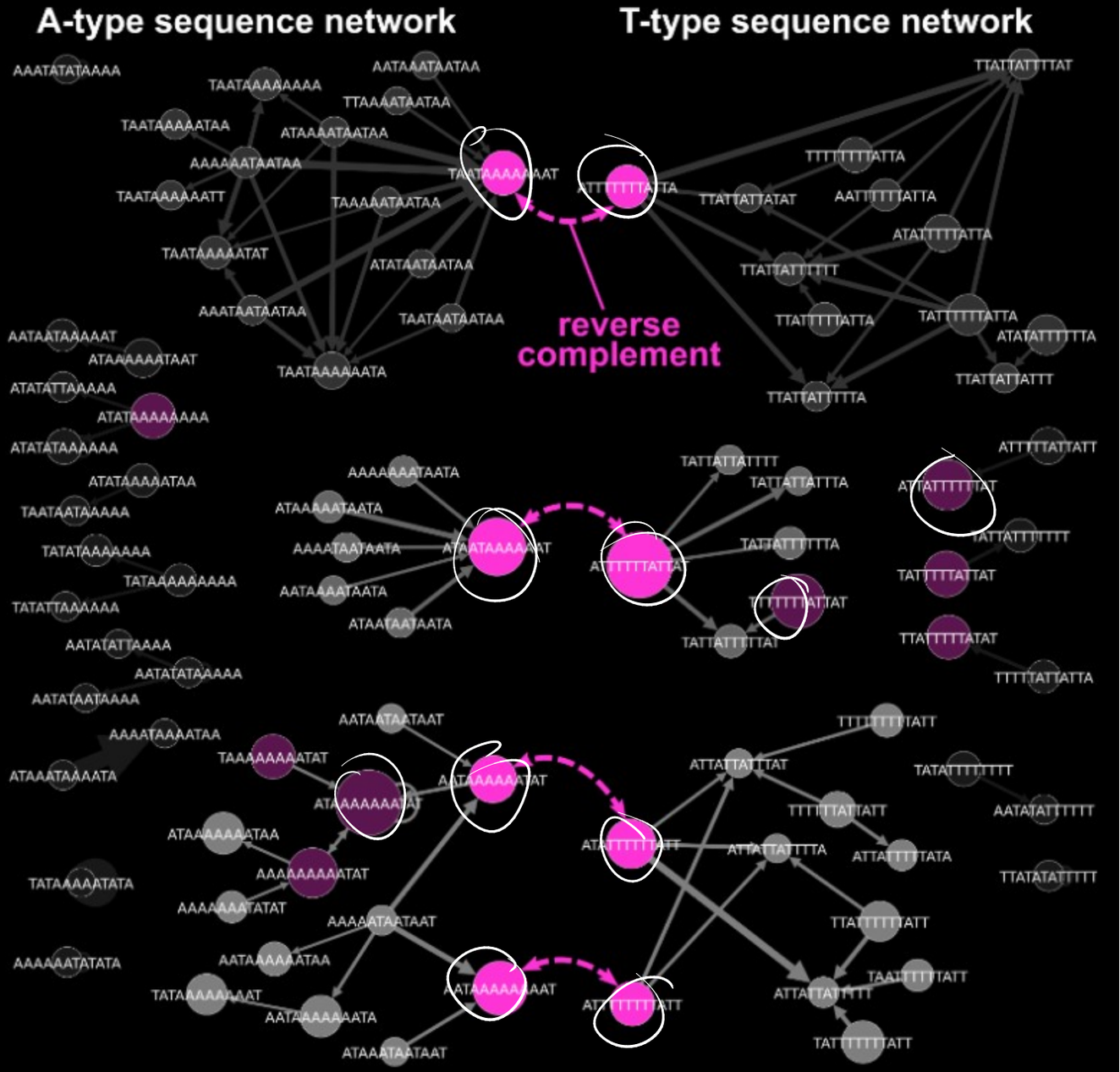


PNAS, under revision

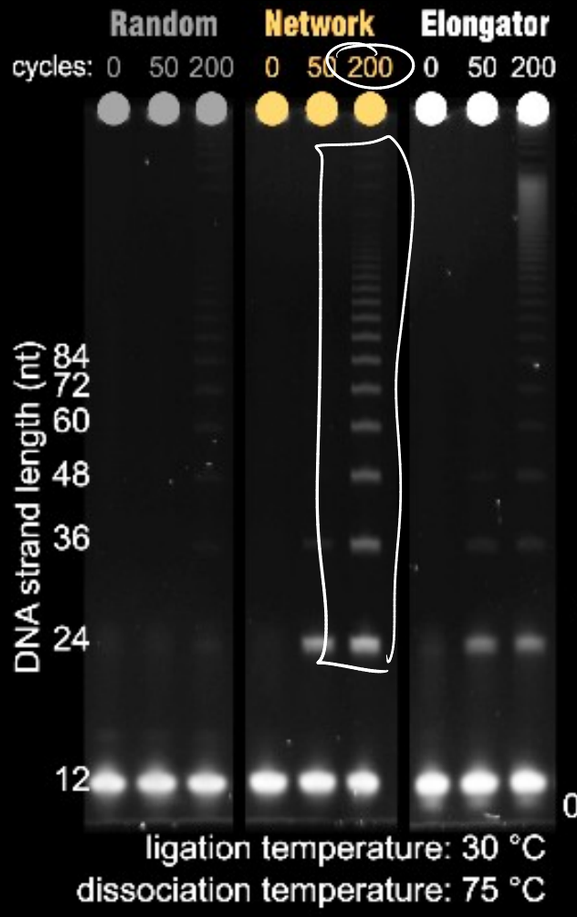
Dynamics in sequence space

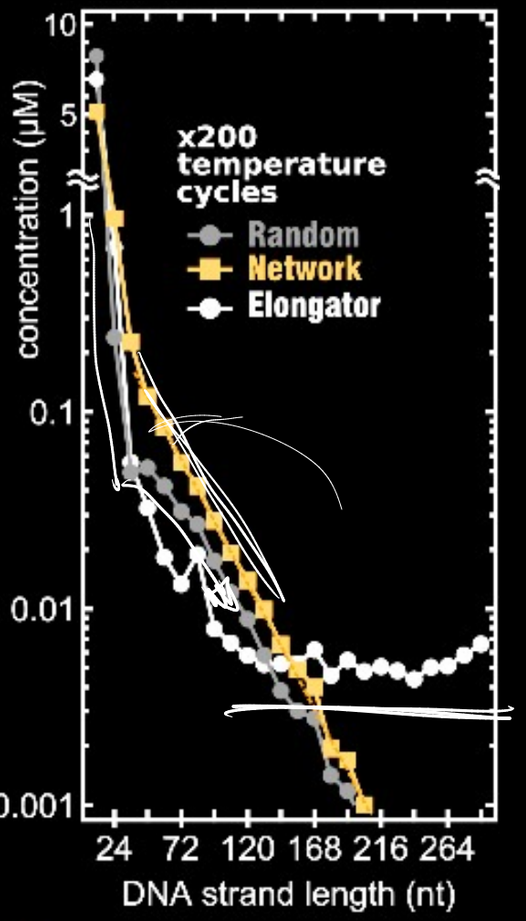


Random	Network	Elongator
AAAATAAAATAT	ATAATAAAAAAT	ATATTTTTTATA
ATAATTAAATAA	AATAAAAAAAAT	TATAAAAAATAT
TAAAAATTATTT	AATAAAAAATAT	AAATATATAAAA
TTAAATTTTATA	TAATAAAAAAAT	TTTTATATATTT
TATTTAATTTTT	ATTTTTTATTAT	AAAATATATAAA
TAAAAATTAATA	ATATTTTTTATT	TTTATATATTTT
AAAATAATTTAT	ATTTTTTTTATT	TATTTTTTTTAT
TTATATAAAATA	ATTTTTTTATTA	ATAAAAAAAATA

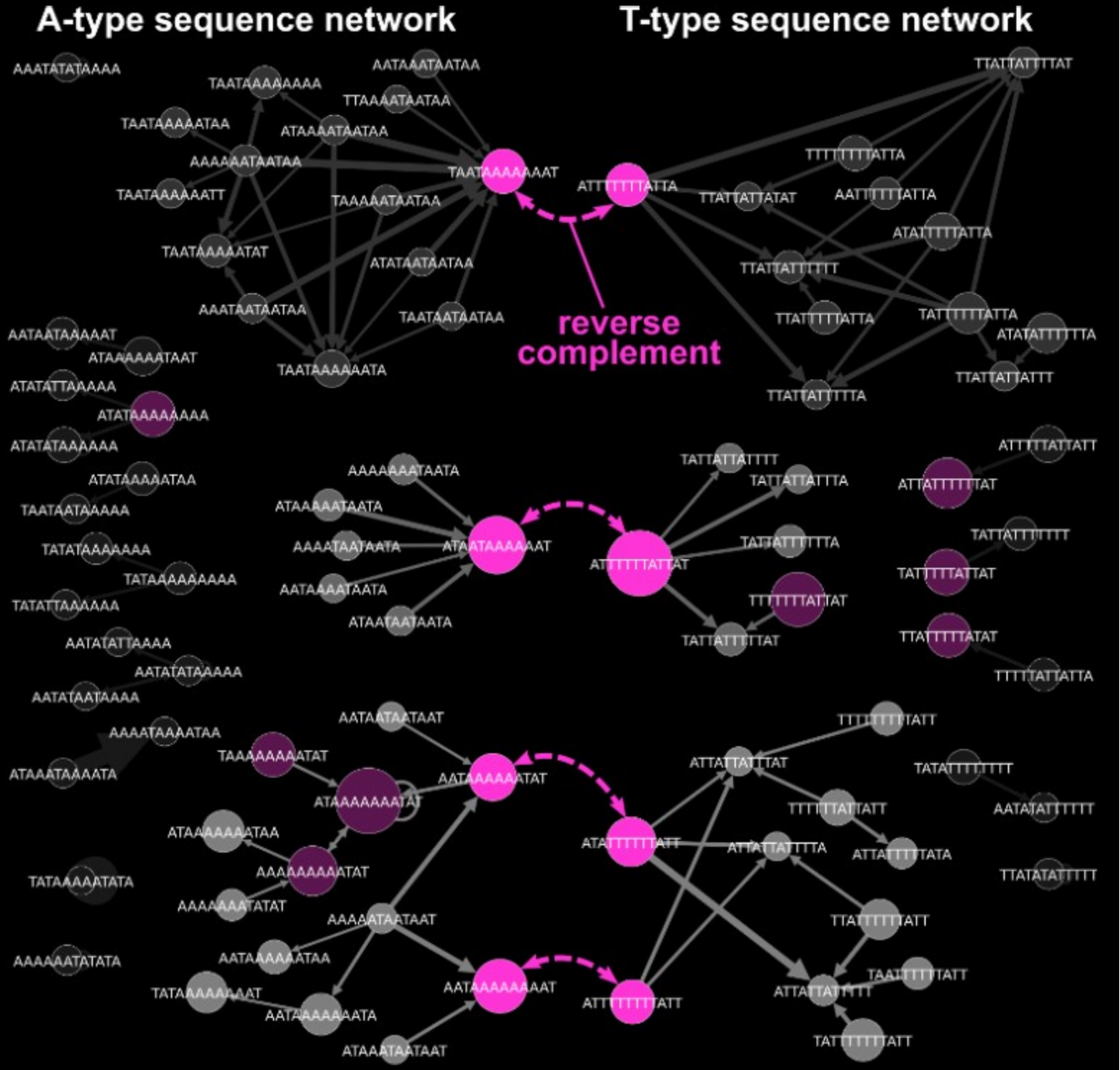


Dynamics in sequence space

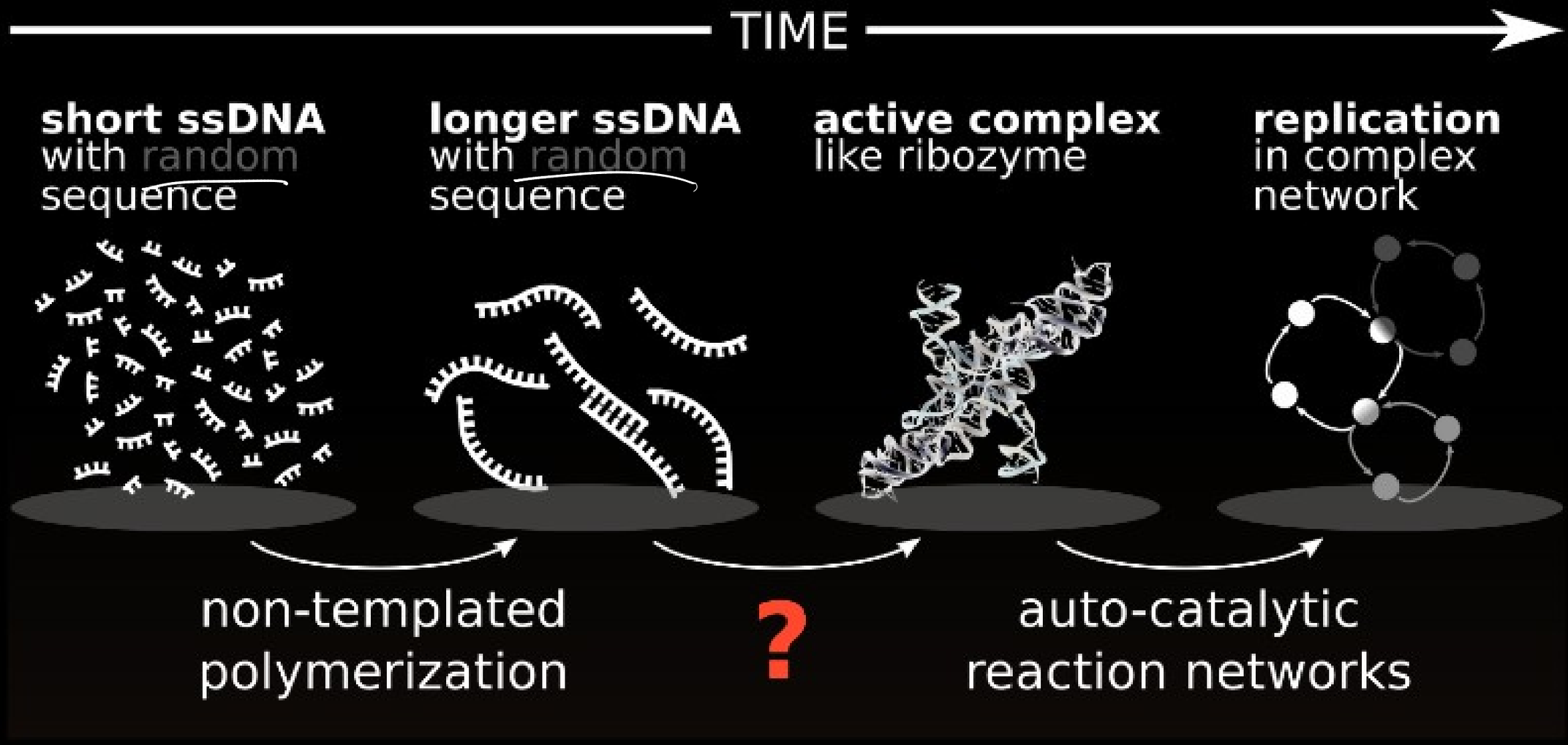




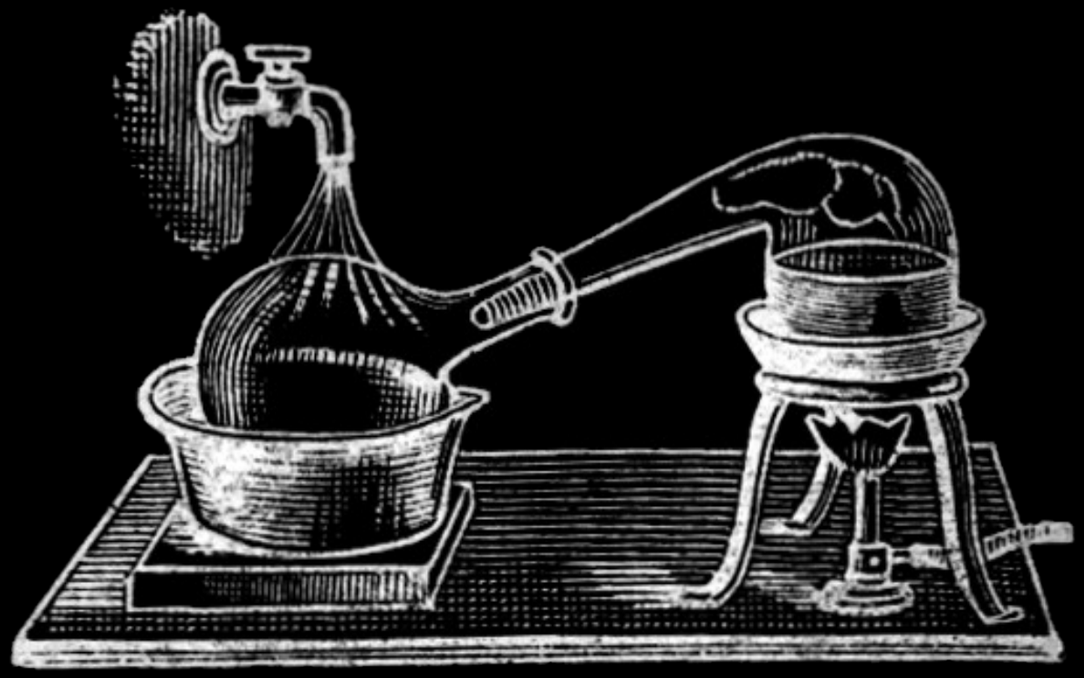
Random	Network	Elongator
AAAATAAAATAT	ATAATAAAAAAT	ATATTTTTTATA
ATAATTAAATAA	AATAAAAAAAAT	TATAAAAAATAT
TAAAAATTATTT	AATAAAAAATAT	AAATATATAAAA
TTAAATTTTATA	TAATAAAAAAAT	TTTTATATATTT
TATTTAATTTTT	ATTTTTTATTAT	AAAATATATAAA
TAAAAATTAATA	ATATTTTTTATT	TTTATATATTTT
AAAATAATTTAT	ATTTTTTTTATT	TATTTTTTTTAT
TTATATAAAATA	ATTTTTTTATTA	ATAAAAAAAATA



