

A: Fundamentals of Life

- Definition of Life
- Logic of Molecular Biology
- History of Biology
- Becoming alive
- Soup of Life
- Selection: before and in life
- Three faces of Entropy
- Death and equilibrium
- Missing non-equilibrium
- Structure of Origin of Life
- Modes of non-equilibrium
- Examples of evolution

B: Physics for Chemistry

Polymerization

- Theory of polymerization
- P. by fast cooling
- P. by stacking with 3'-5'-Ph.
- Activation groups
- P. on clay
- P. by thermophoresis
- Phase transitions with DNA
- Sedimentation of DNA
- Drying and its problems
- Elegance of air interface

Replication

- Templated polymerization
- Ligation
- Strand separation problem
- PCR in convection
- Ribo-PCR in convection

C: Evolution Machines

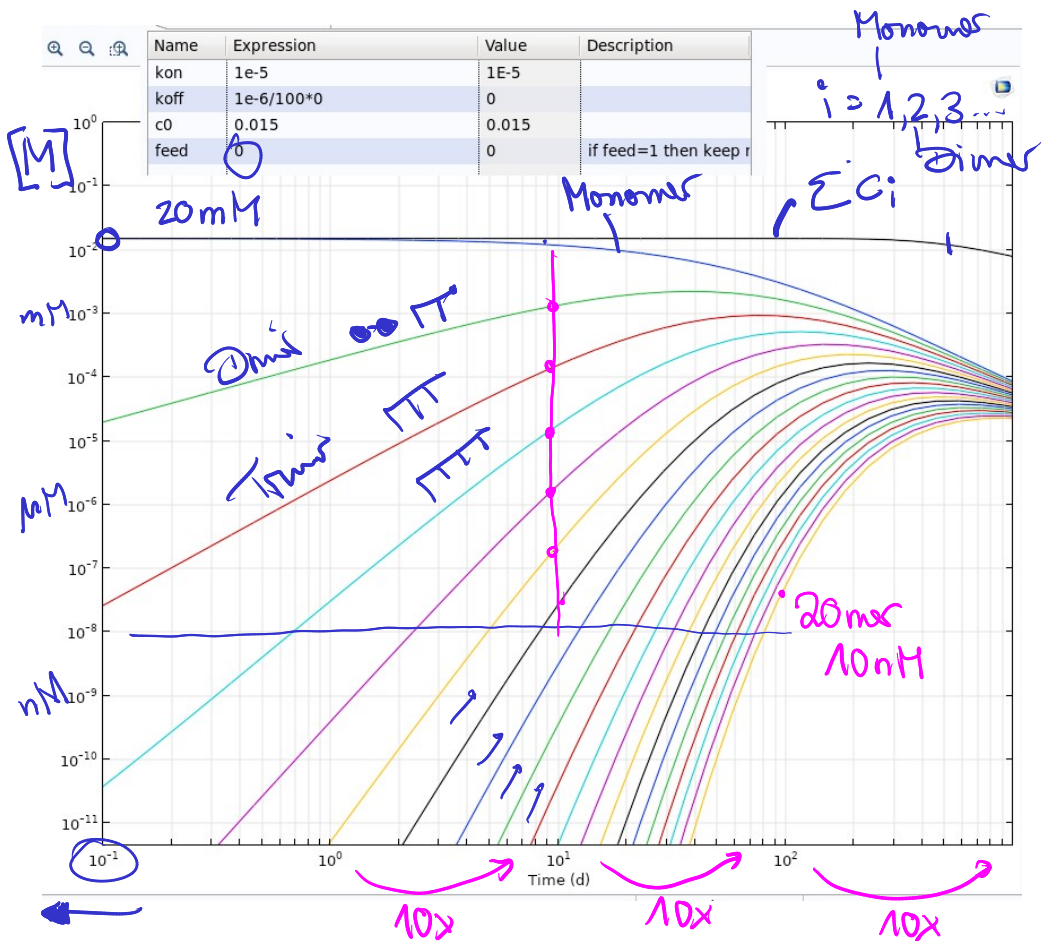
Replication with accumulation

- Case of Ribo-PCR
- Spiegelman problem
- Case of trapped PCR
- Trapped PCR with flow
- Feeding problem
- Replication with heated tRNA
- Replication in driven Fog