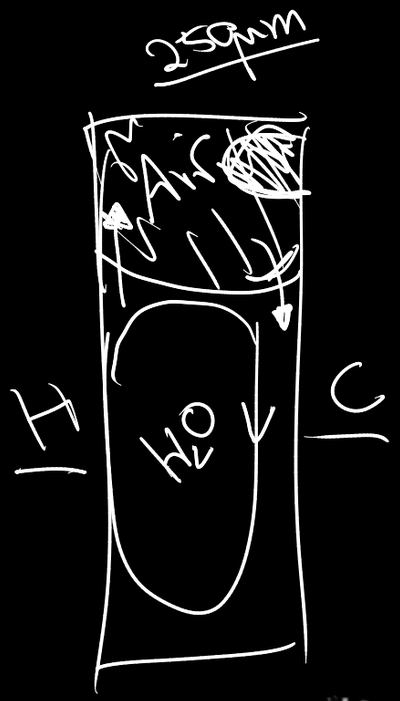
Dynamics in sequence space

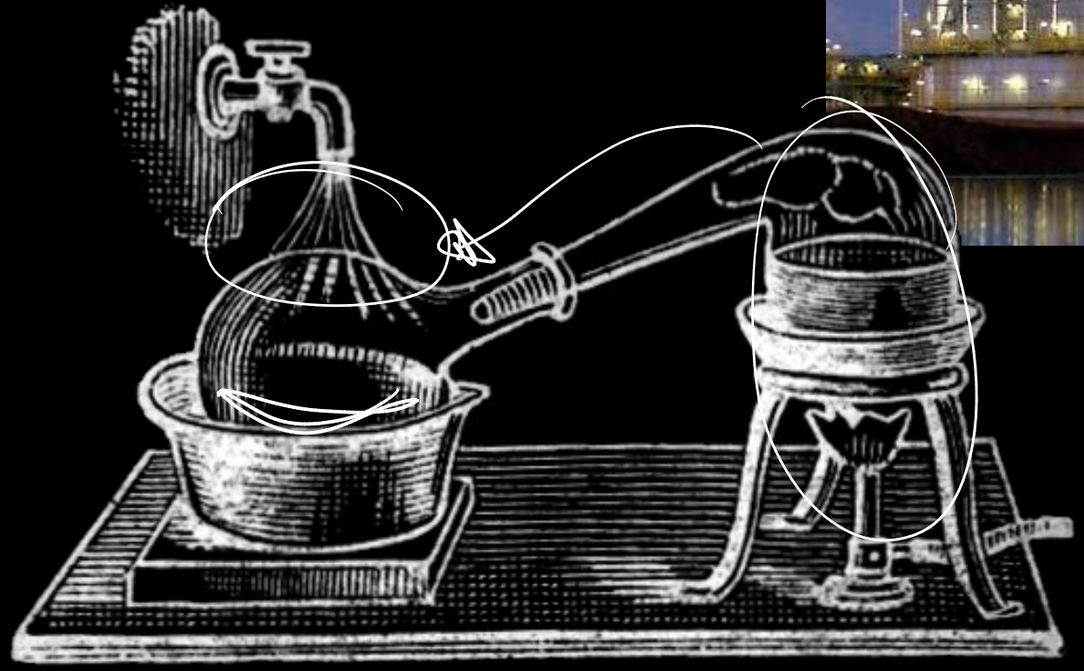


Microdistilleries

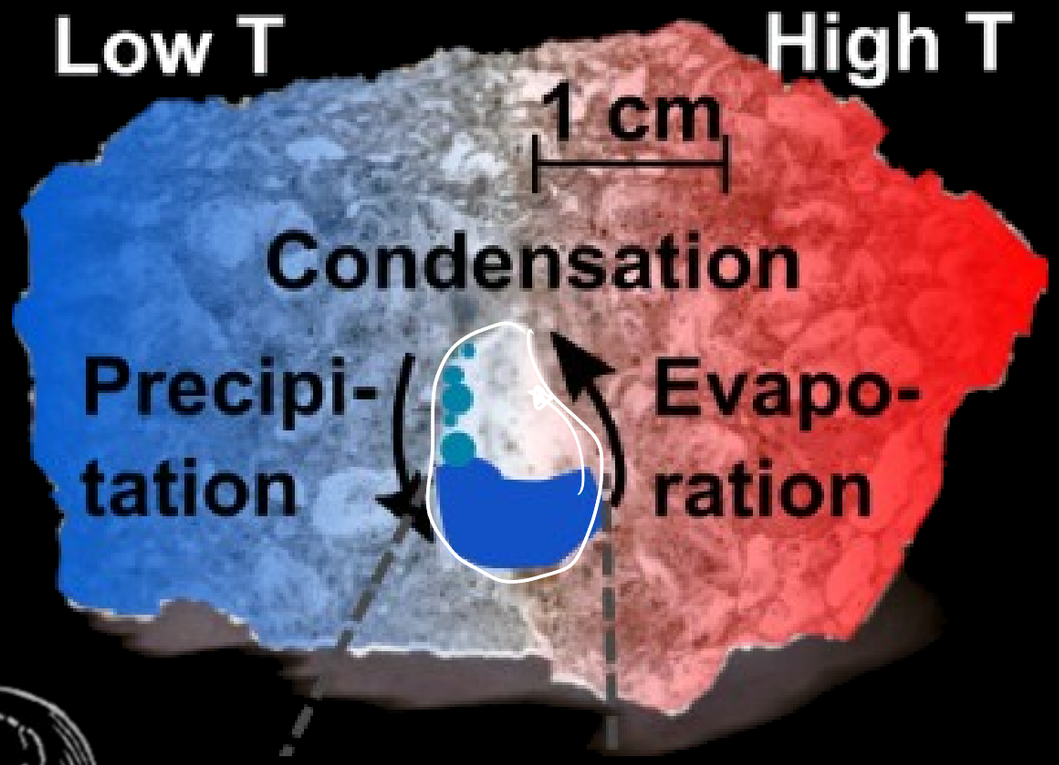


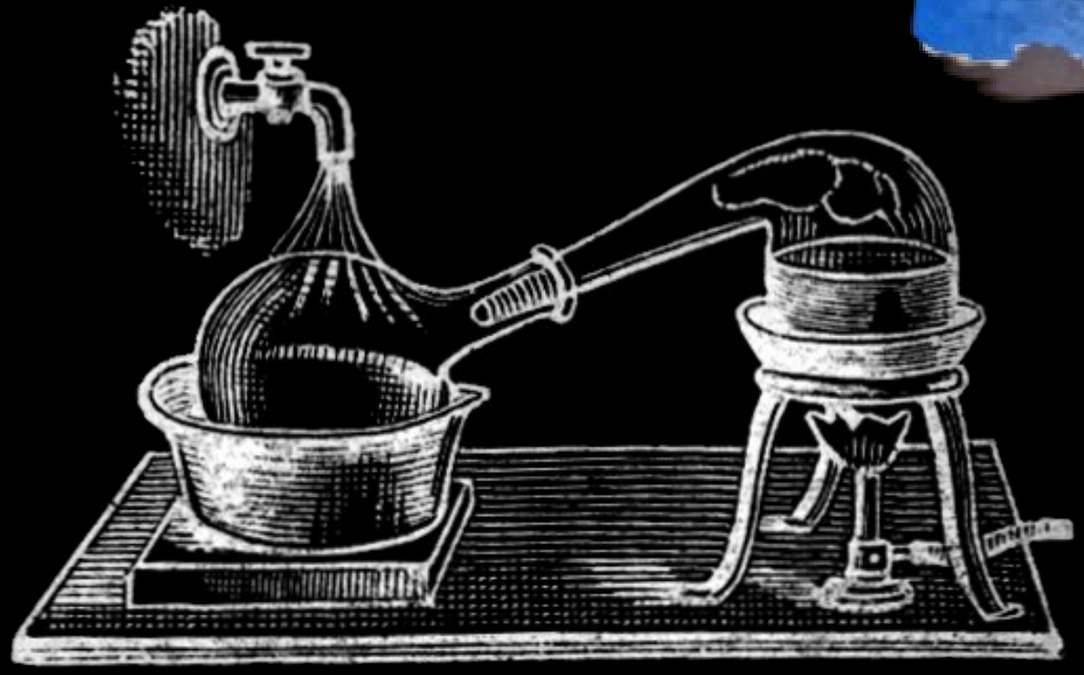
Microdistilleries



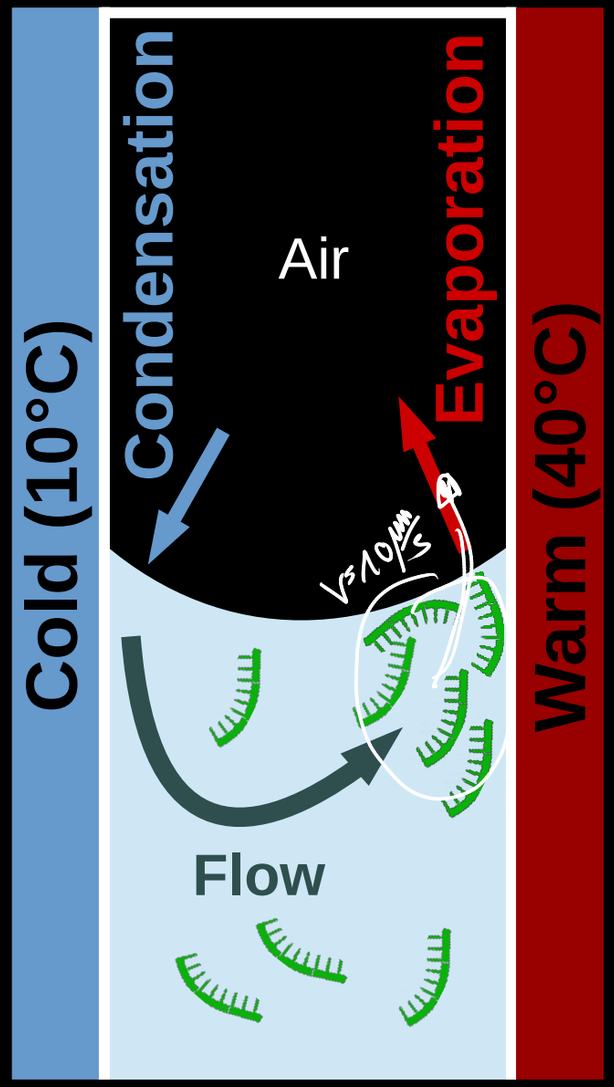


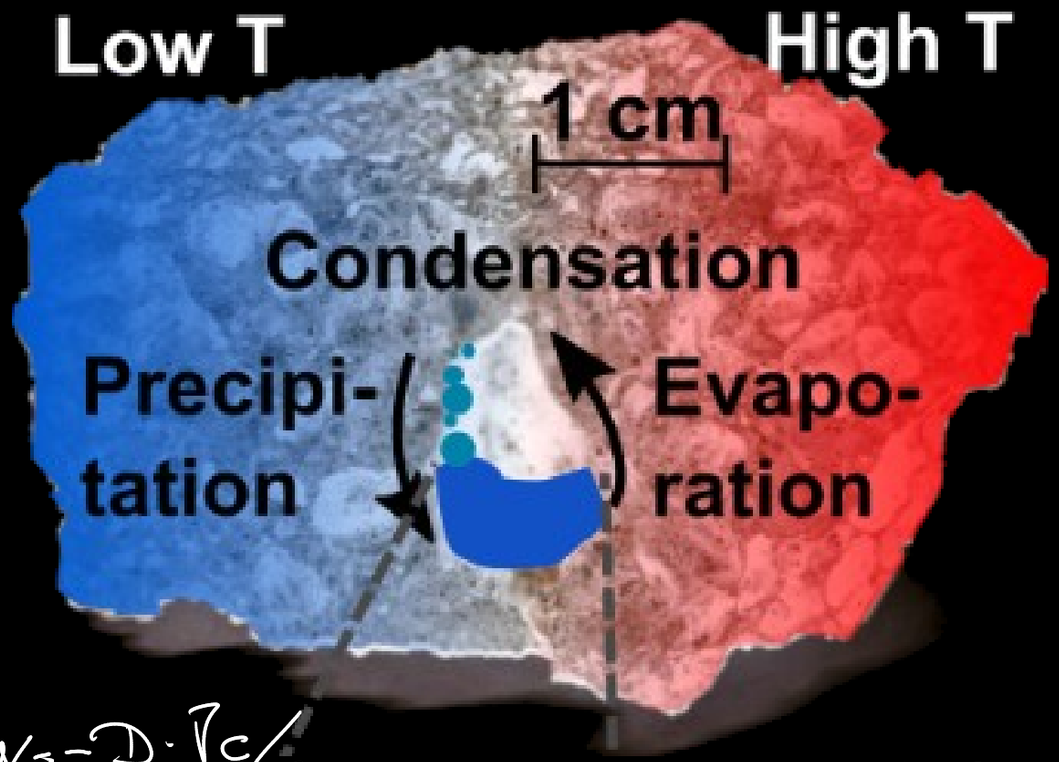
Microdistilleries





Microdistilleries: Accumulation





$v = v_s - D \cdot \nabla c / c$

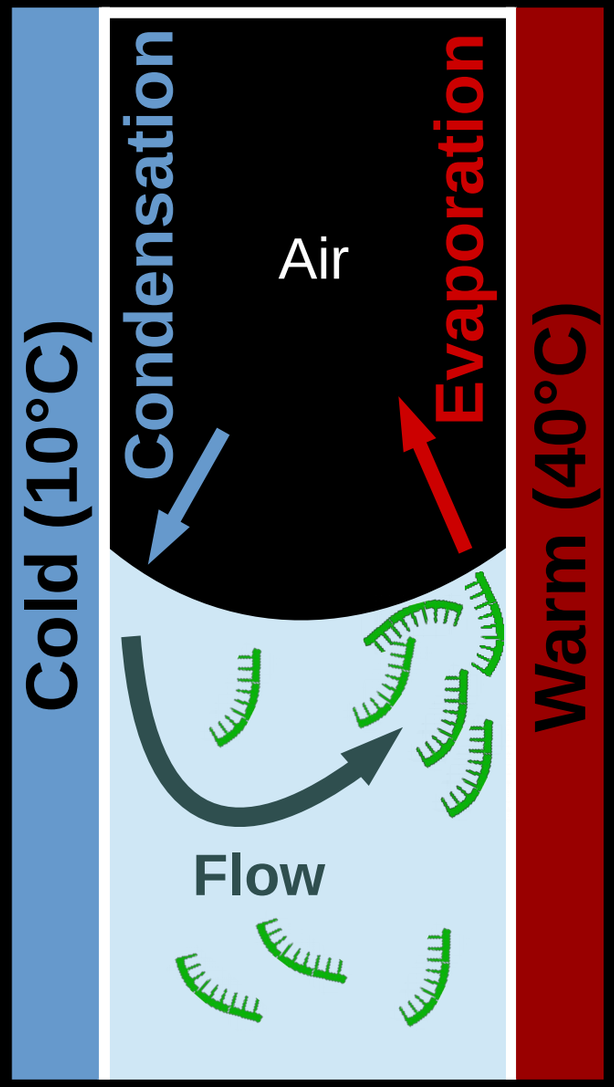
Air 10µm/s

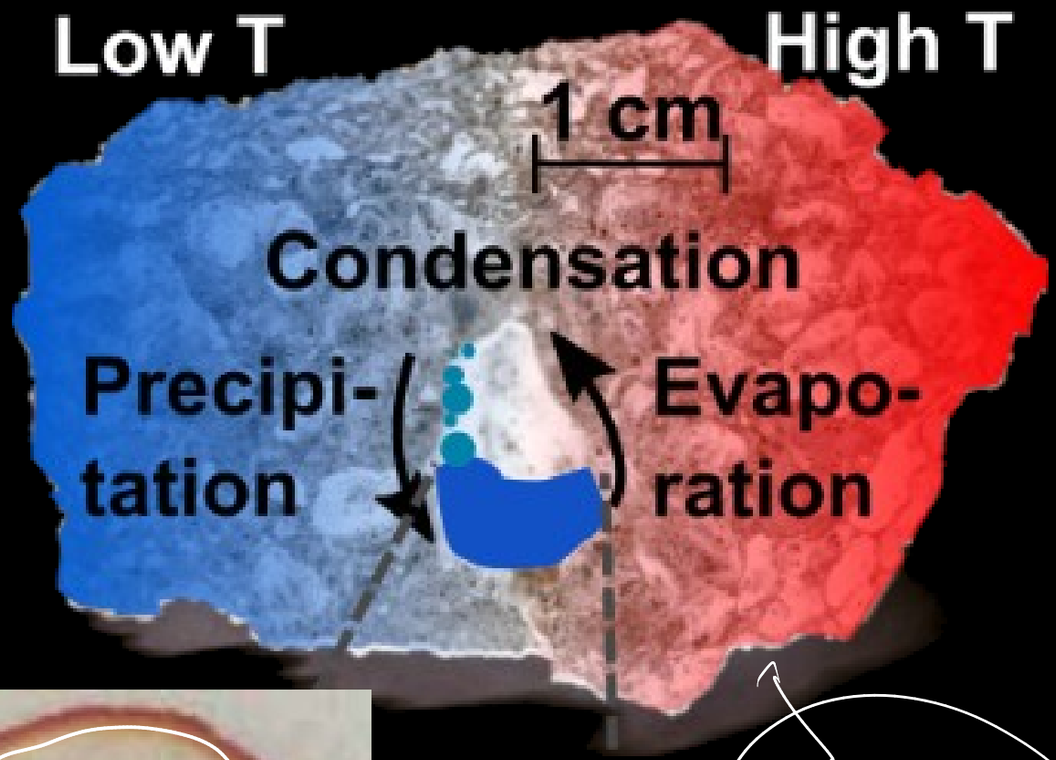
$v_s = -D \cdot \frac{\nabla c}{c}$

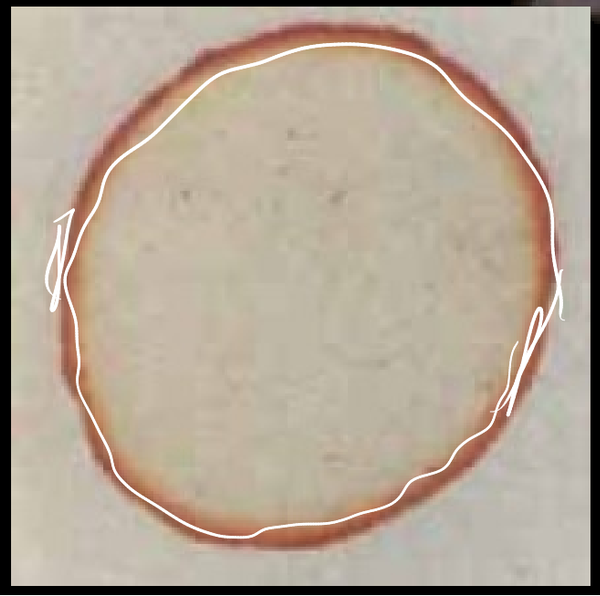
$v = -D \cdot \nabla \ln c$

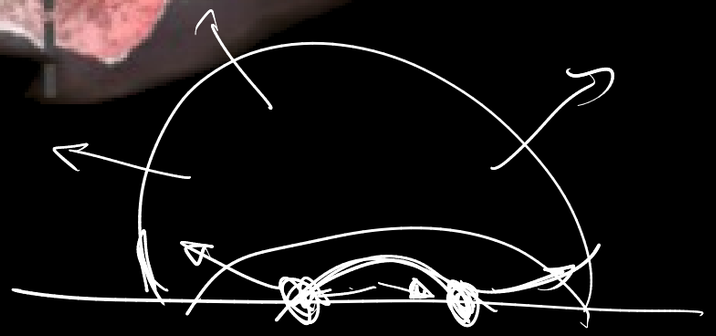
$j = v \cdot c$

Microdistilleries: Accumulation



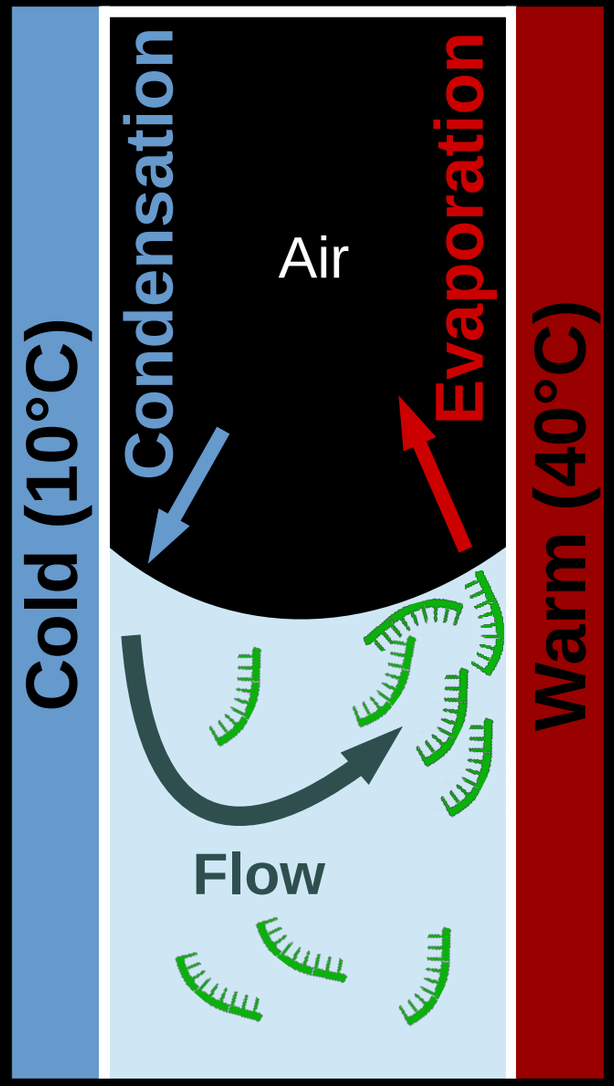


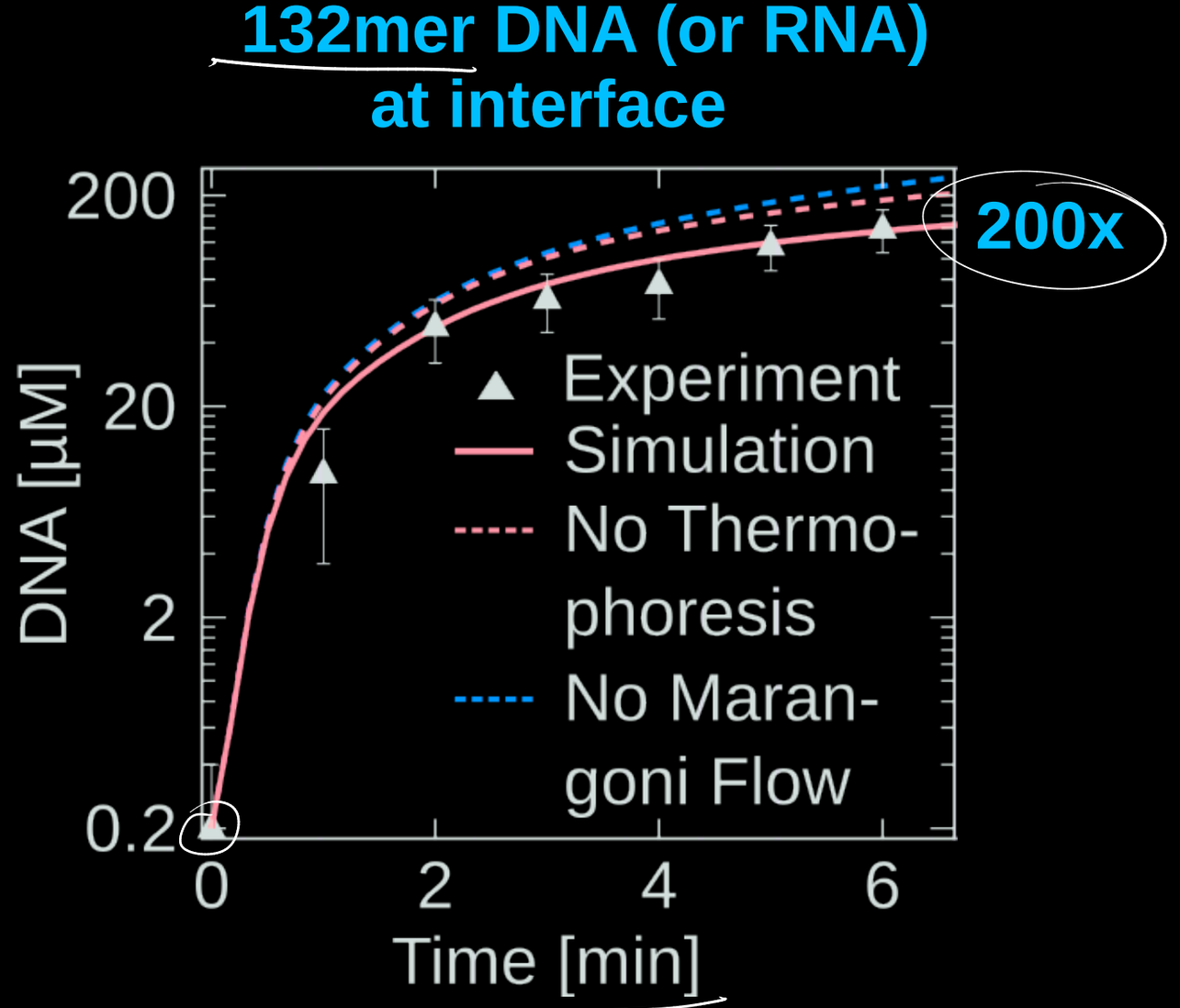




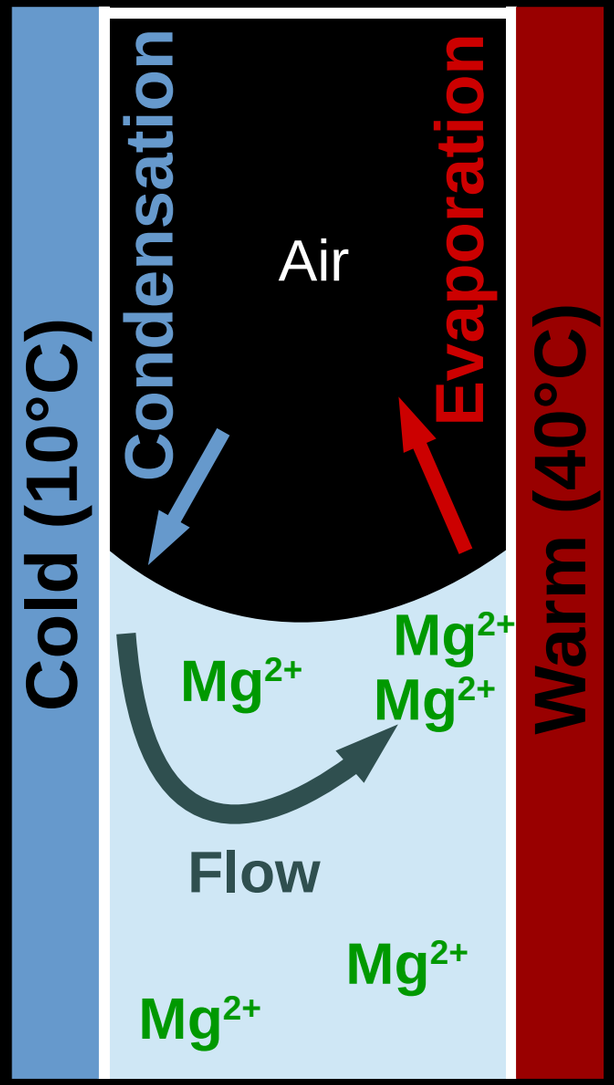
Continuous
Coffee ring effect

Microdistilleries: Accumulation

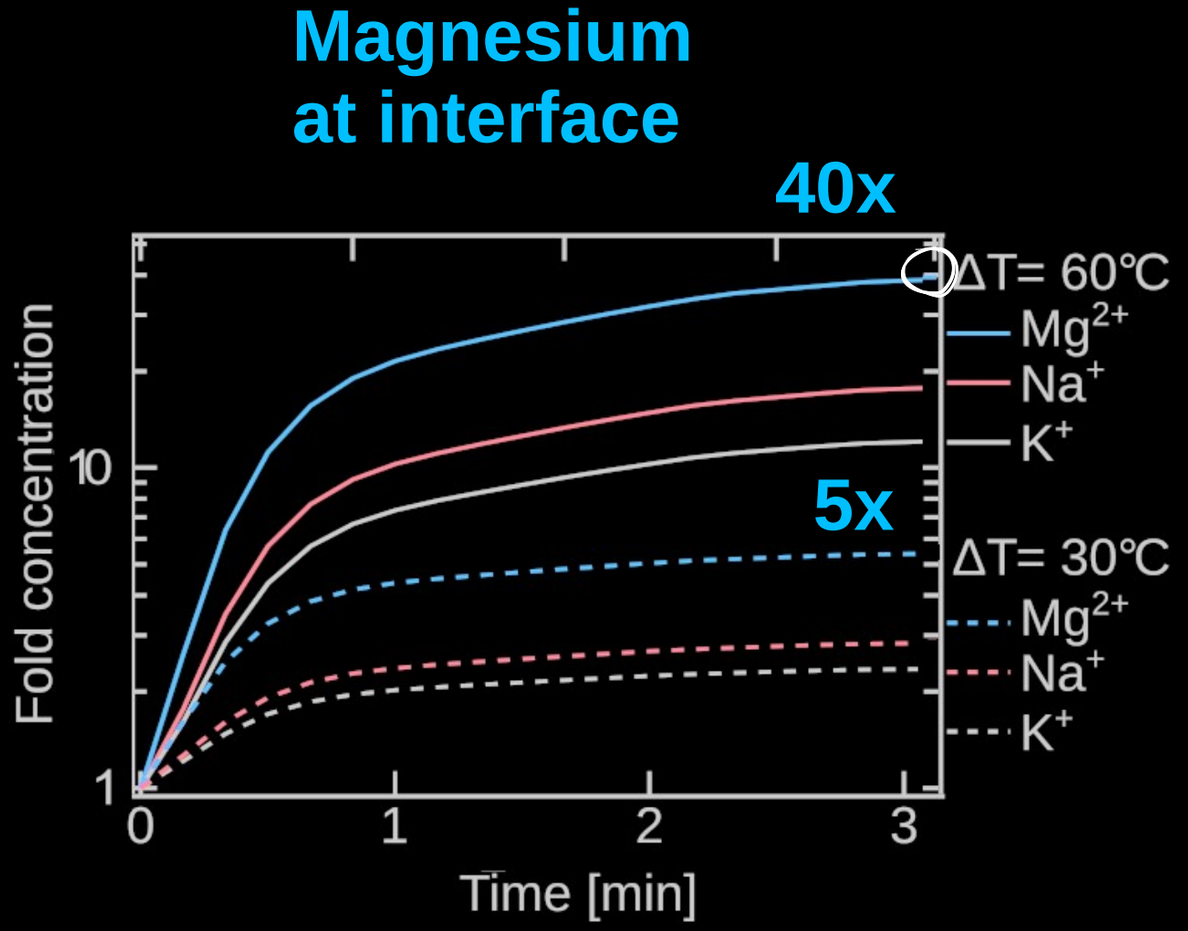


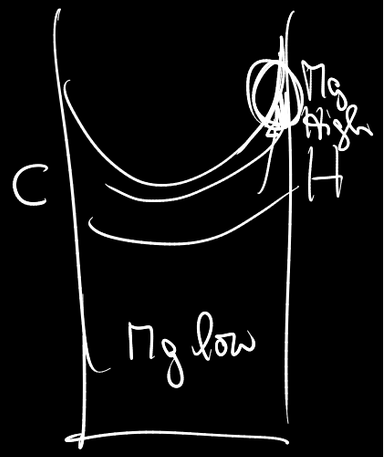


Microdistilleries: Accumulation



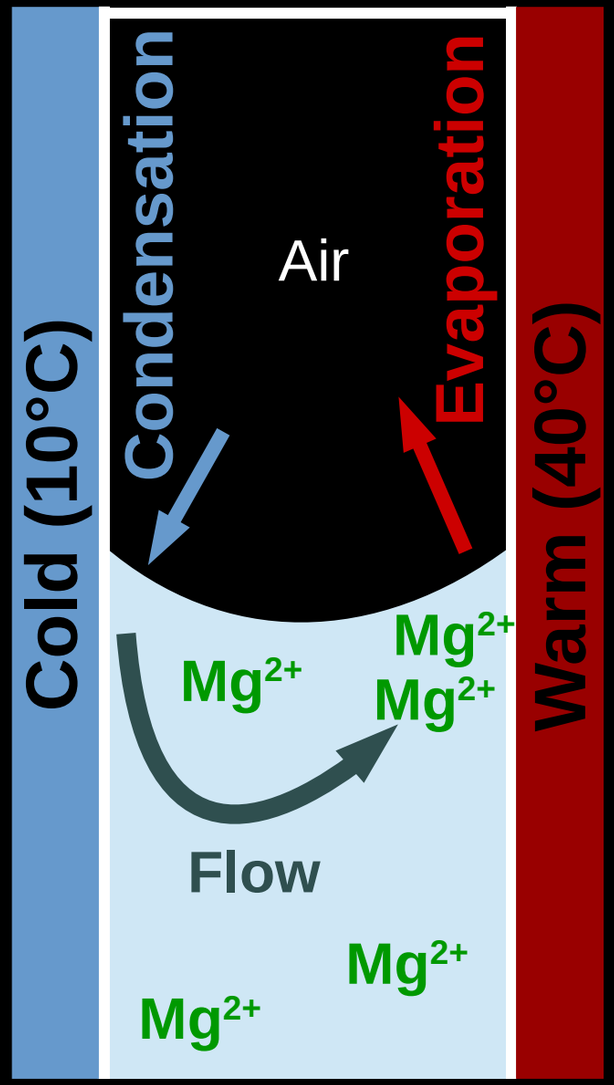
250µm





Nature Chemistry, 2019

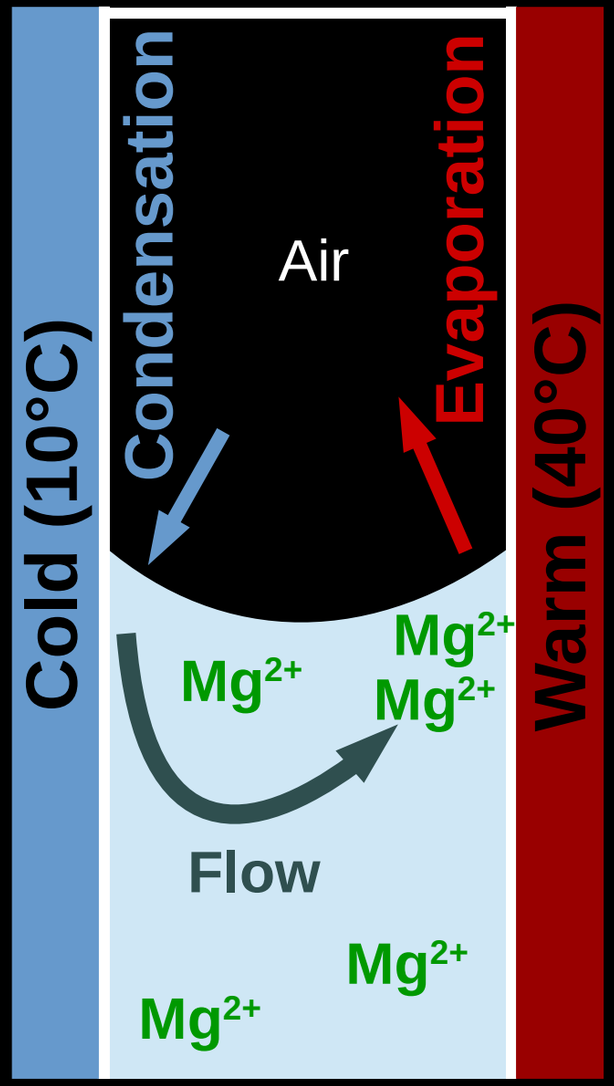
Enhanced RNA Catalysis ?



0.1µM Ribozyme
0.5µM Substrate
0.4mM $MgCl_2$

Nature Chemistry, 2019

Enhanced RNA Catalysis



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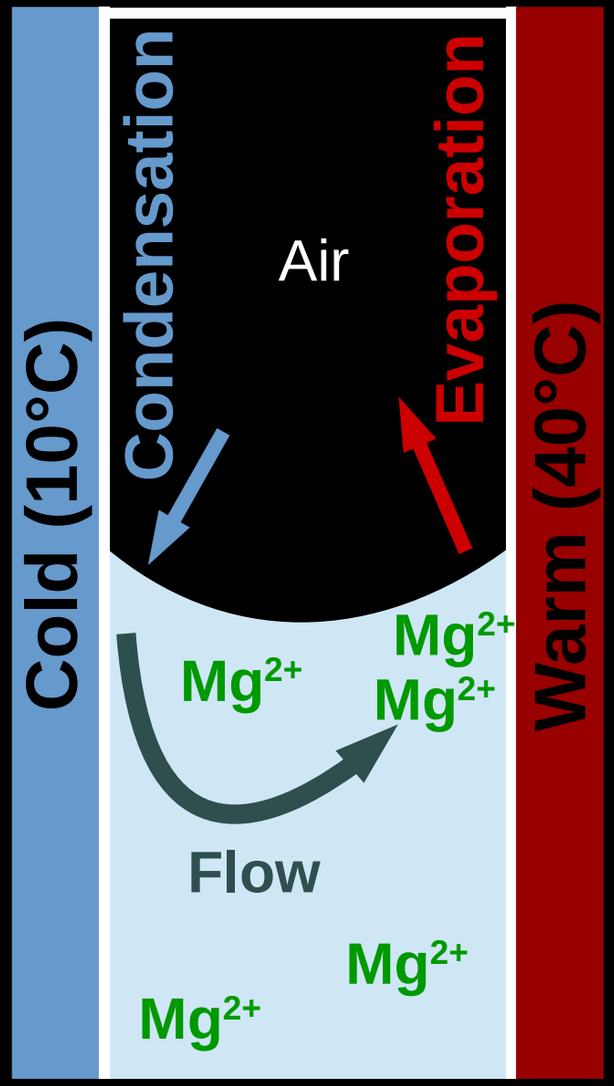
0.5µM Substrate
0.4mM $MgCl_2$

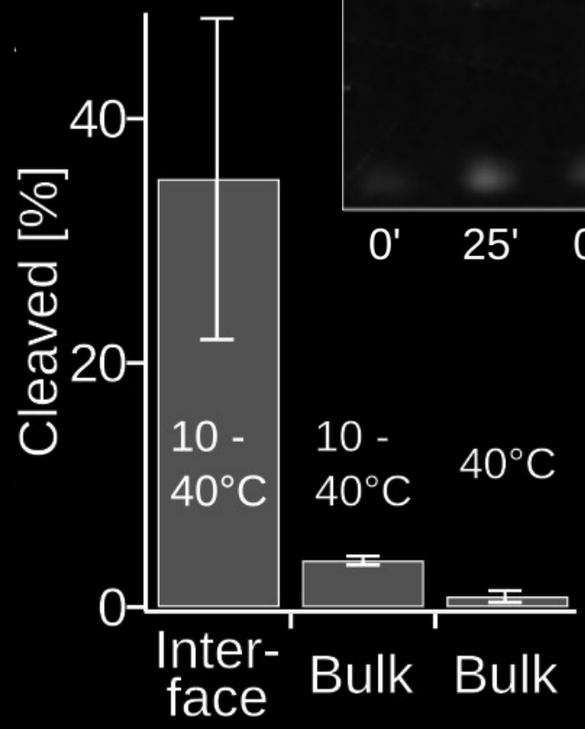
Nature Chemistry, 2019

Enhanced RNA Catalysis



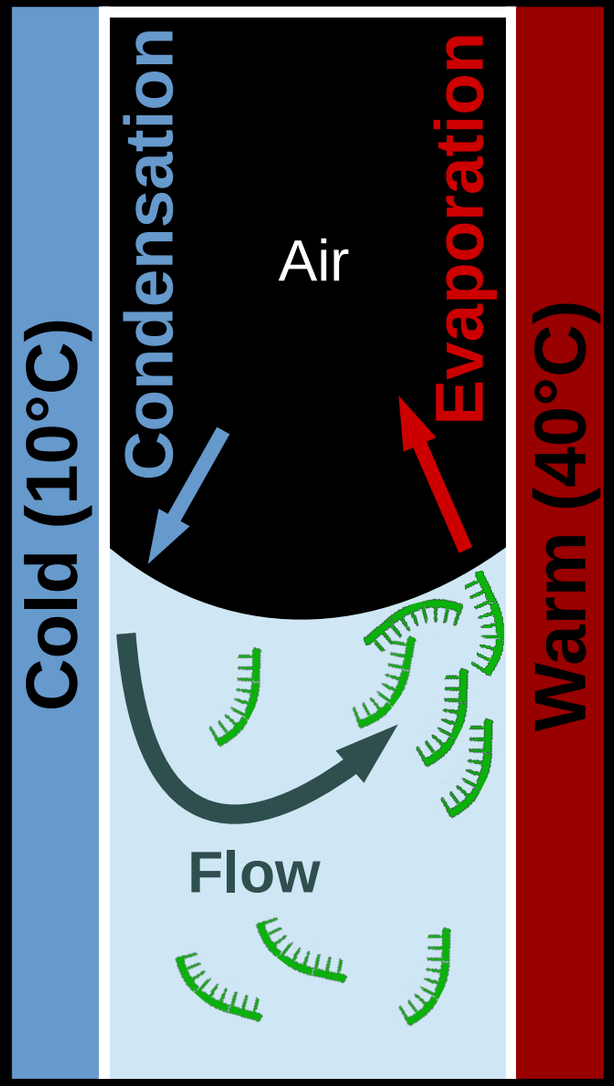
250µm

0.1µM Ribozyme
0.5µM Substrate
0.4mM $MgCl_2$

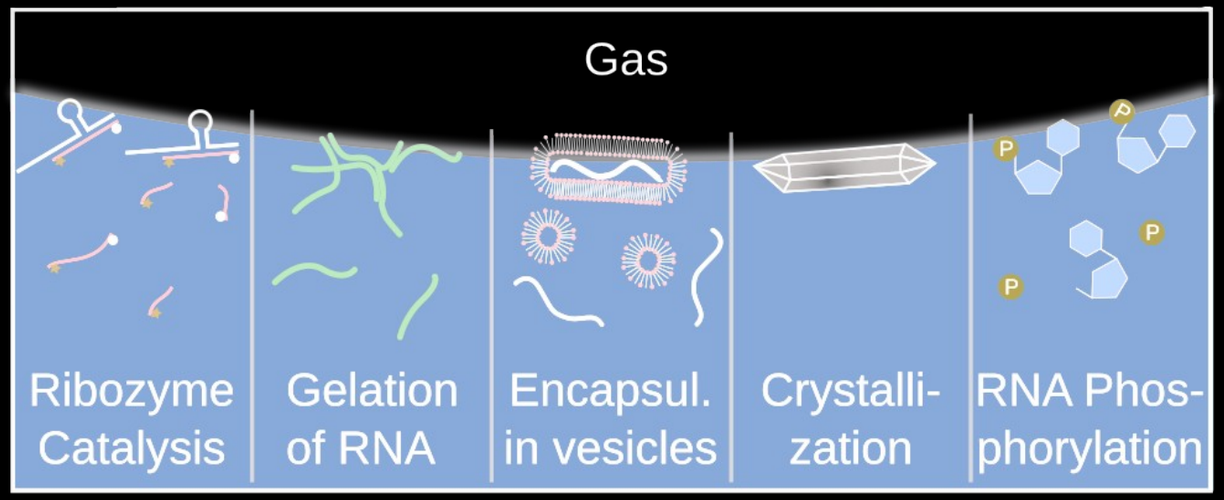


Nature Chemistry, 2019

Microdistillery

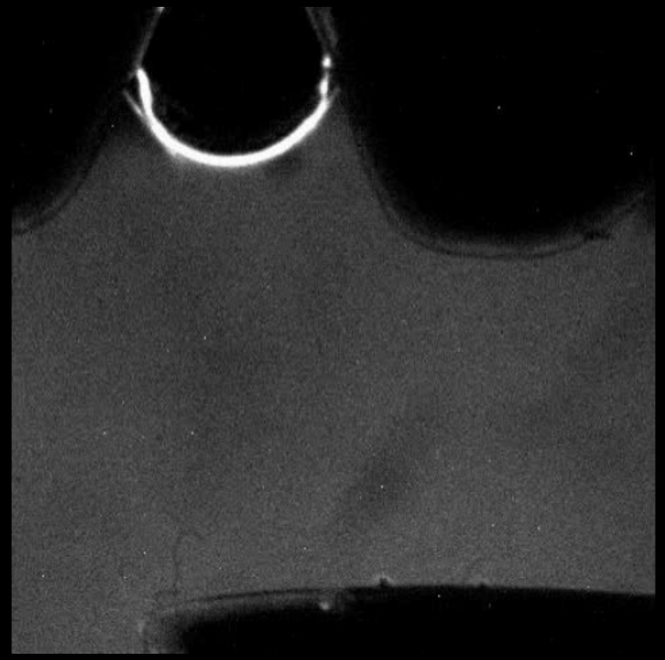


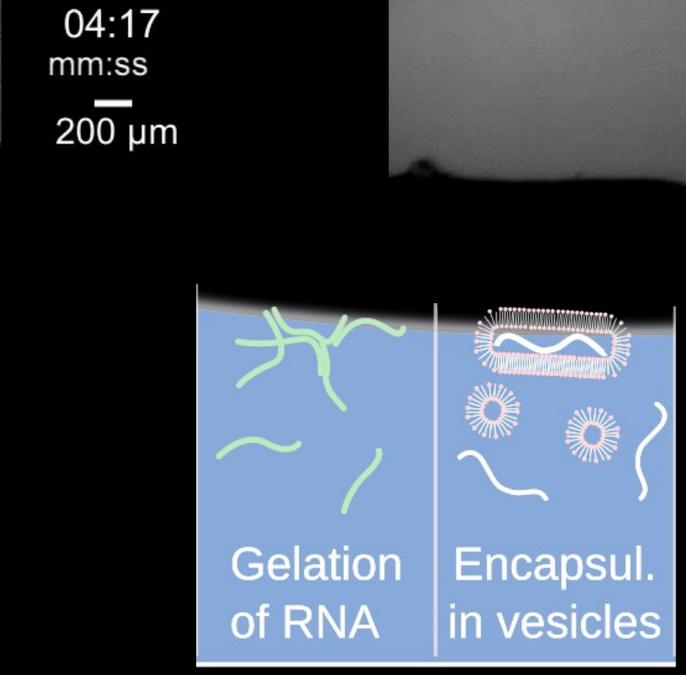
- 1000x Accumulation of DNA
- Dry-wet cycles for Phosphorylation
- **Surface enhanced catalysis**
- Incorporation into Vesicles
- Driven crystallization at air interface
- DNA/RNA - Gelation at interface