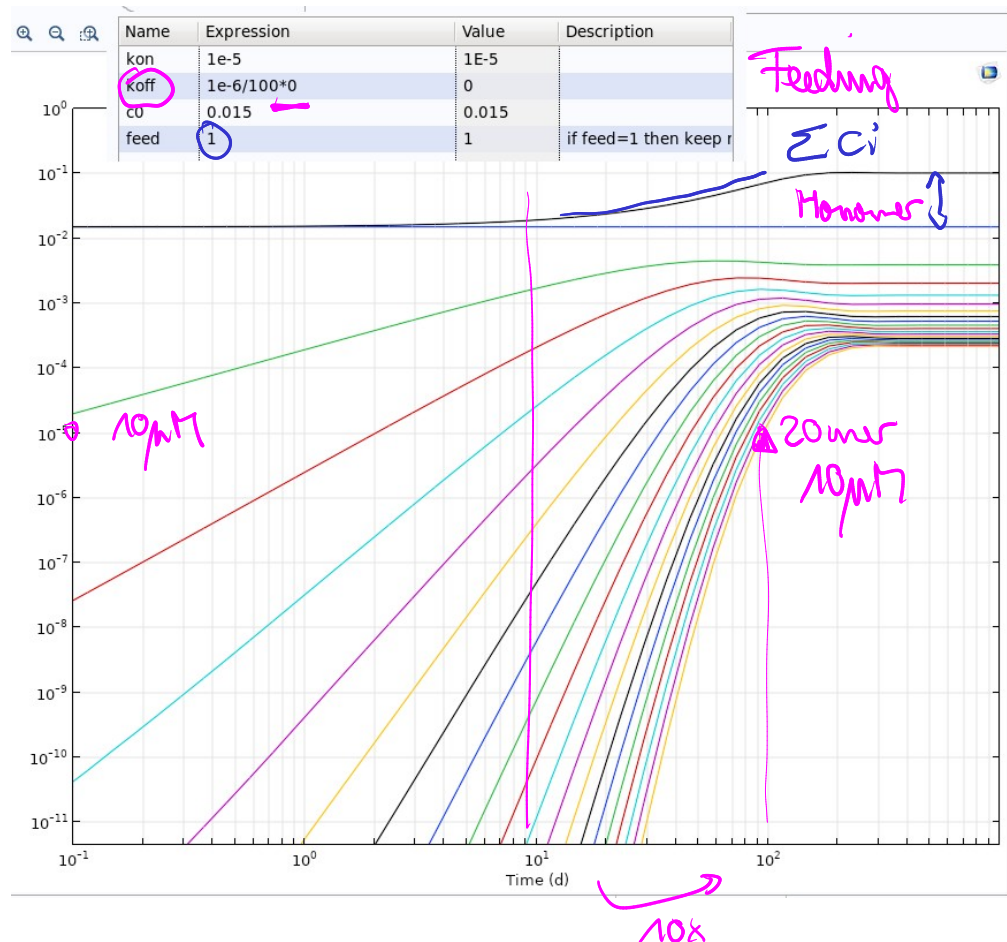
Robustness of evolution

- Error threshold
- Instability of four bases
- Hypercycles with ligation
- Spont. Symmetry breaking
- Spont. sequence selection
- Cooperation within cells