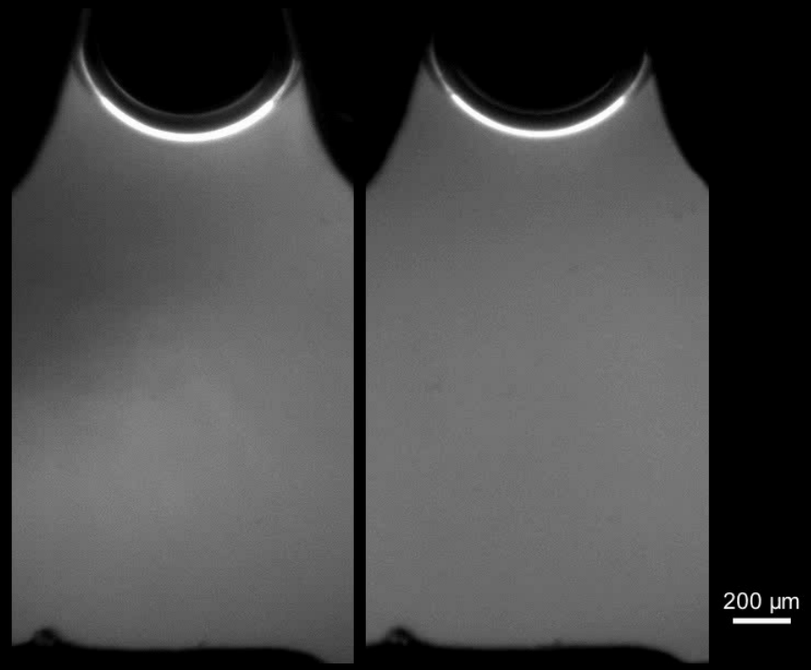


Nature Chemistry, 2019

Nonequilibrium gelation and vesiculation

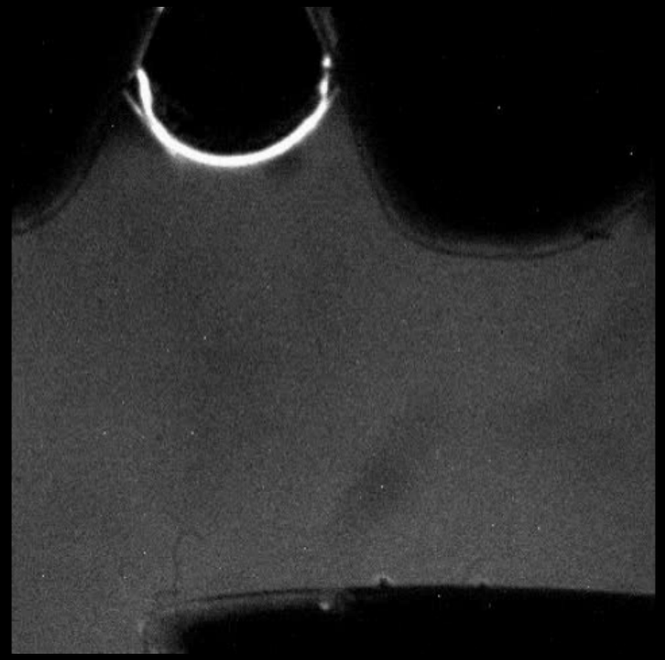


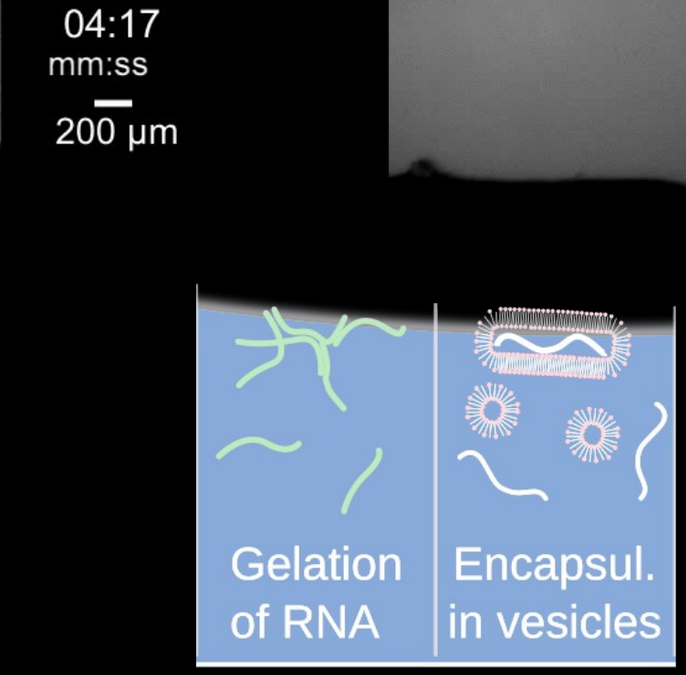


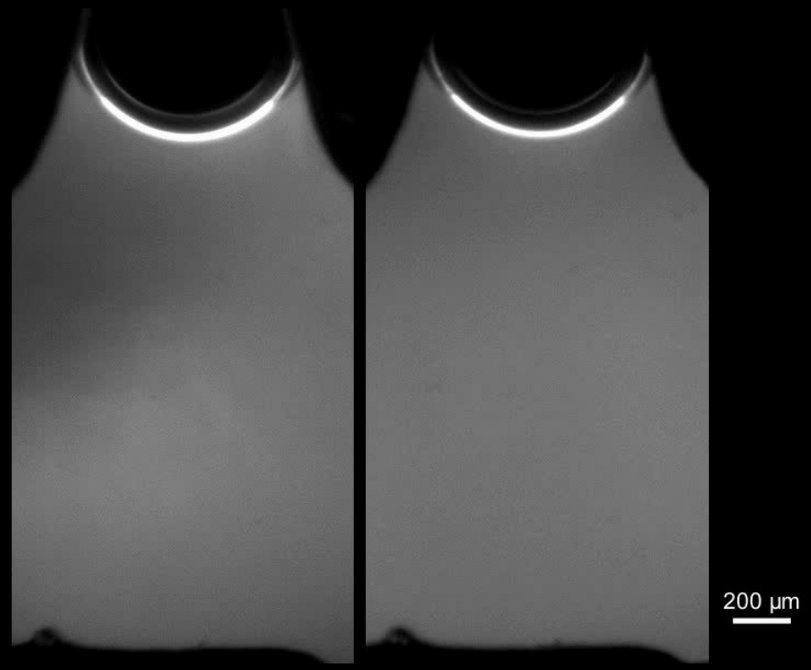


Nature Chemistry, 2019

Nonequilibrium gelation and vesiculation

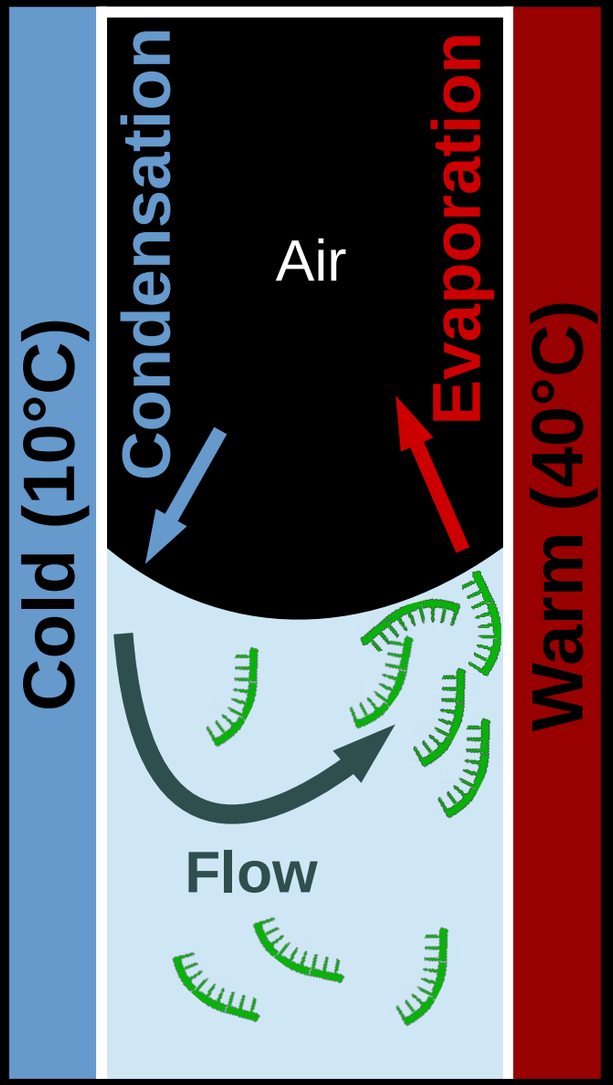






Nature Chemistry, 2019

Microdistillery



- 1000x Accumulation of DNA
- Dry-wet cycles for Phosphorylation
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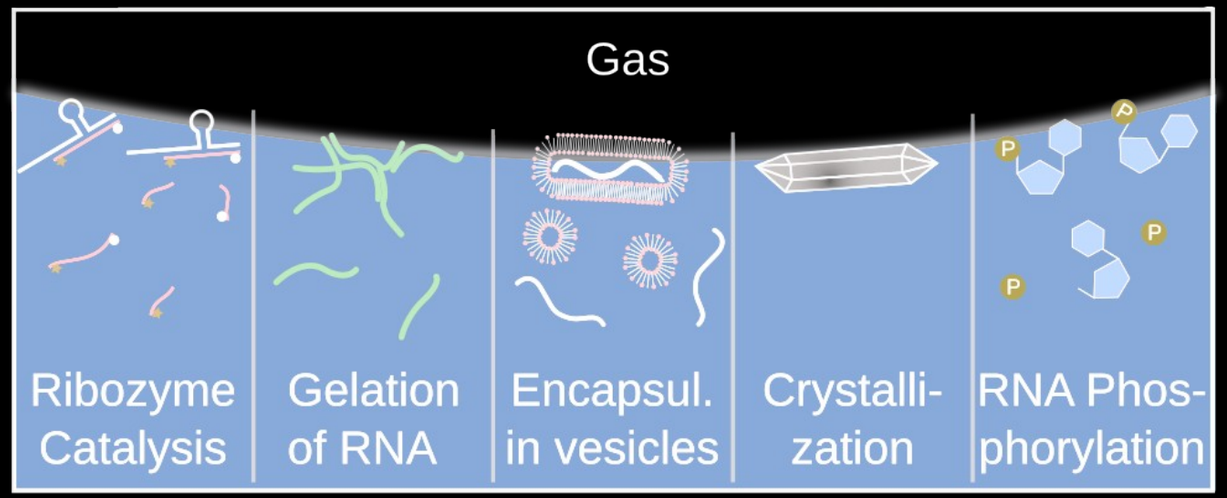
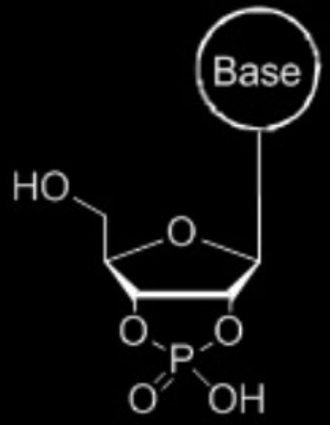
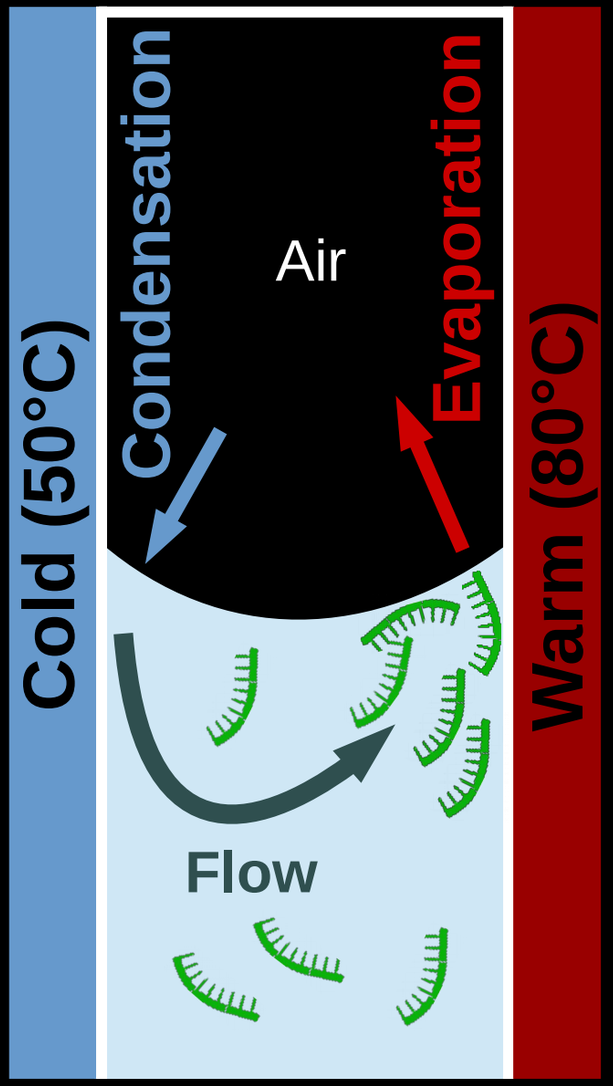


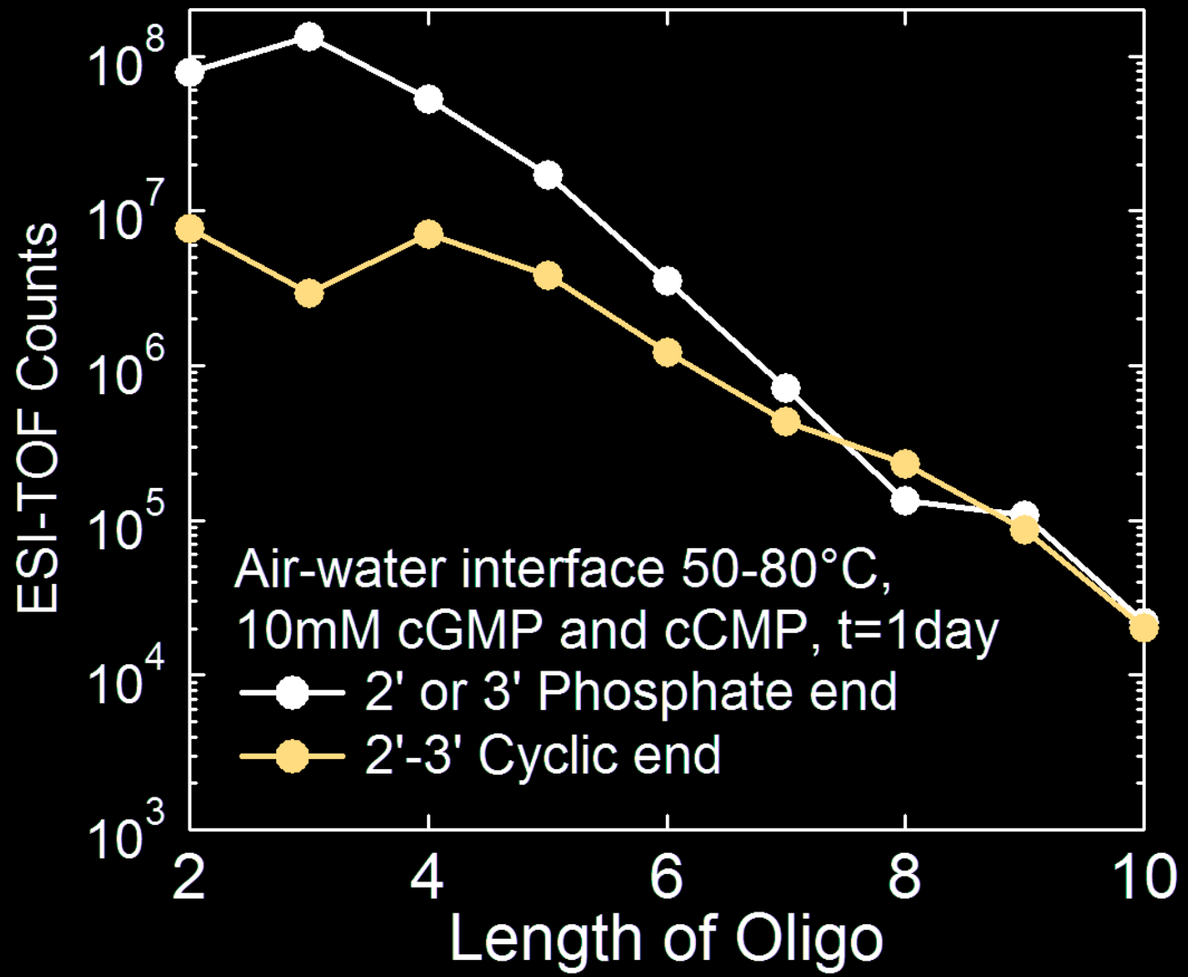
Polymerization of RNA



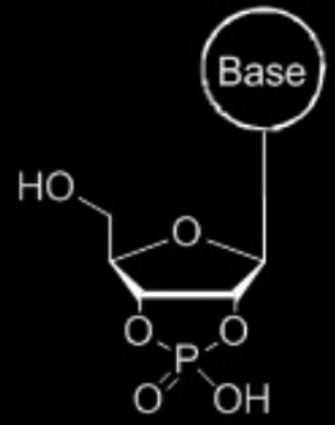
Nature Chemistry, 2019

Microdistillery



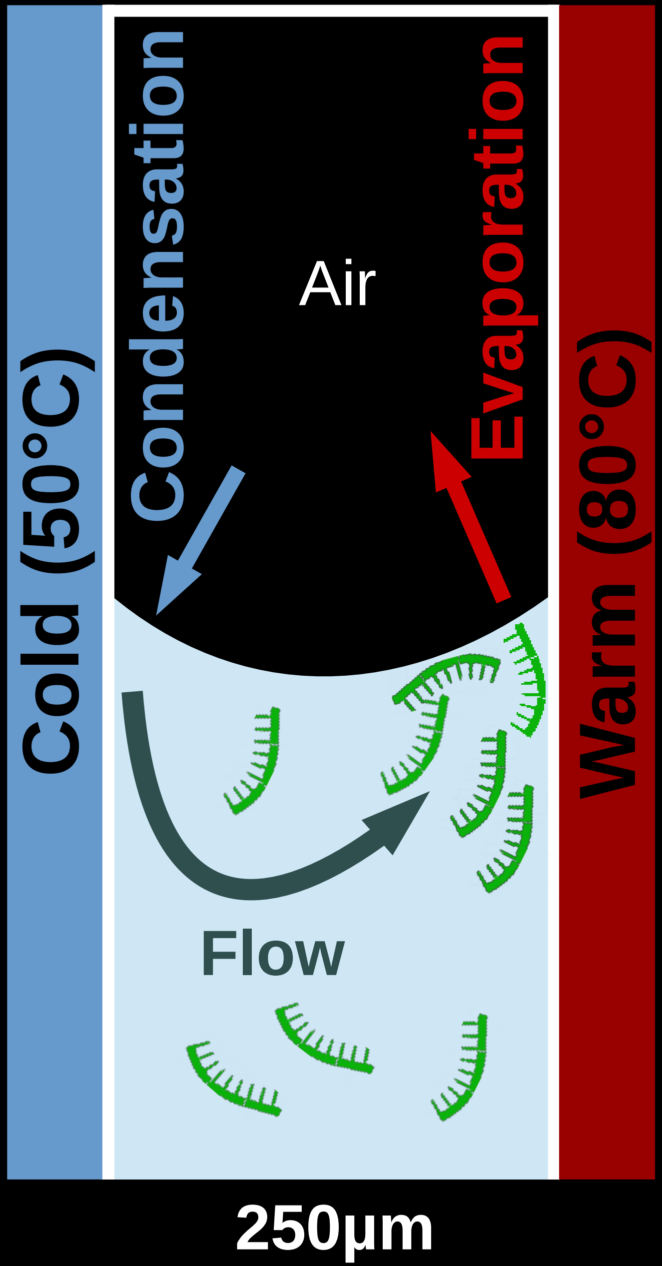


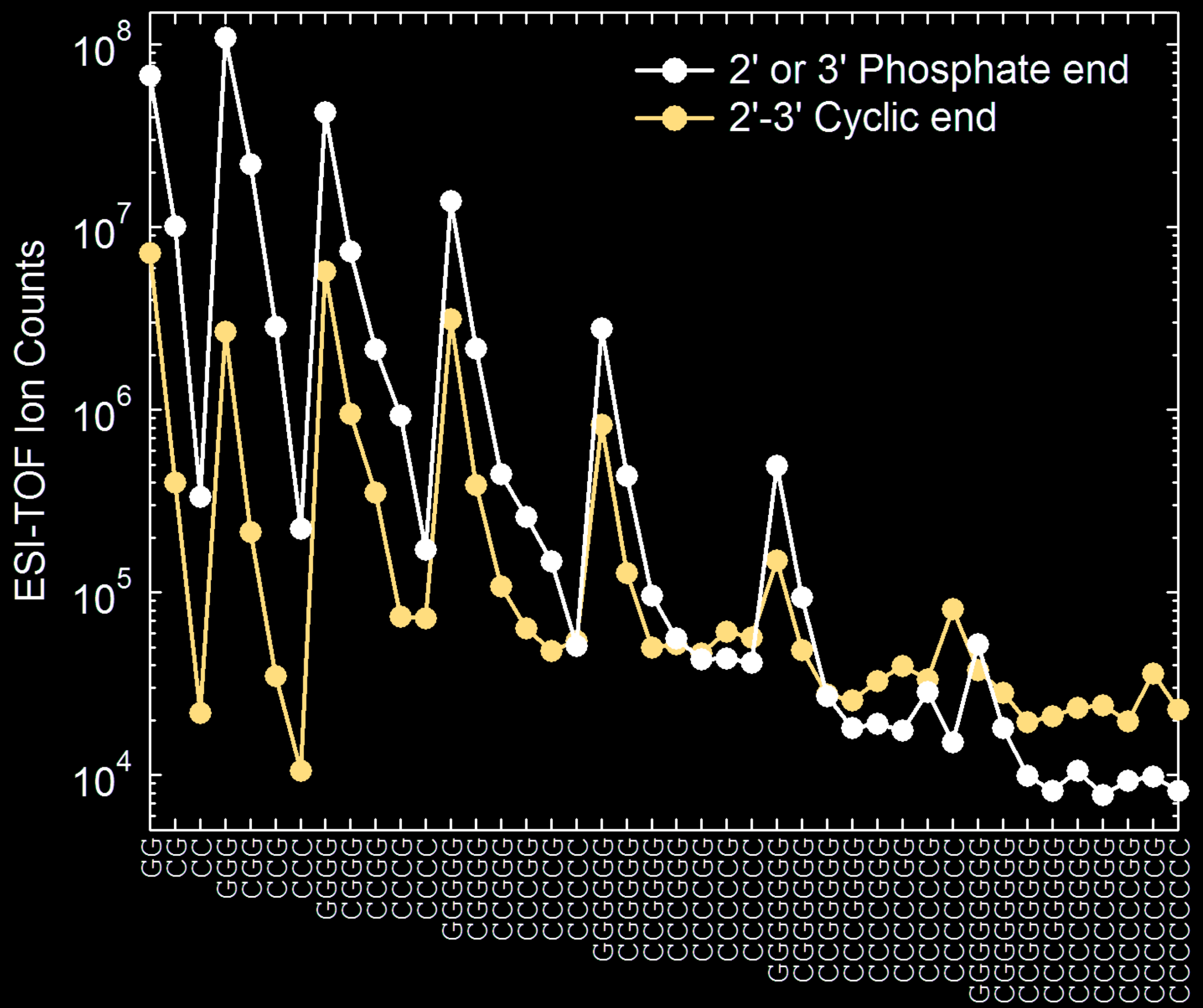
Polymerization of RNA



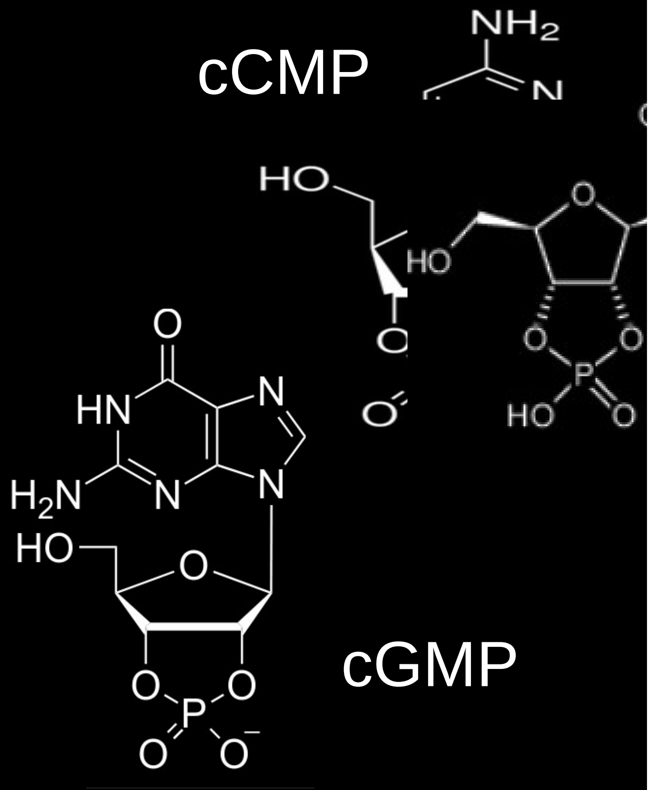
Polymerization of 2’-3’cG/CMP at Air-Water, pH8-10, 1day

Microdistillery

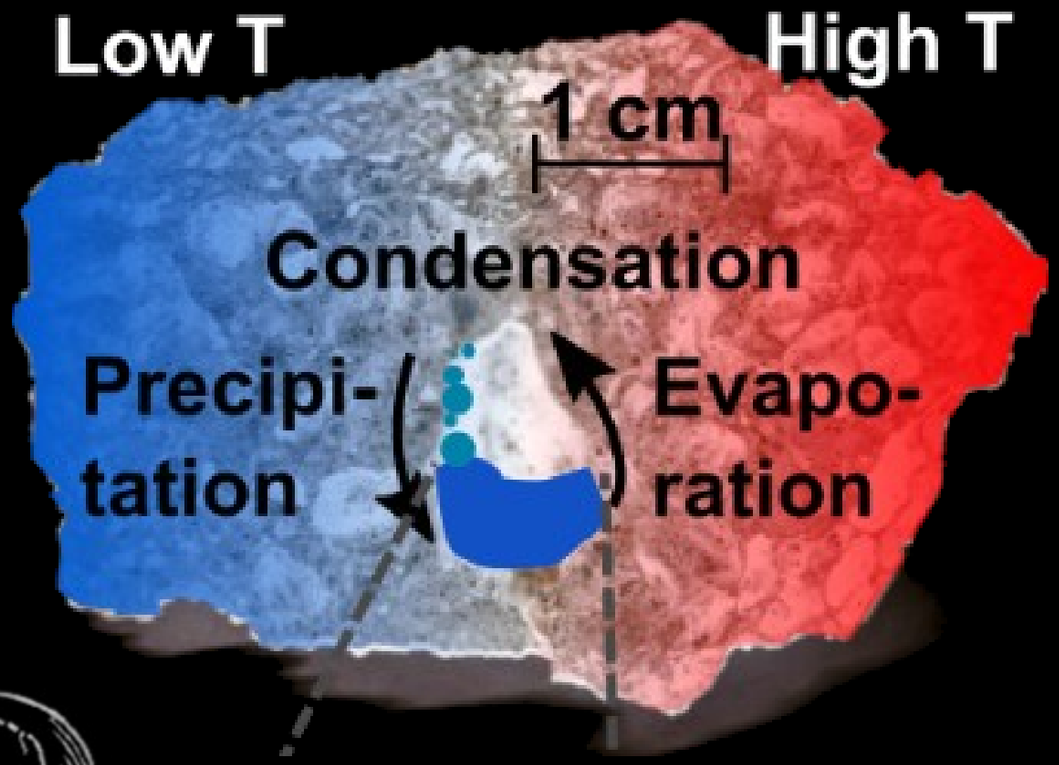


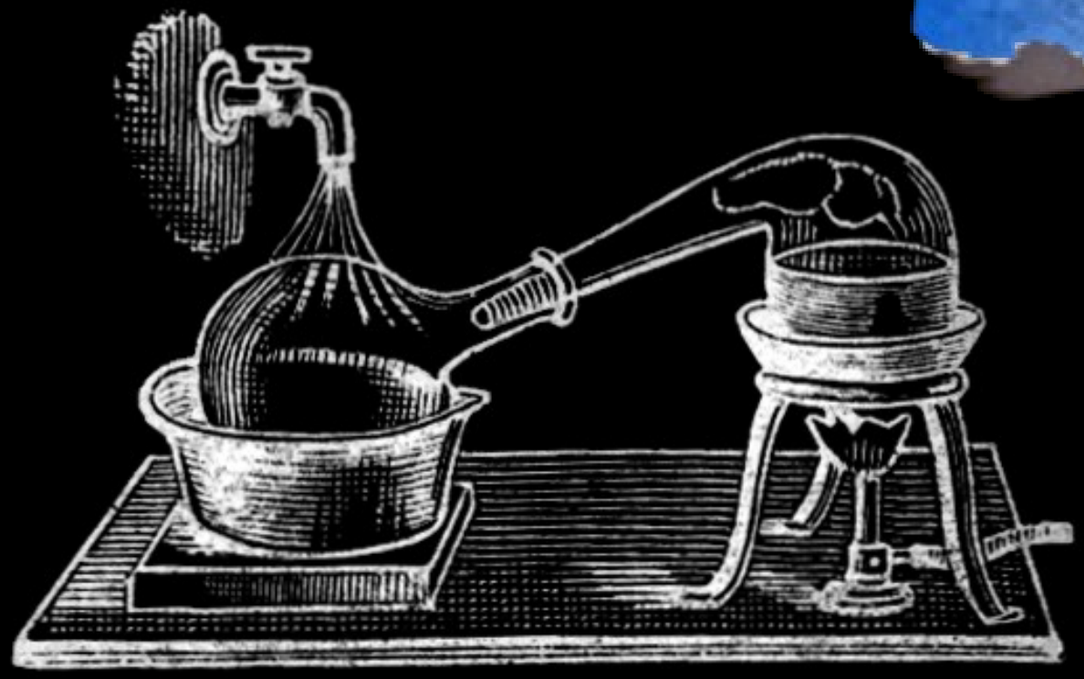


Polymerization of RNA

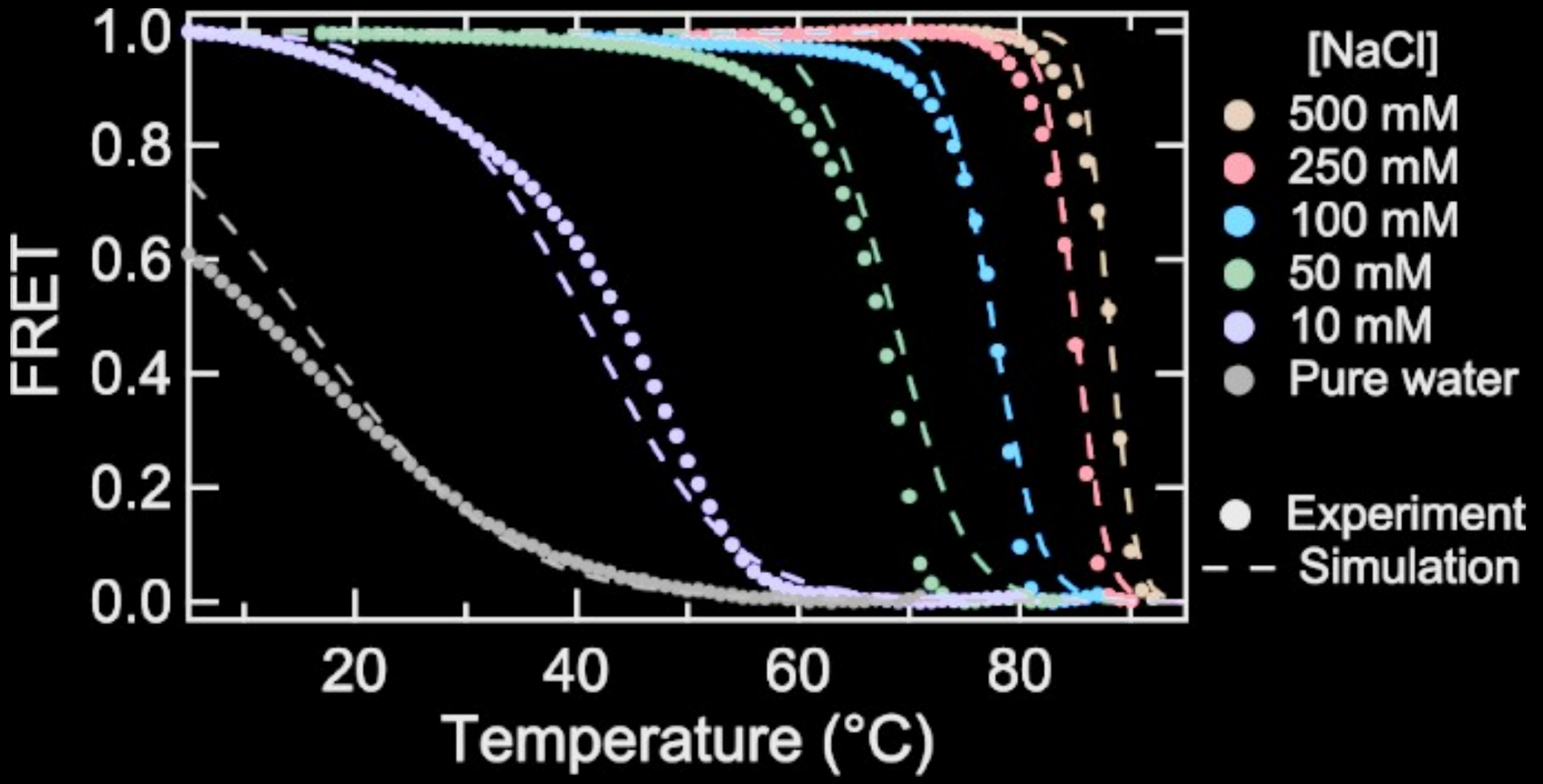


Microdistillery: Pure water





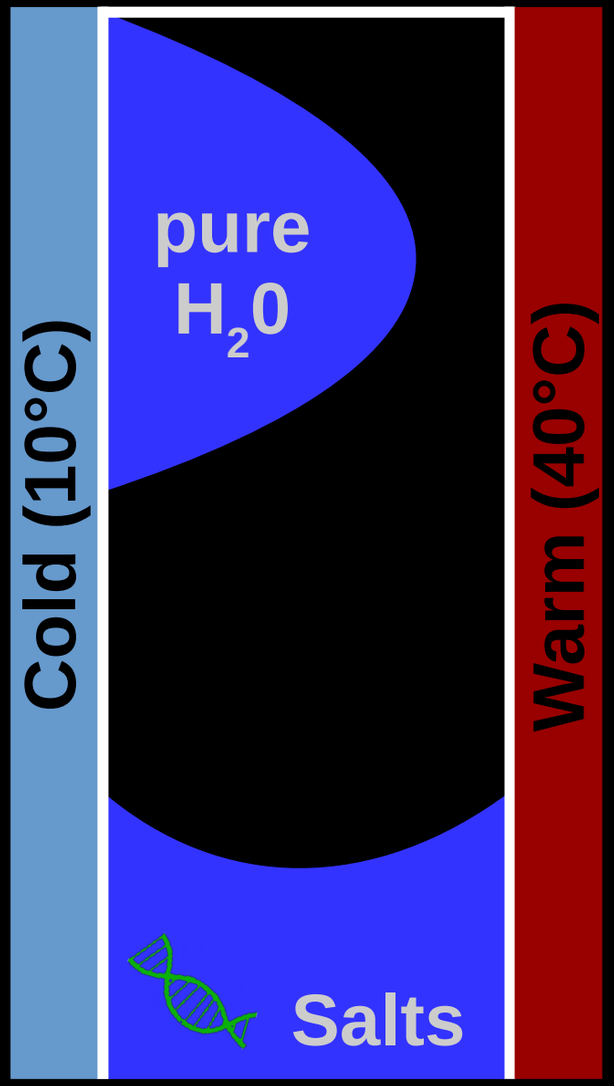
Microdistillery: Pure water

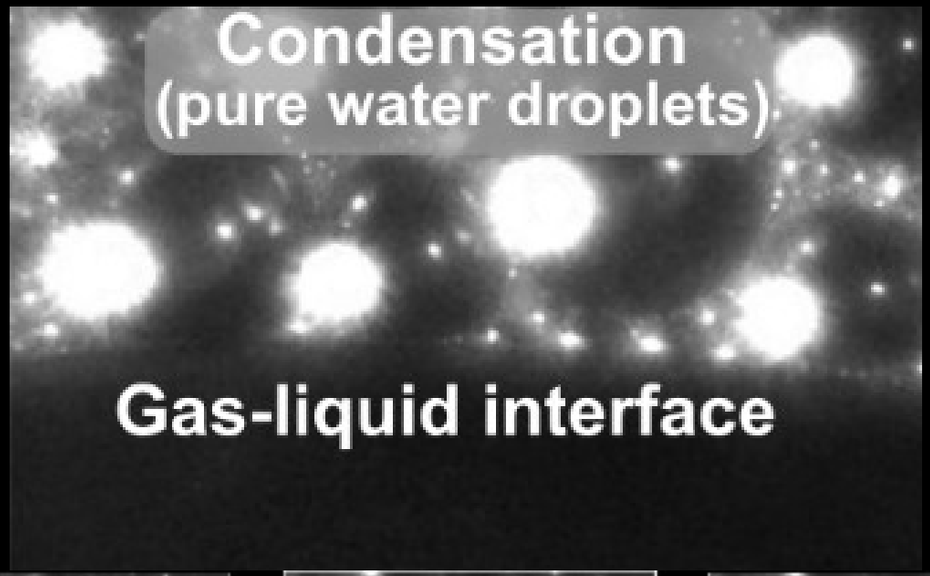


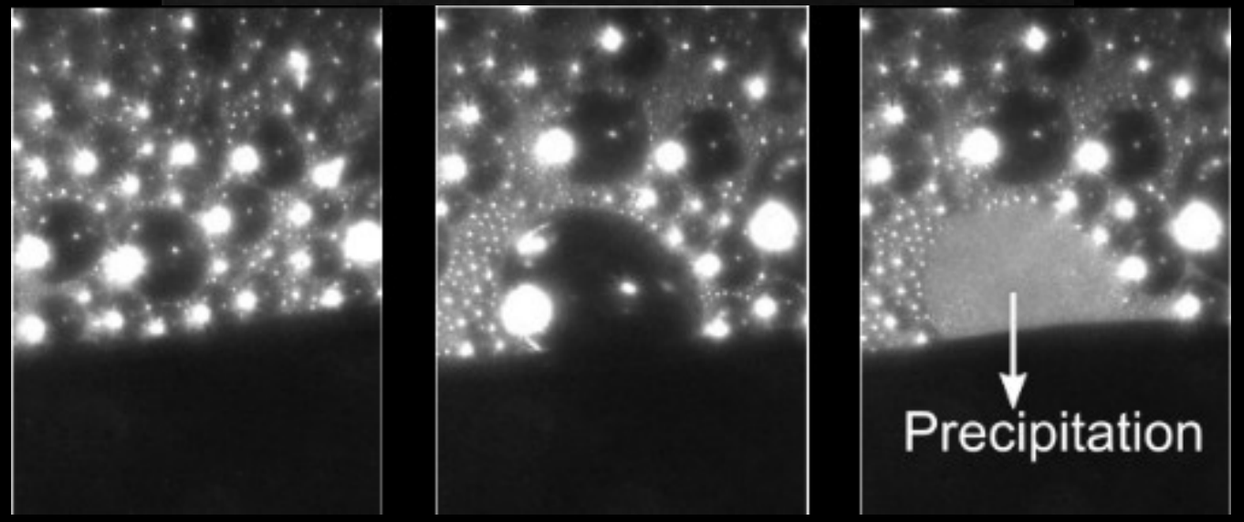
51bp DNA (or RNA)
no $MgCl_2$

Angewandte, 2019

Microdistillery: salt oscillations

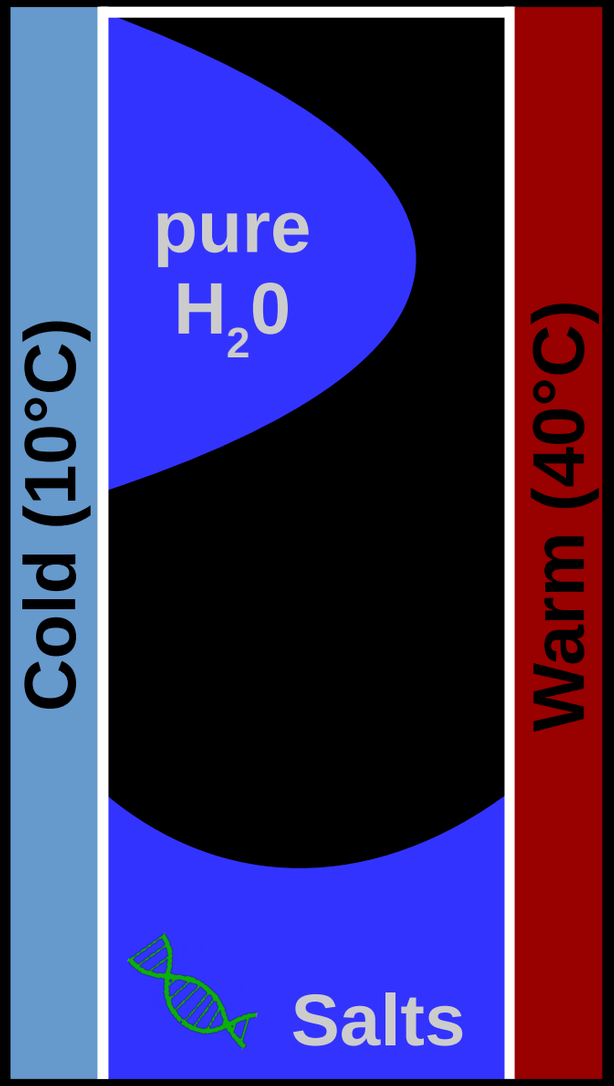


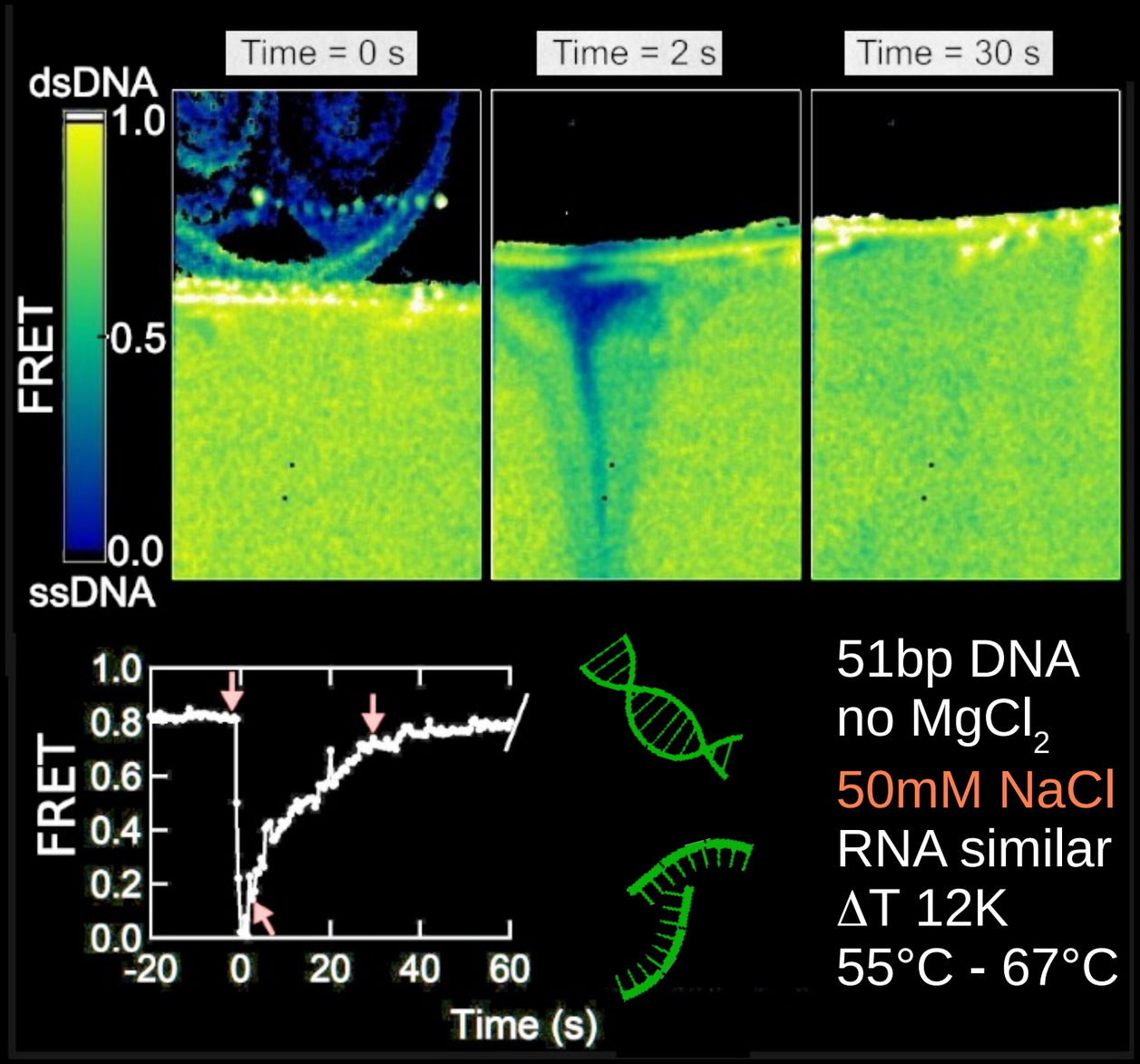




Angewandte, 2019

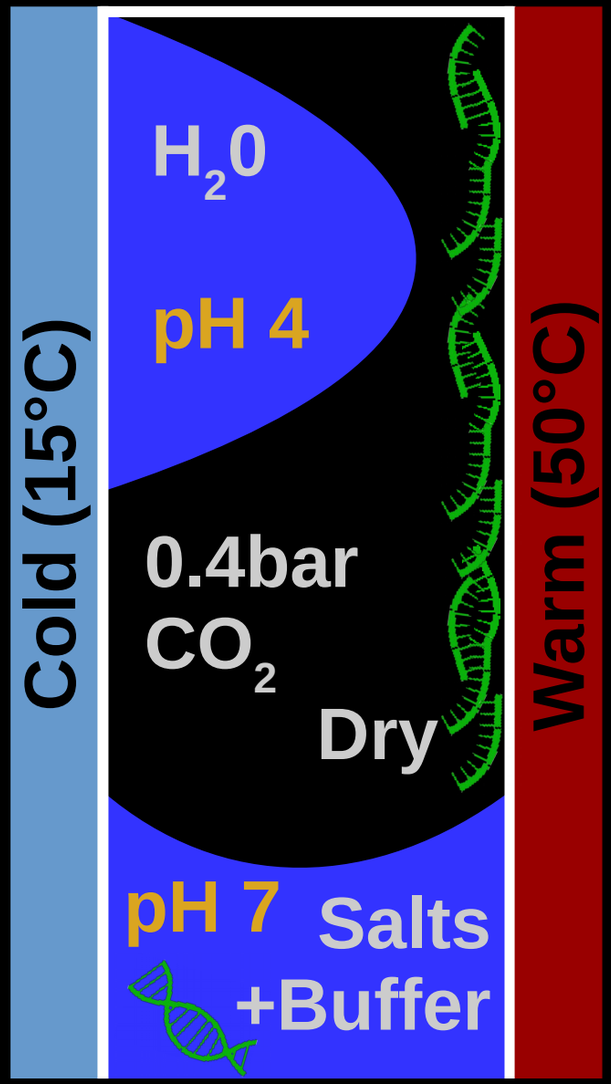
Microdistillery: salt oscillations