Theory of polymerization



Comsol no feeding of monomers



Comsol with feeding of monomers

Theory of polymerization

Kinetics_system_generator_2.0.vi Front Panel

File Edit View Project Operate Tools Window Help

15pt Application Font

of Monomers: 20

Rate equation system

Conc. string: c

Kon String: kon

Koff String 2: koff

Not only Monomer addition

Add time derivative for Consol ODE

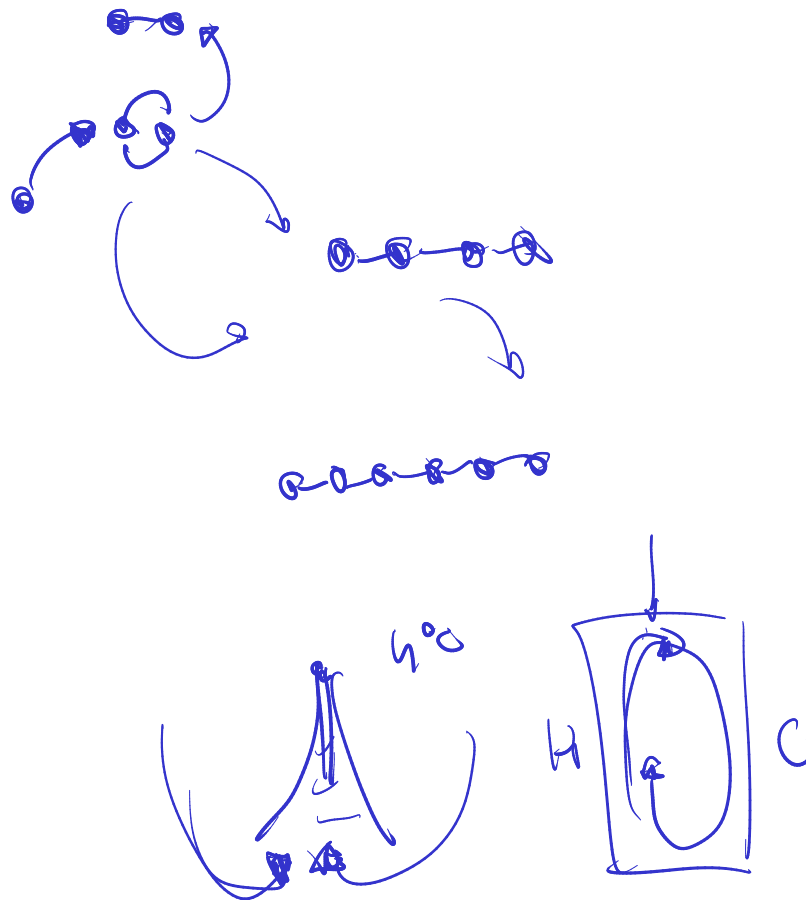
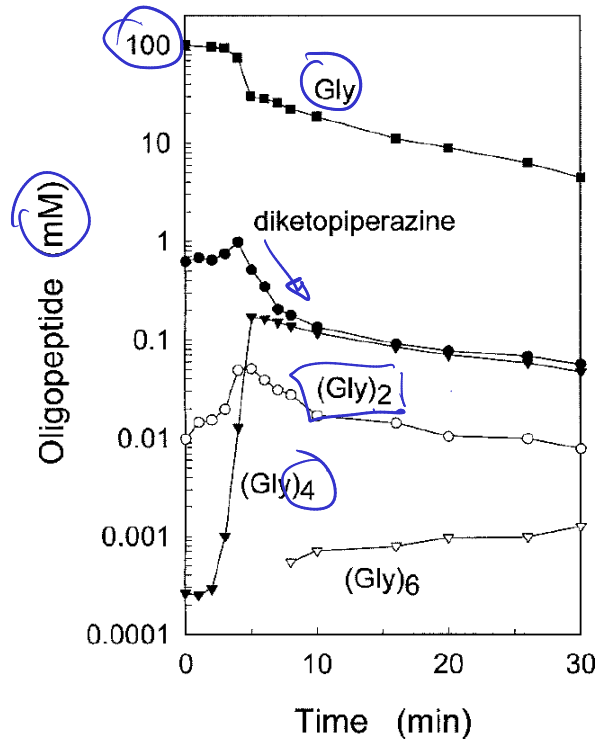
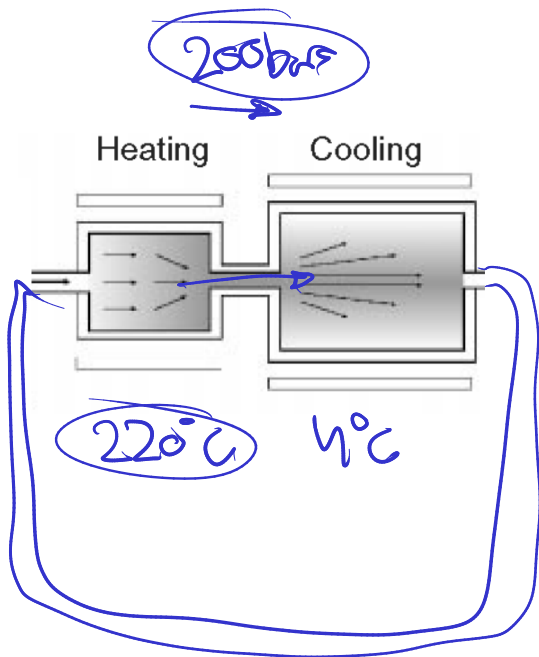
Open end (have off-rates for last term)

```
-c1t-2*kon*c1*c1-2*kon*c1*c2-2*kon*c1*c3-2*kon*c1*c4-2*kon*c1*c5-2*kon*c1*c6-2*kon*c1*c7-2*kon*c1*c8-2*kon*c1*c9-2*kon*c1*c10-2*kon*c1*c11-2*kon*c1*