Angewandte, 2019

pH Oscillation in droplets with CO_2

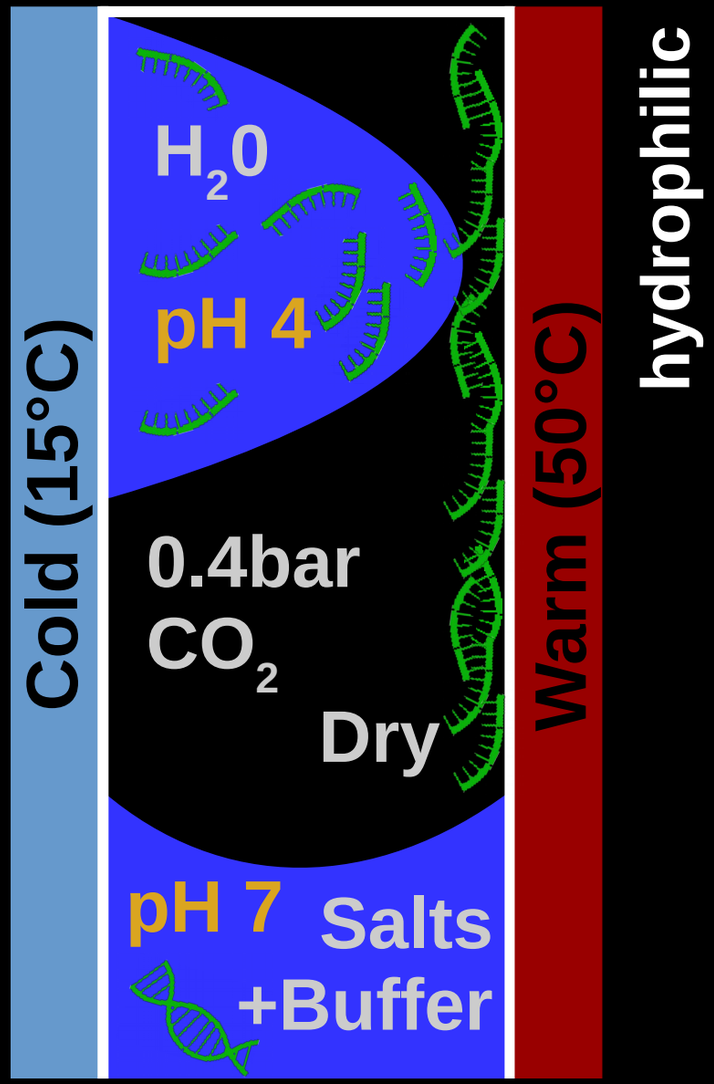


unpublished

24bp RNA (4 bases), Tm=74°C
50mM TRIS, pH 7.4 in bulk

12.5 mM $MgCl_2$

pH Oscillation in droplets with CO_2



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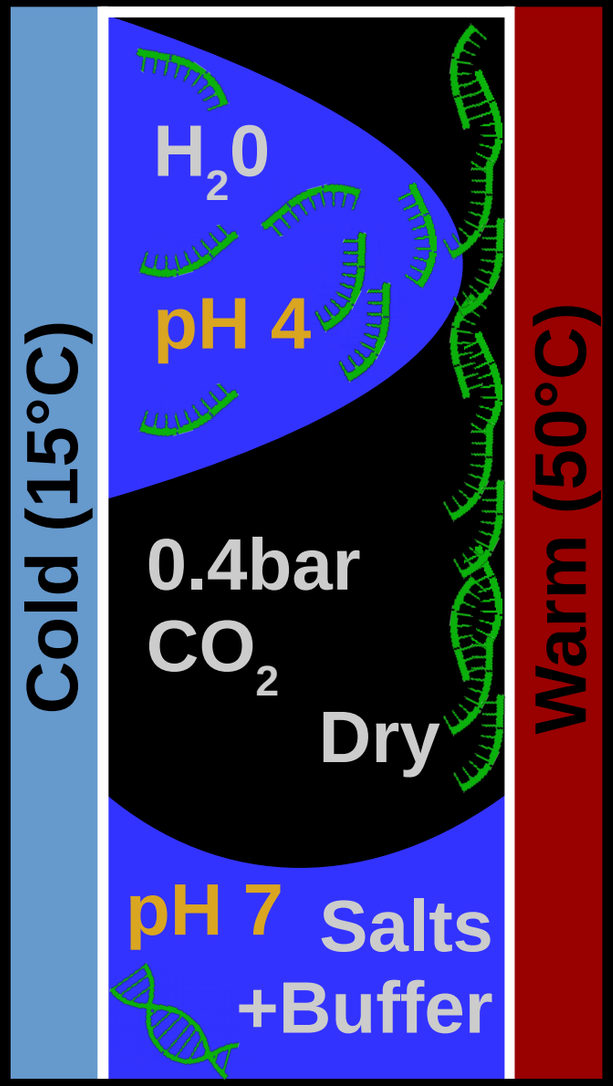
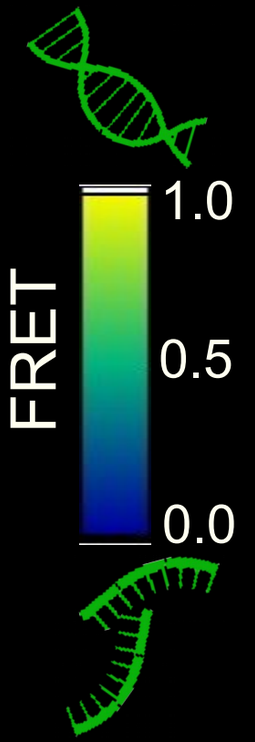
12.5 mM $MgCl_2$ (> at interface)
Temp: 15°C – 50°C (avg. 33°C)

pH Oscillation with CO_2



hydrophilic



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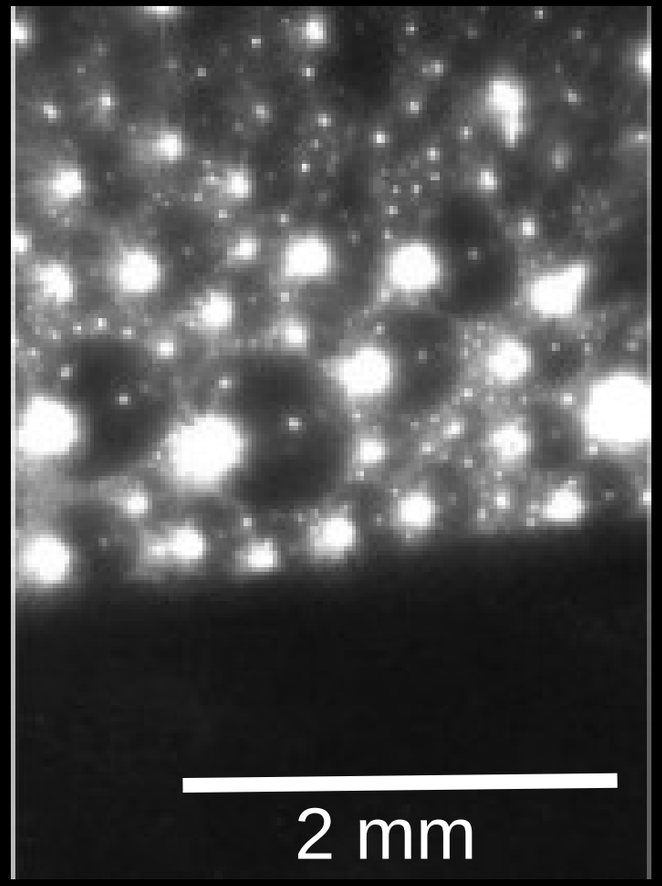
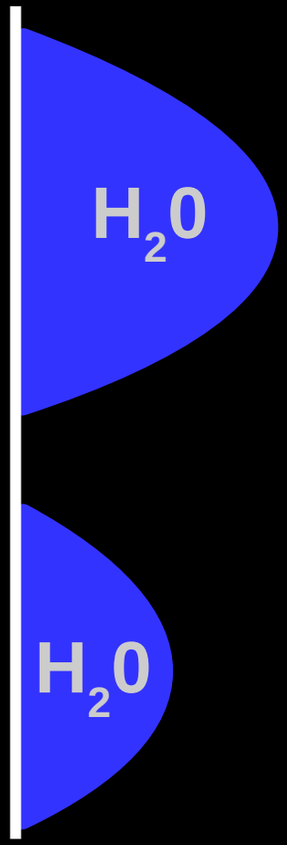
Temp: 15°C – 50°C (avg. 33°C)

Droplet Compartmentalization

Hydrophobic

Cold
10°C

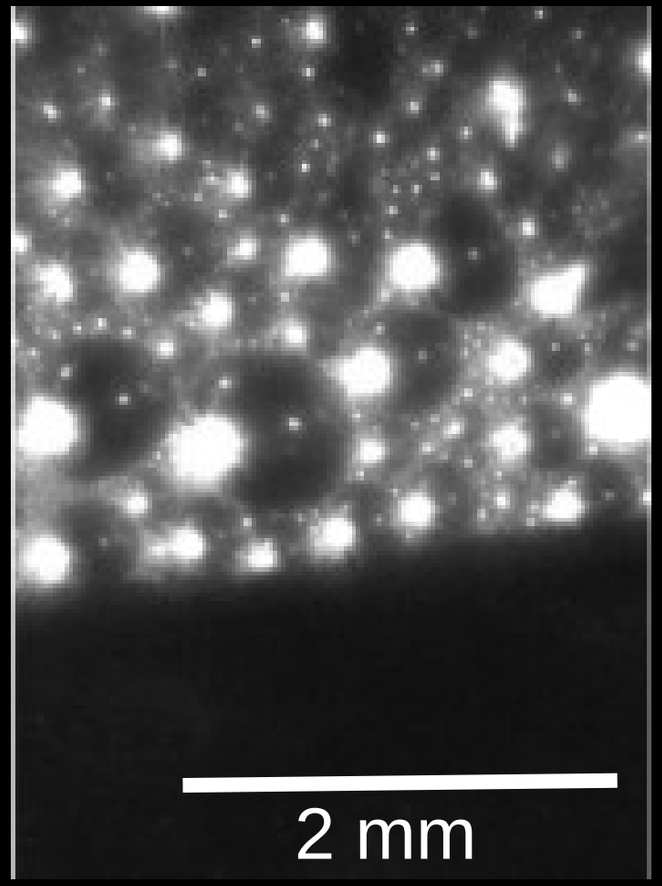


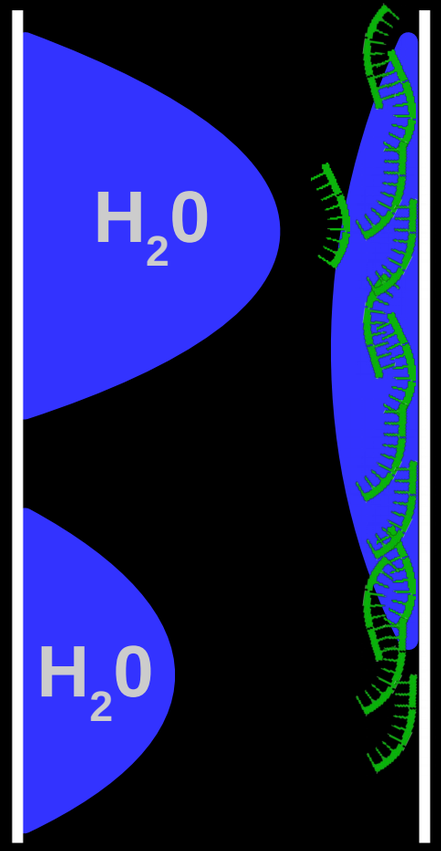


Droplet Compartmentalization

Hydrophobic

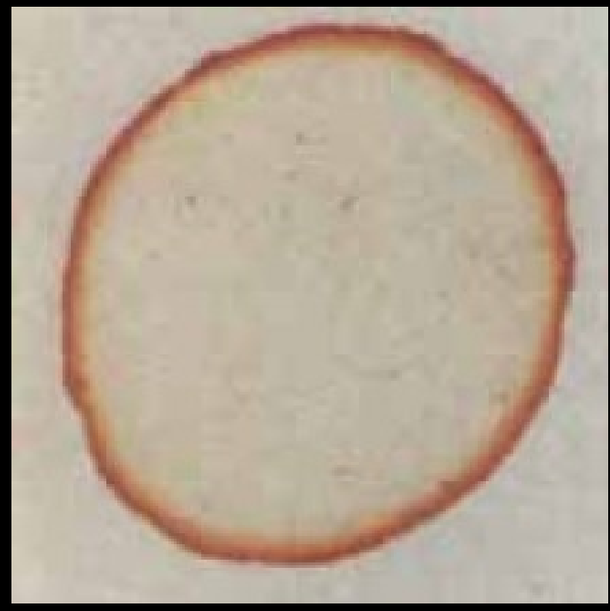
Cold
10°C





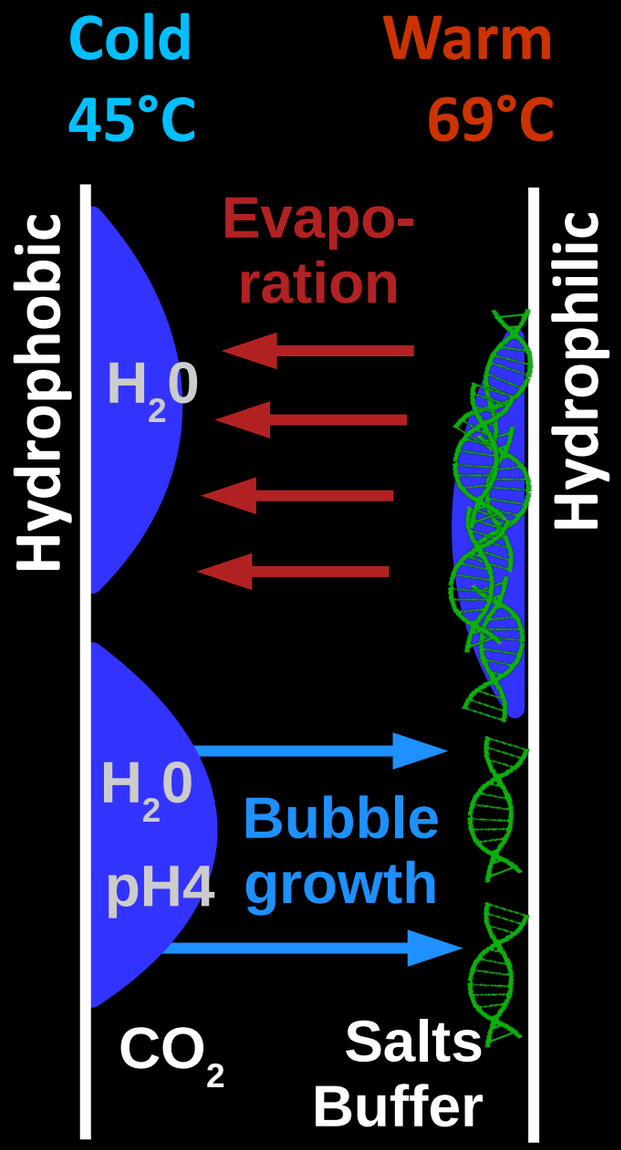
Hydrophilic

Warm
40°C

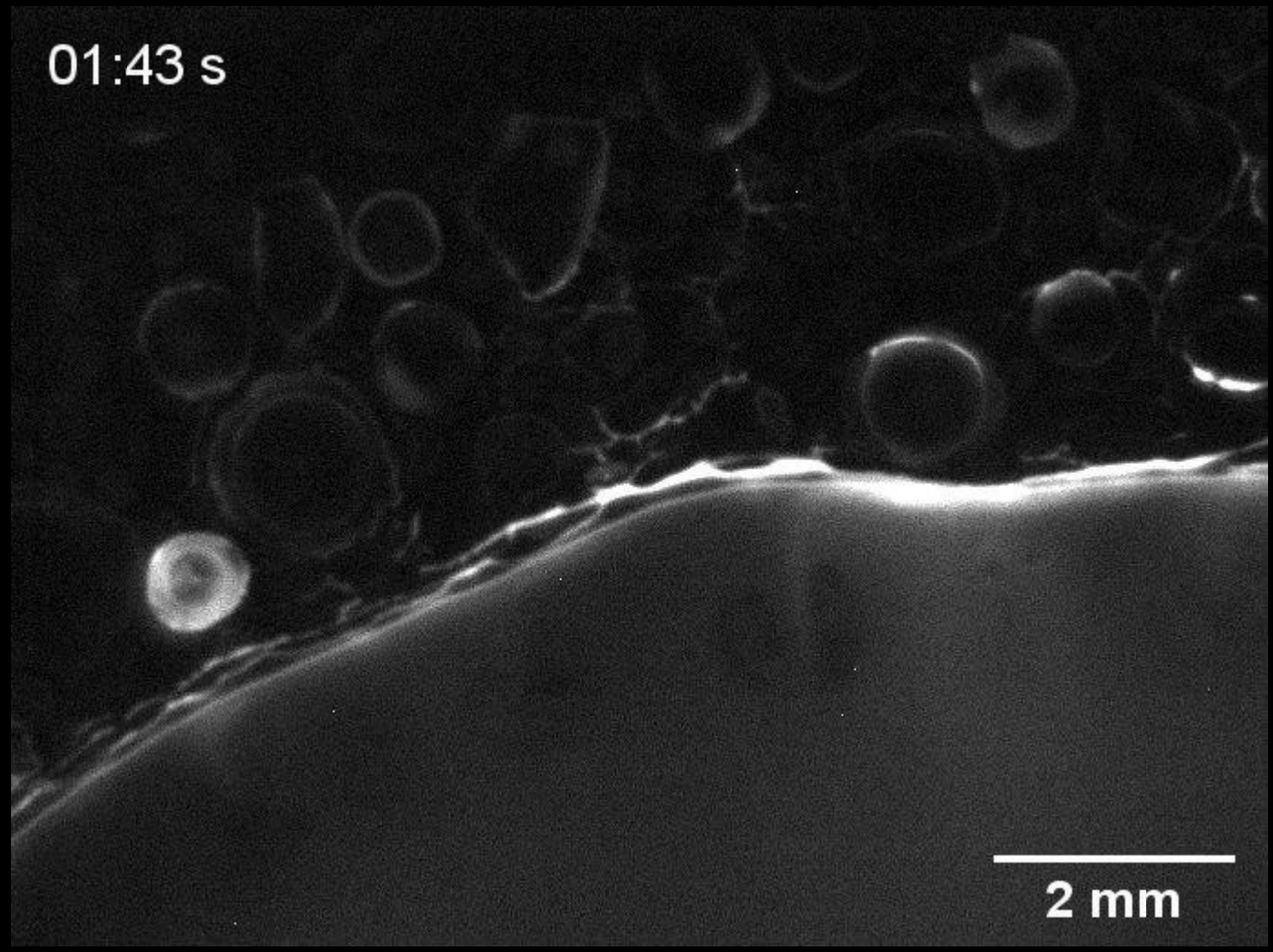


Drying with
Coffee ring effect

Salt and pH cycling in Fog Droplets

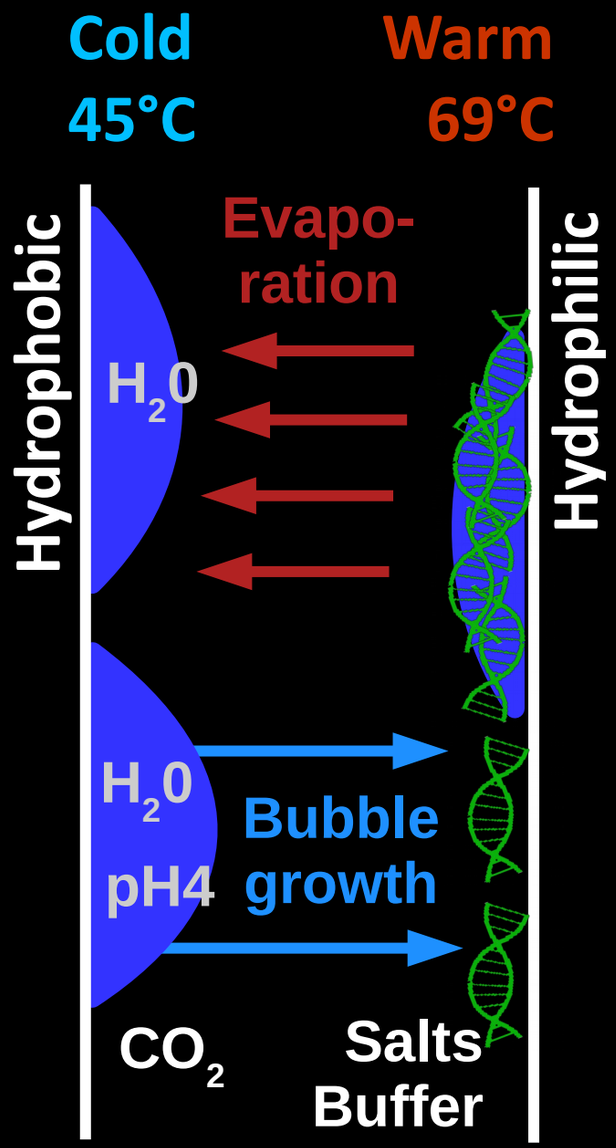


Monitoring Coffee Ring Effect

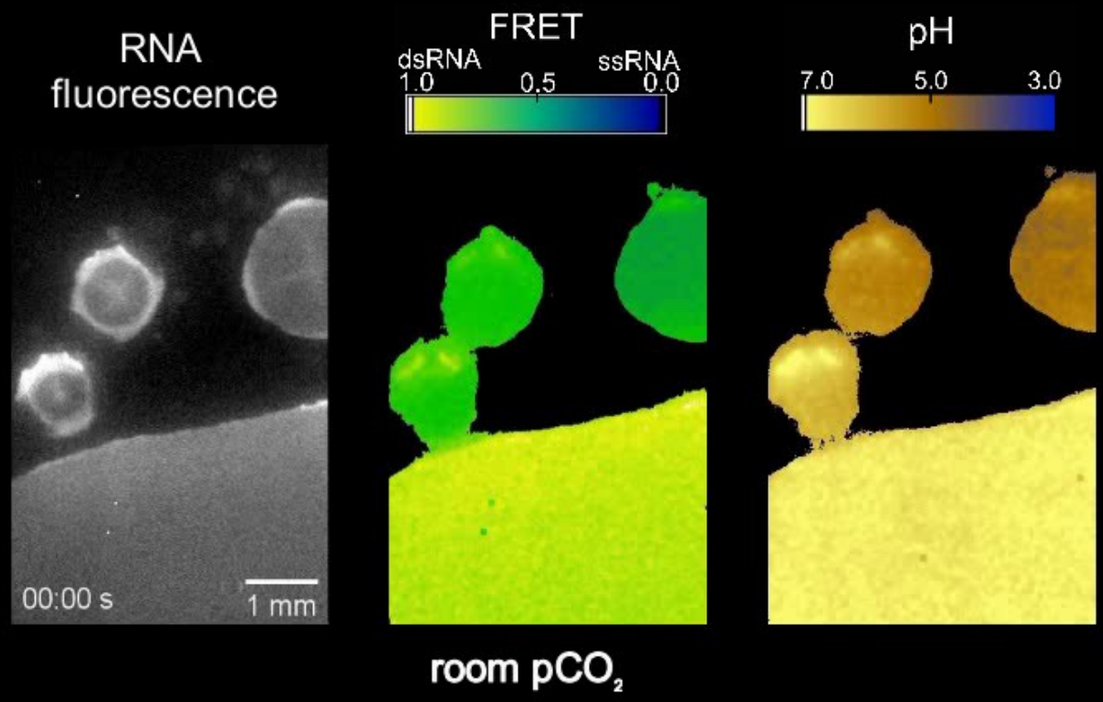


unpublished

Salt and pH cycling in Fog Droplets



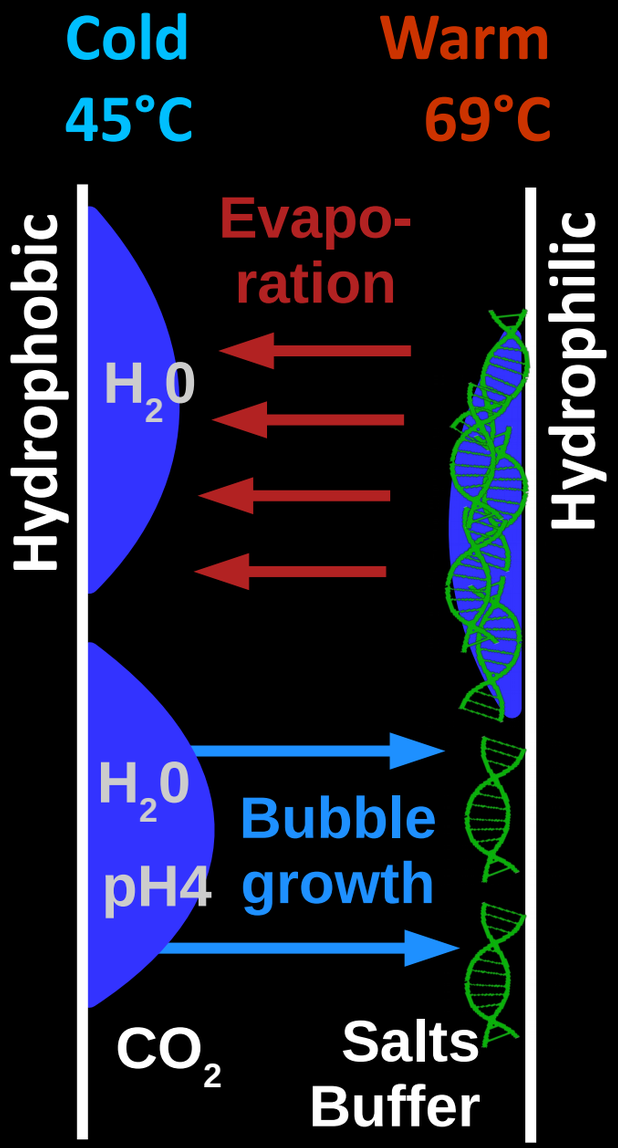
Imaging pH and strand separation



RNA 24mer (AT only) 4 μM, Tm 48 °C, 10 mM $MgCl_2$, 10 mM Tris (initial pH 7.0), Lysosensor 20 μM. Temperatures: hot side 27 °C, cold side 22 °C

unpublished

Fog PCR



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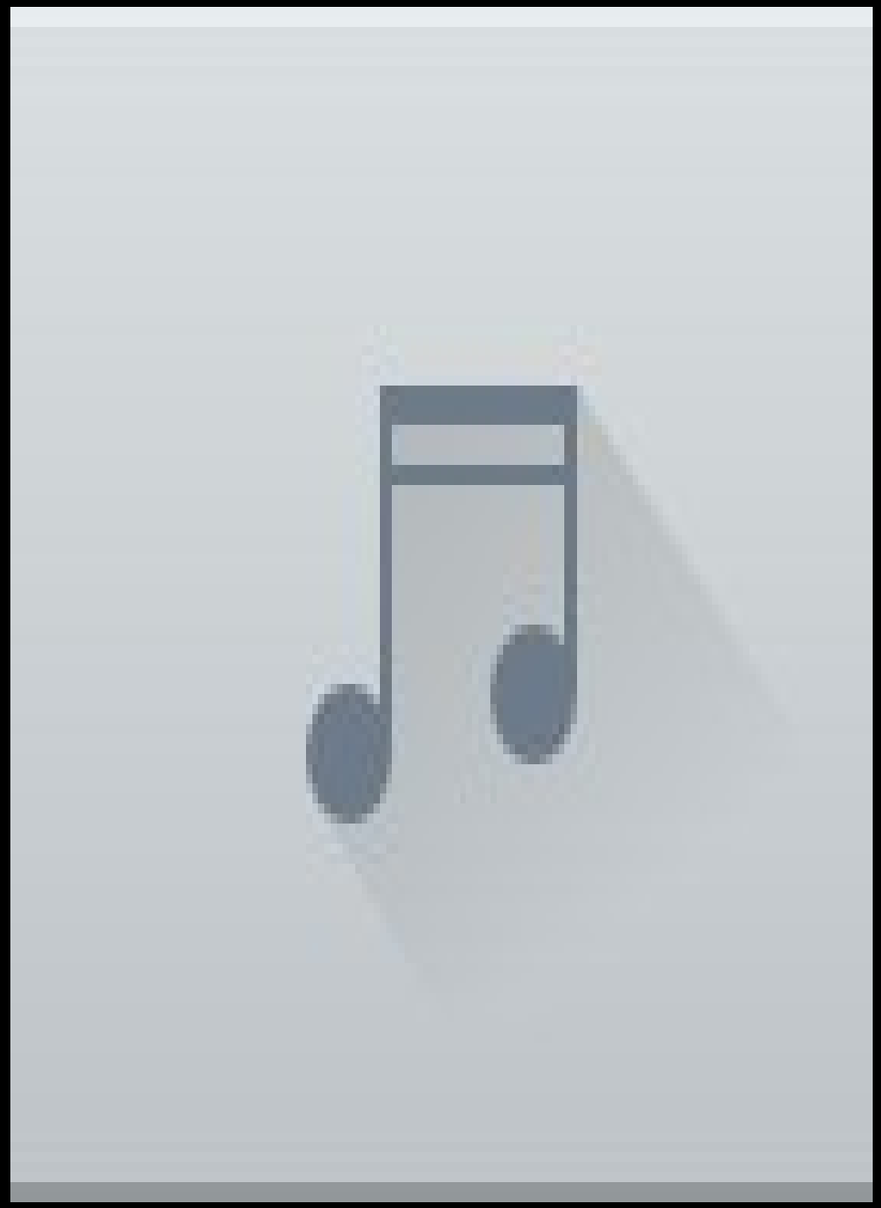
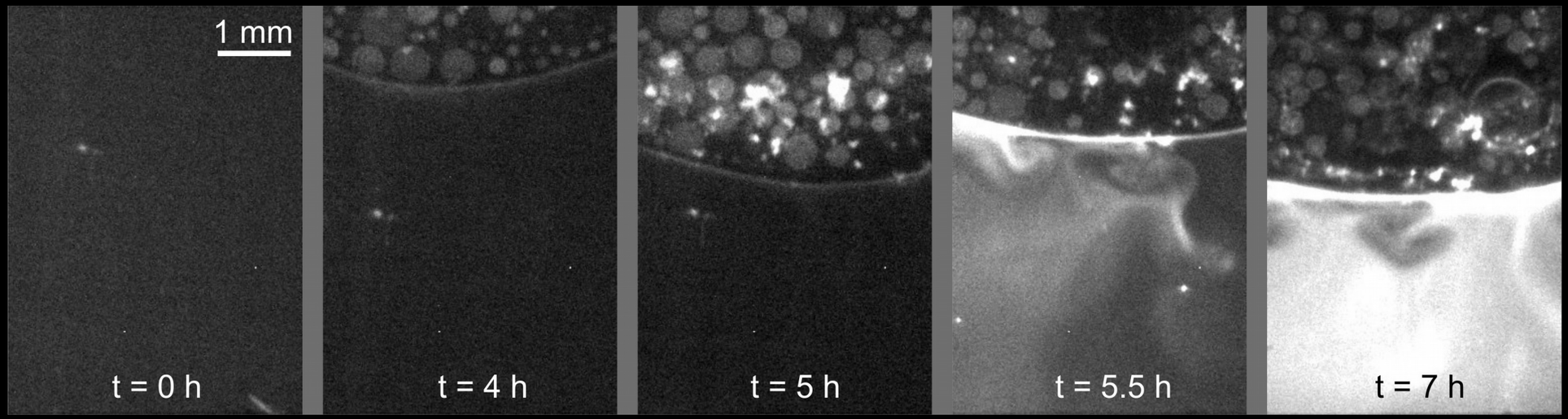
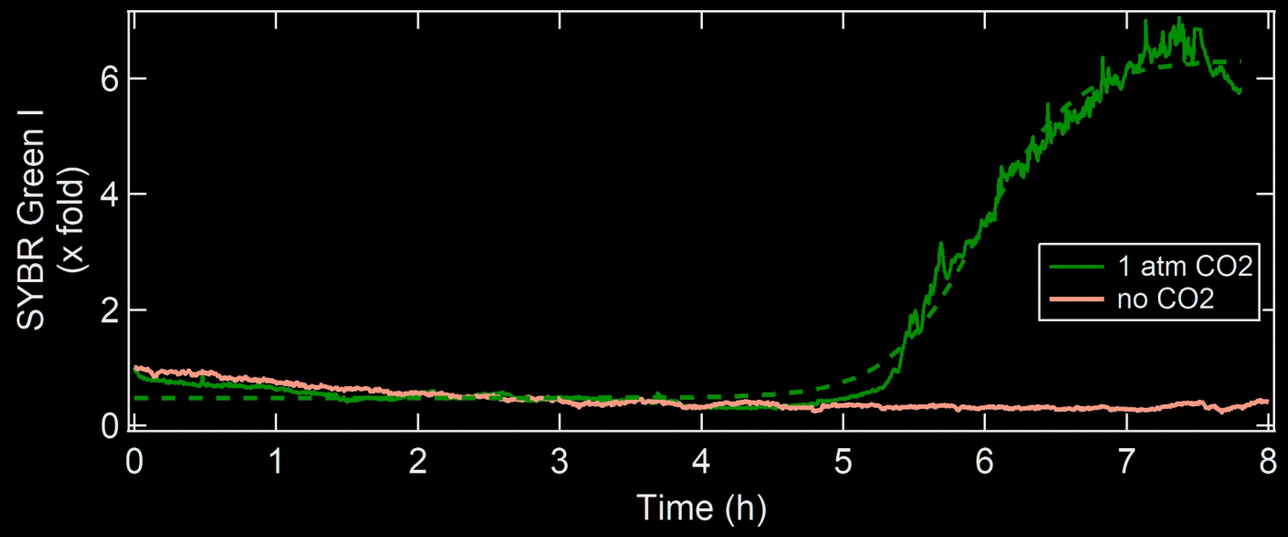


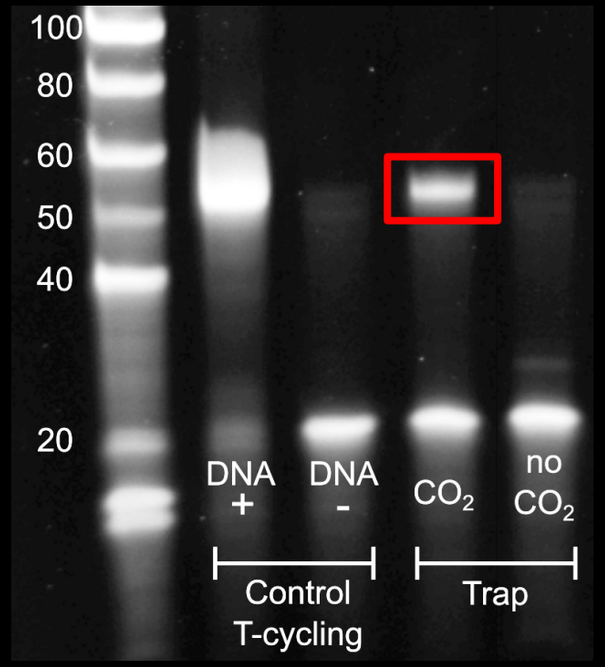
Alan
Ianeselli

T gradient:
45 °C - 69 °C
51mer T_m = 83 °C
1 bar CO_2
1 nM template DNA
0.5 µM primers
Taq polymerase
1.5 mM $MgCl_2$
0.1% BSA
2x SYBR Green

Fog PCR







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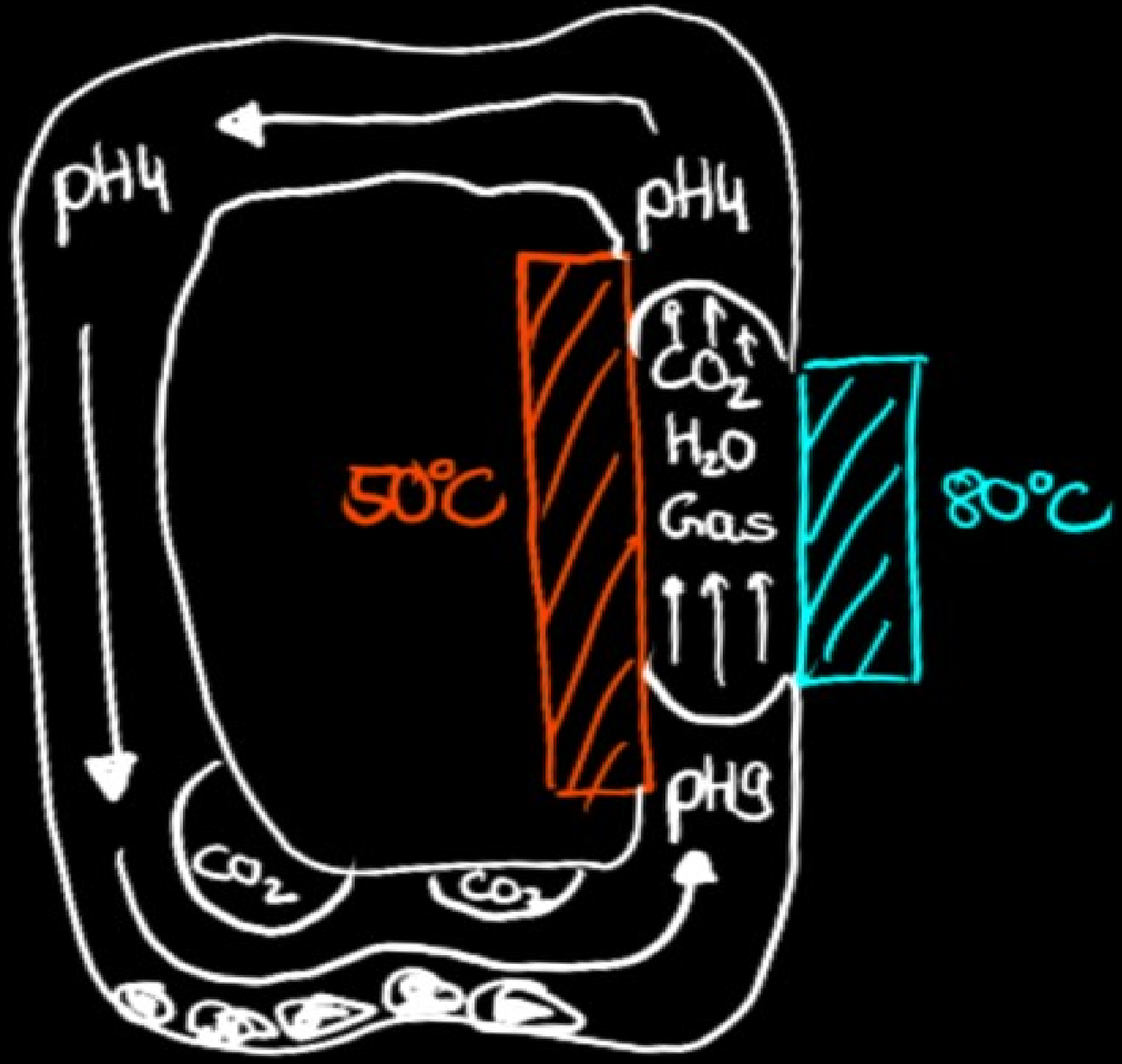
Connecting the Pieces: the Distillery of Life ?