c12-2*kon*c1*c13-2*kon*c1*c14-2*kon*c1*c15-2*kon*c1*c16-2*kon*c1*c17-2*kon*c1*c18-2*kon*c1*c19-2*kon*c1*c20+
-c2t+1*kon*c1*c1-2*kon*c2*c1-2*kon*c2*c2-2*kon*c2*c3-2*kon*c2*c4-2*kon*c2*c5-2*kon*c2*c6-2*kon*c2*c7-2*kon*c2*c8-2*kon*c2*c9-2*kon*c2*c10-2*kon*c2*c11-2*kon*c2*c12-2*kon*c2*c13-2*kon*c2*c14-2*kon*c2*c15-2*kon*c2*c16-2*kon*c2*c17-2*kon*c2*c18-2*kon*c2*c19-
-c3t+2*kon*c1*c2-2*kon*c3*c1-2*kon*c3*c2-2*kon*c3*c3-2*kon*c3*c4-2*kon*c3*c5-2*kon*c3*c6-2*kon*c3*c7-2*kon*c3*c8-2*kon*c3*c9-2*kon*c3*c10-2*kon*c3*c11-2*kon*c3*c12-2*kon*c3*c13-2*kon*c3*c14-2*kon*c3*c15-2*kon*c3*c16-2*kon*c3*c17-2*kon*c3*c18-2*kon*c3*c19-
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-c7t+2*kon*c1*c6+2*kon*c2*c5+2*kon*c3*c4-2*kon*c7*c1-2*kon*c7*c2-2*kon*c7*c3-2*kon*c7*c4-2*kon*c7*c5-2*kon*c7*c6-2*kon*c7*c7-2*kon*c7*c8-2*kon*c7*c9-2*kon*c7*c10-2*kon*c7*c11-2*kon*c7*c12-2*kon*c7*c13-2*kon*c7*c14-2*kon*c7*c15-2*kon*c7*c16-2*kon*c7*c17-
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```

Creating kinetic terms with a LabVIEW program

Esoteric? Protein Polymerization by fast cooling

Matsuno: Polymerisation by fast cooling



Koichiro Matsuno, Science 283, 831 (1999)

Polymerization on clay

Needs ion washing: Correct mechanism?

Ferris: Clay-based polymerisation

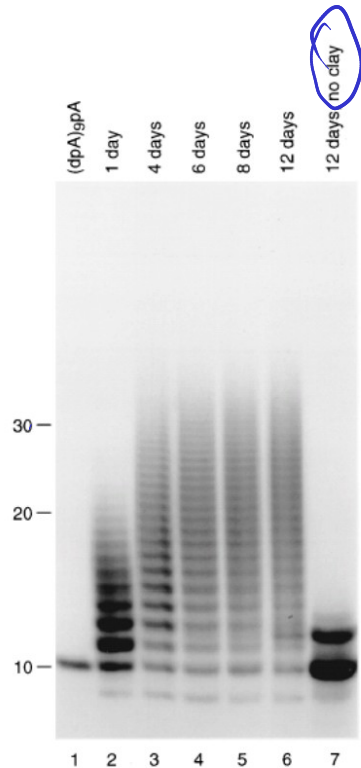
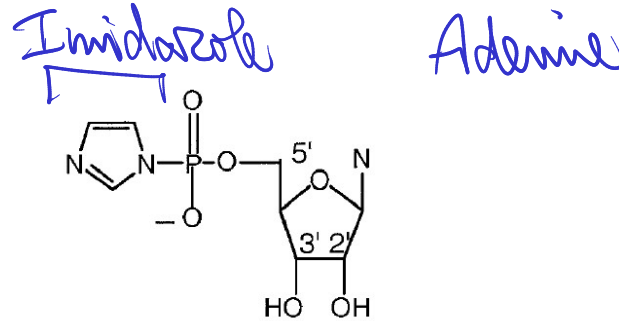