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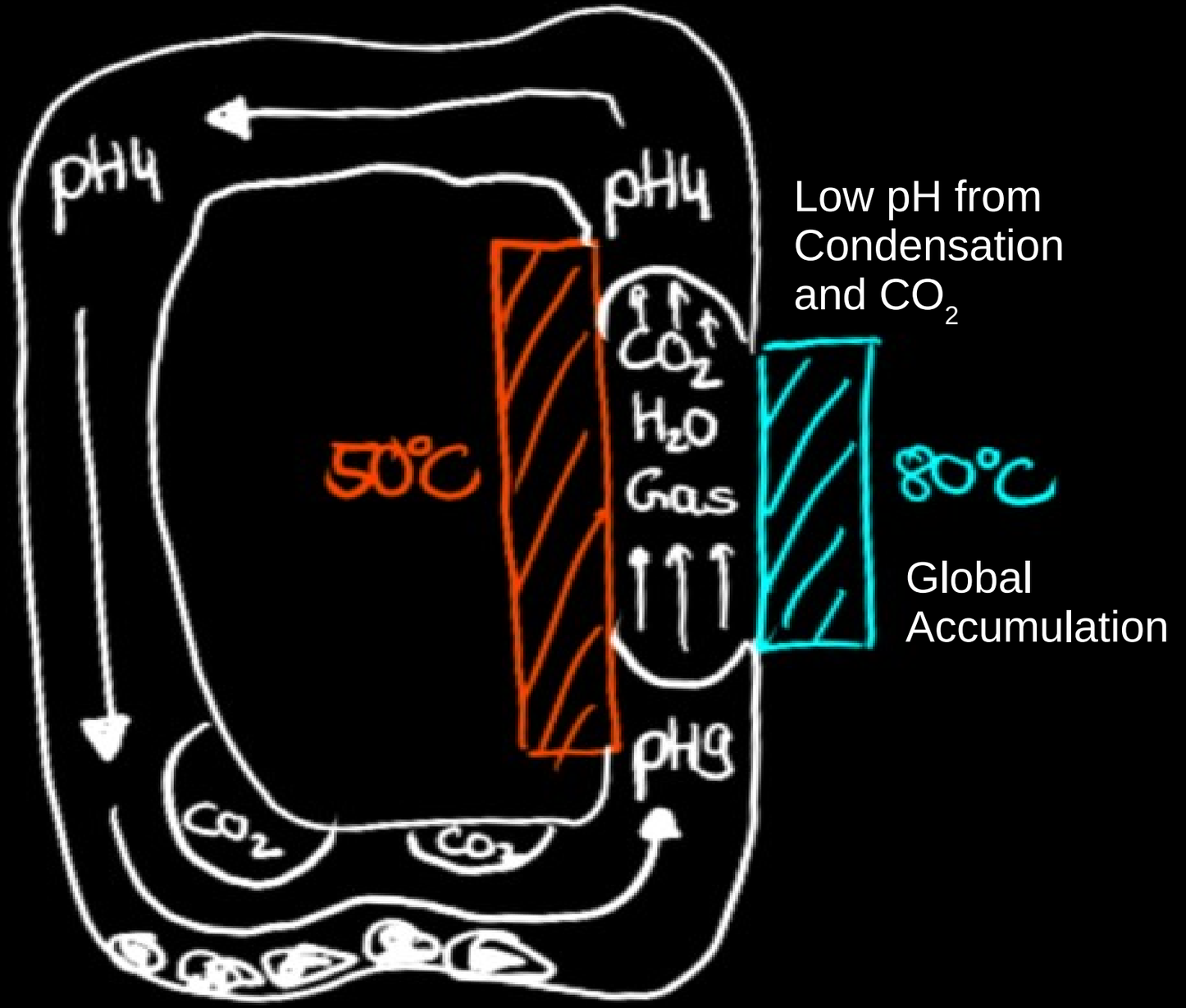

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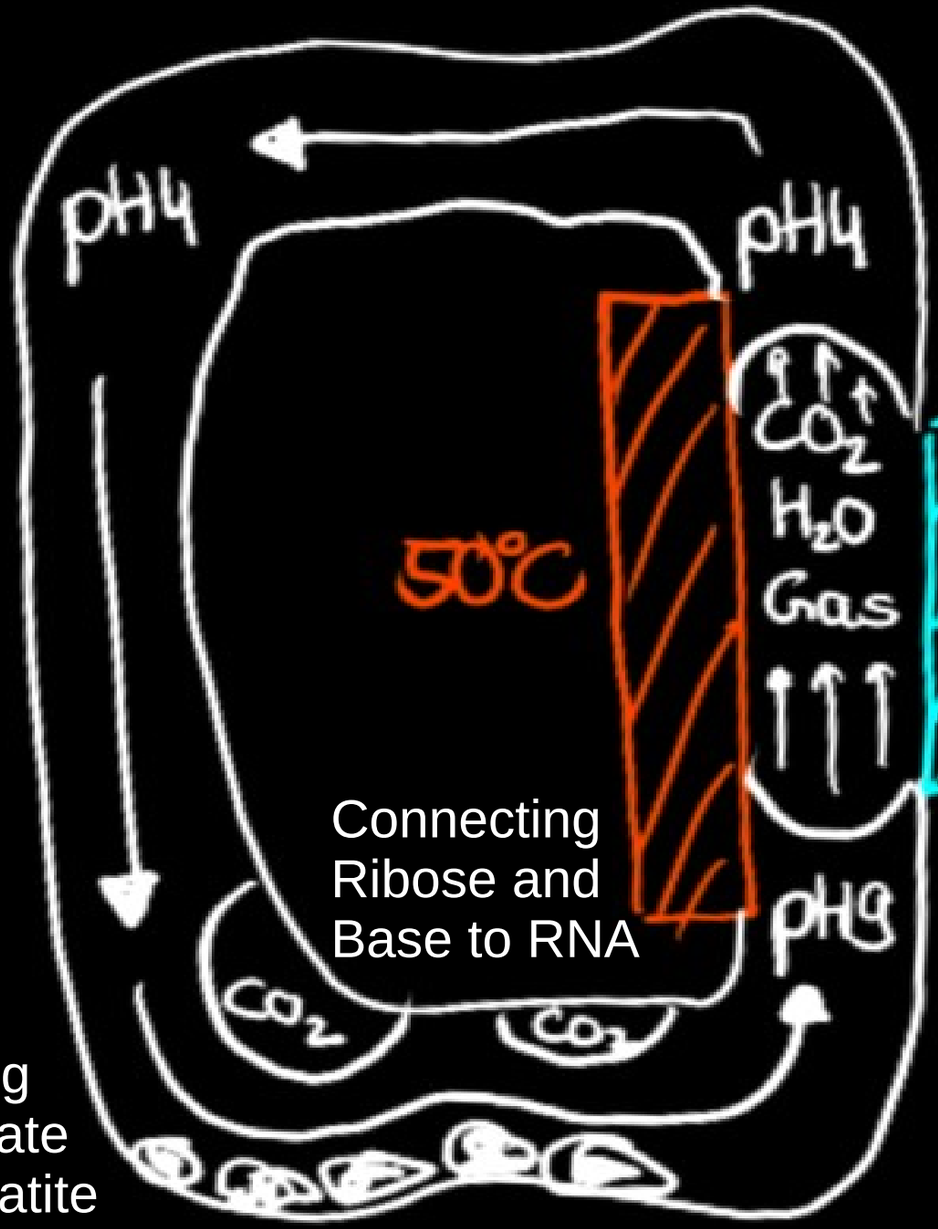


Low pH from Condensation and CO_2

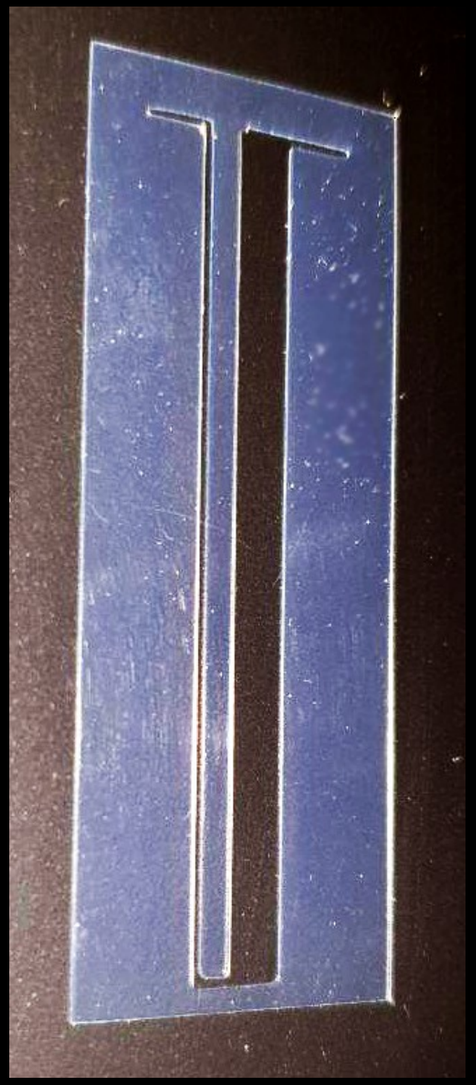
Global Accumulation

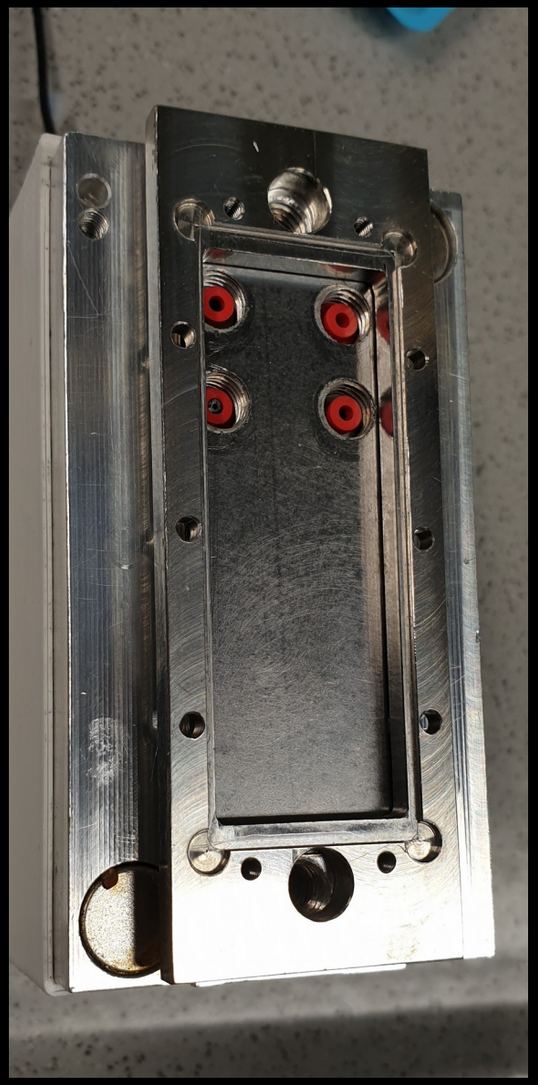
Connecting Ribose and Base to RNA

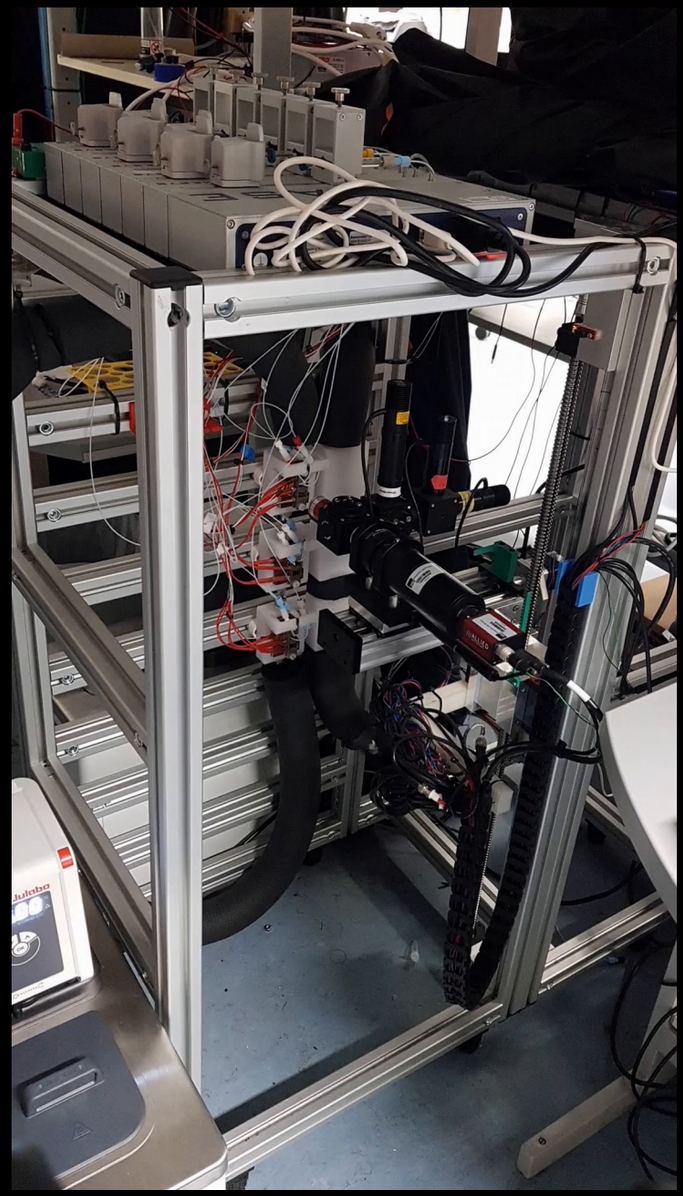
Phosphorylation
Polymerization
Hydrolysis
Recycling
Replication
Gelation

Leaching Phosphate from Apatite

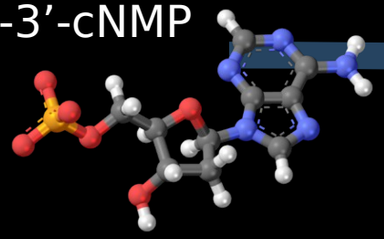
Emergence of Life Scenario







2’-3’-cNMP



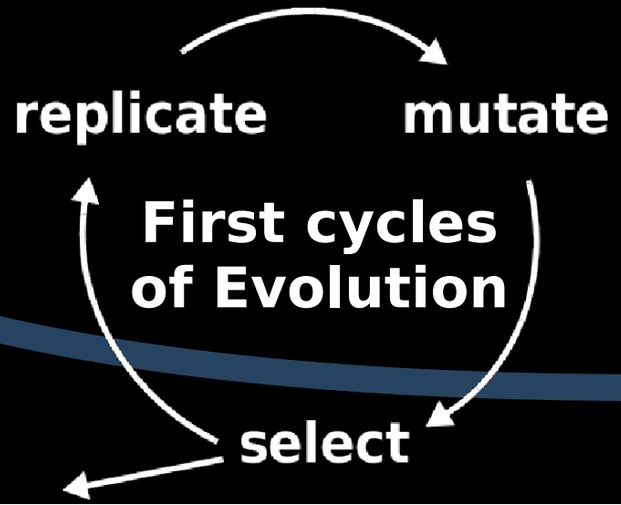
Polymerization
to random sequences

Replication
base-wise, by ligation
by hydrogelation, by
mechano-selection

Nucleotides

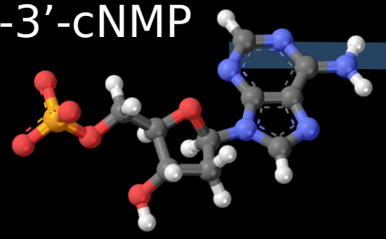
Symmetry breaking
by nonlinear sequence
cooperation mechanisms

Selection
for function between
purified phenotypes



Life

2’-3’-cNMP



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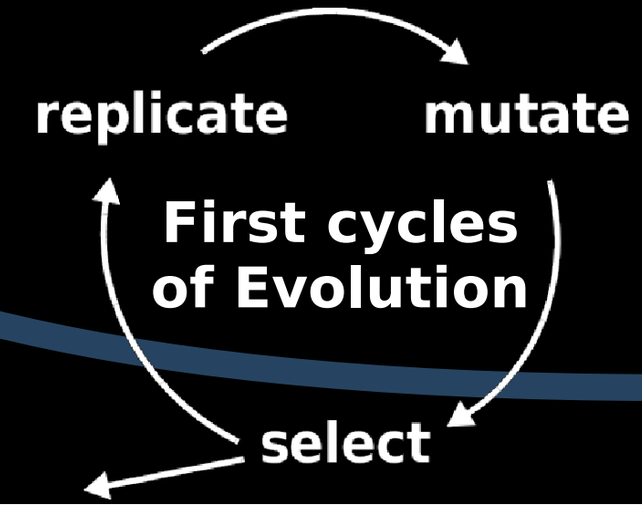
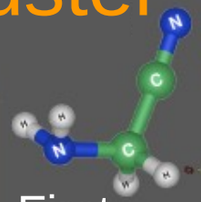


Life

DPG Technology
Transfer Price 2019

Origins Cluster

Clouds



First Organics

Dust Grains

Disks

Planets

Early Earth

Amino Acids

Nucleic Acids

Chirality

Activation

Polymer-ization

Encap-sulation

Non-equilibrium

Length Selection

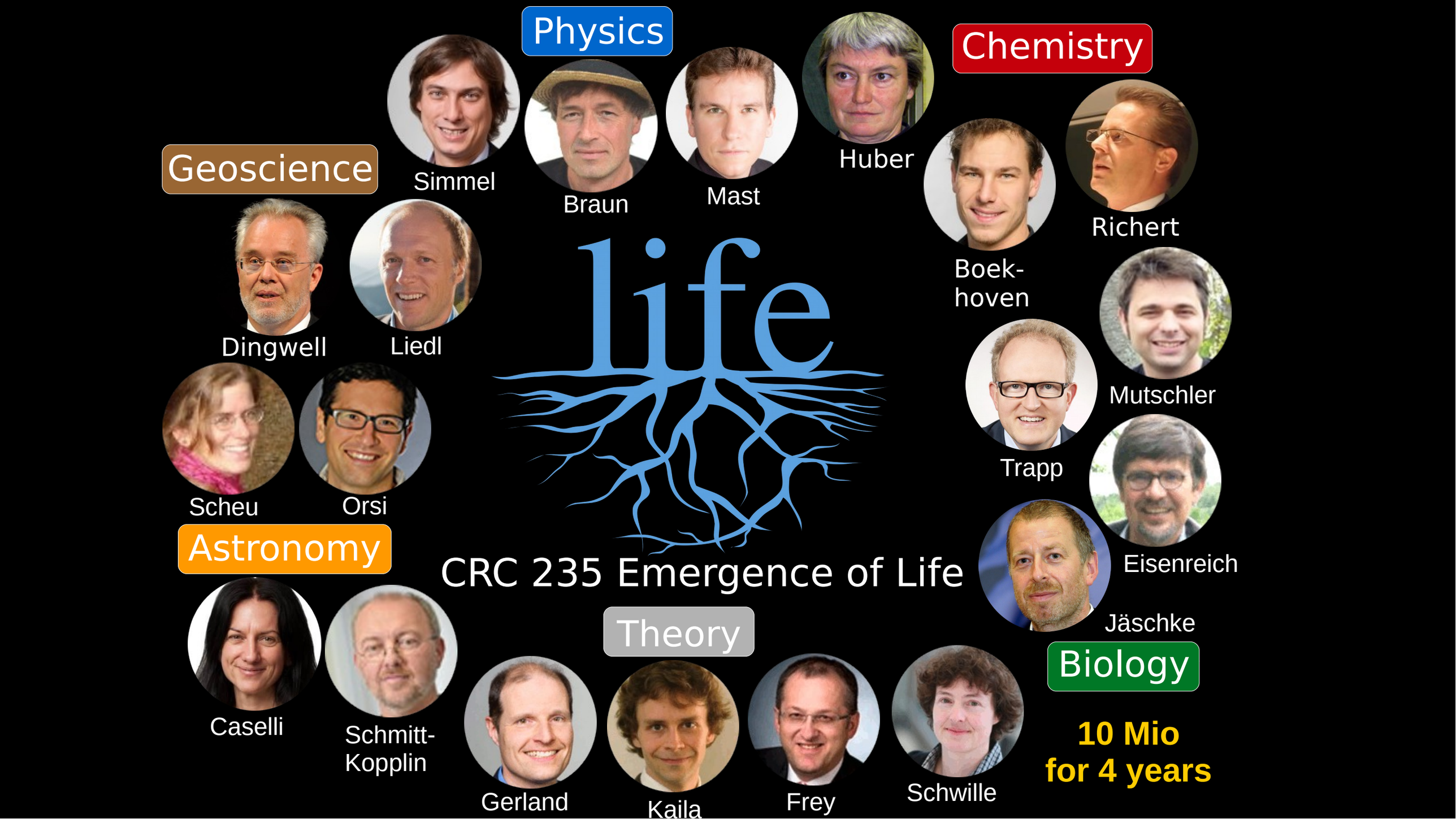
Replication

Complex Sequences

RNA Phases

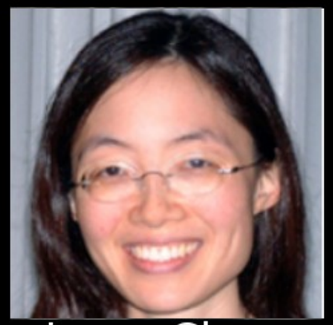
Darwinian Molecular Evolution

5 Million Euro for 7 years


Physics
Chemistry
Geoscience
Astronomy
Theory
Biology
life
CRC 235 Emergence of Life
Simmel
Braun
Mast
Huber
Richert
Boek-
hoven
Dingwell
Liedl
Mutschler
Trapp
Scheu
Orsi
Eisenreich
Jäschke
Caselli
Schmitt-
Kopplin
Gerland
Kaila
Frey
Schwille
10 Mio
for 4 years

Simons Collaboration on the Origins of Life


Donna Blackmond


Irene Chen


Karin Öberg


Gerald Joyce


Roger Summons


Matthew Powner


Dimitar Sasselov


Dieter Braun


Jack Szostak


John Sutherland


Ram Krishnamurthy


George Whitesides

Christof Mast

Annelena Salditt

Patrick Kudella

Christina Dirscherl

Alexandra Kühnlein

Alan Ianeselli

Max Weingart

Julian Stein

Matthias Morasch

Thomas Matreux

Adriana Serrao

Sreekar Wunnava

Philipp Schwintek

Noel Martin

Simons Foundation
Klung-Wilhelmy Price
Volkswagen Life!

erc Starting 2010-15

erc Advanced 2018-23

nano agents SFB 1032

QMO

nano TEMPER

Collaborators

Ulrich Gerland, Erwin Frey, Thomas Franosch, Hermann Gaub, Irene Chen, John Sutherland, Matt Powner, Andres Jäschke, Oliver Trapp, Don Dingwell, Judith Sponer, Gerald Joyce, Dora Tang, Hannes Mutschler.