Figure 2. Gel electrophoresis of the elongation of ³²PdA(pdA)₈pA with ImpA in microcentrifuge tubes. Lane 1, ³²PdA(pdA)₈pA; lanes 2-6 elongation in the presence of montmorillonite; lane 7, elongation in the absence of montmorillonite.

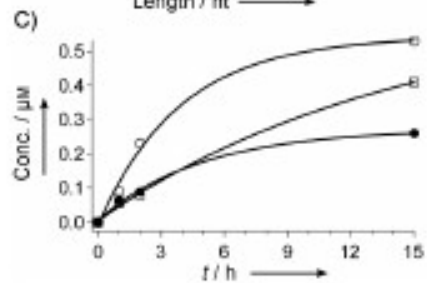
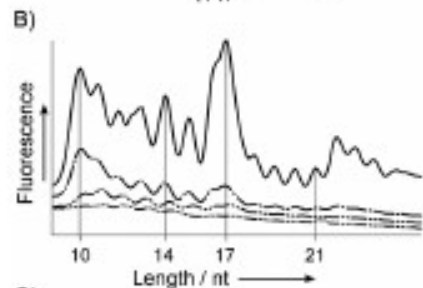
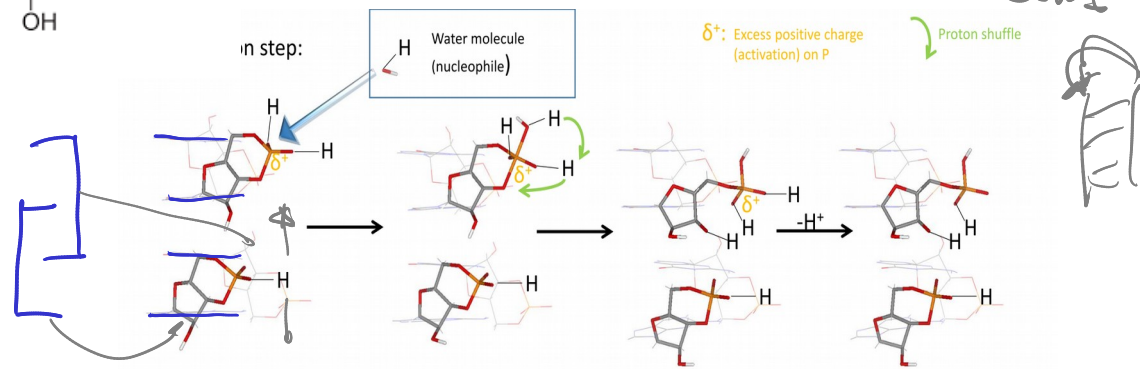
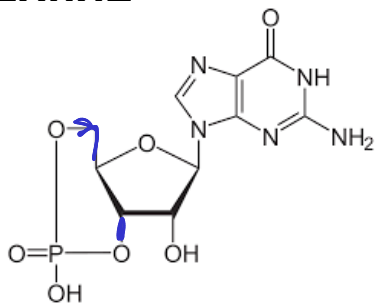
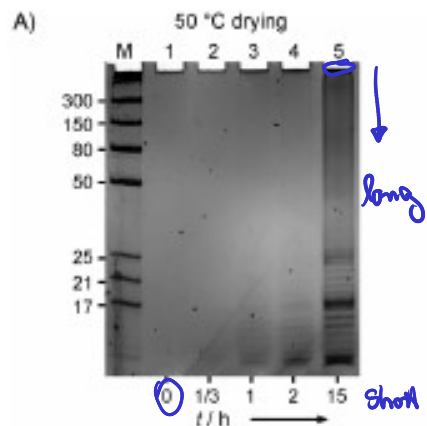


On the **surface of negative charged montmorillonite** clay, energy rich nucleotide-primers can undergo efficient polymerization. One can reach **30-50-mers within some days**. Surfaces are therefore interesting places for catalysis of prebiotic reactions since they can enhance the concentration of the molecules. Problem is the removal of the polymerized species from the surface and replication priming.

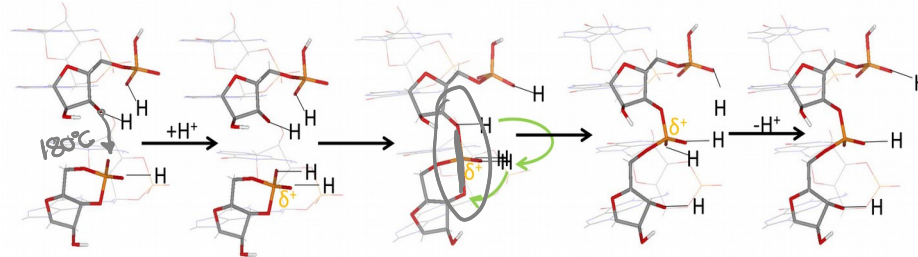
Polymerization by drying of 3'-5' cyclic G-Nucleotide

Dry Polymerization of 3',5'-Cyclic GMP to Long Strands of RNA

Matthias Morasch,^[a] Christof B. Mast,^[a] Johannes K. Langer,^[a] Pierre Schilcher,^[b] and Dieter Braun^{*[a]}



Chain-extension step:



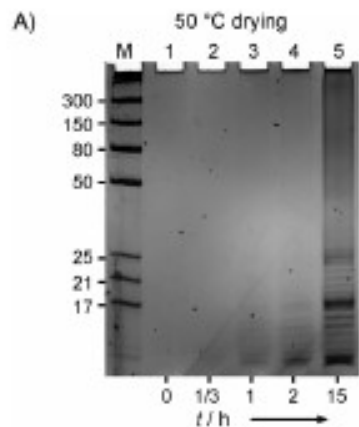
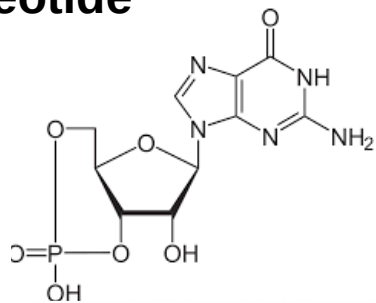
Atom coloring: P, O, H, C, N

See papers by di Mauro and Judith Sporer

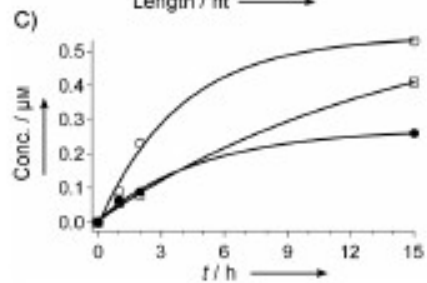
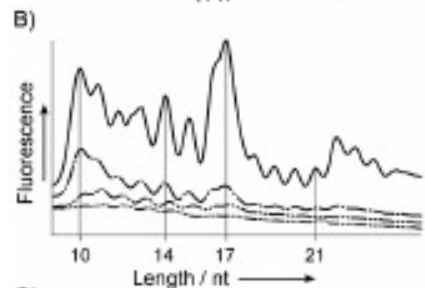
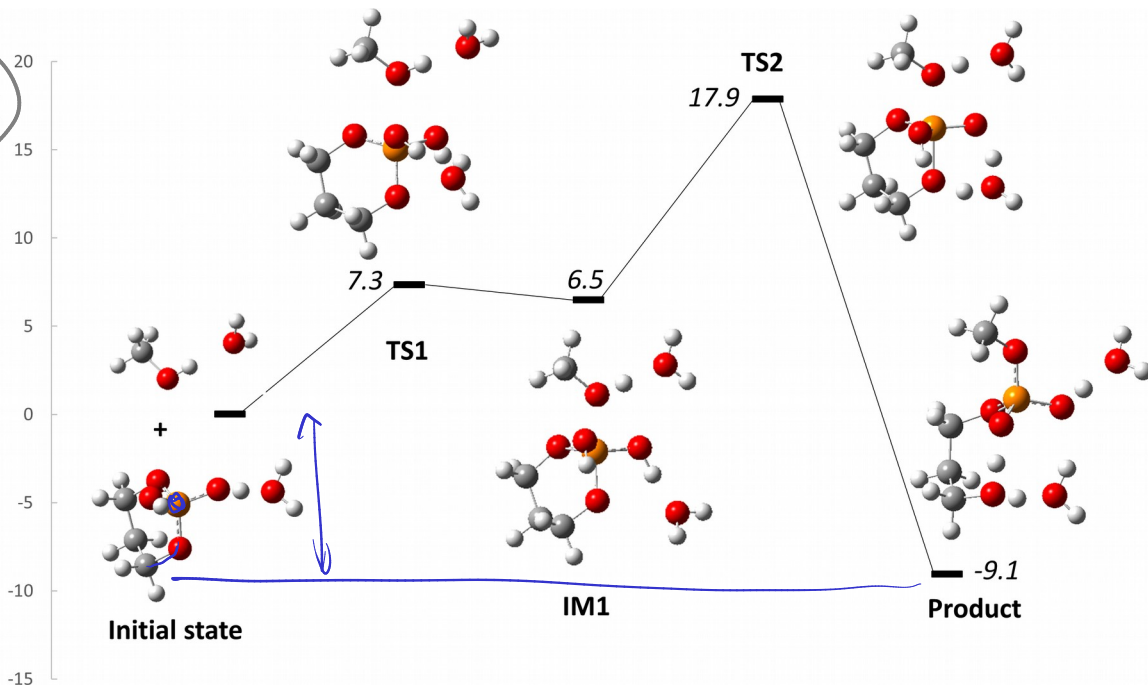
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ΔG ,
kcal/mol



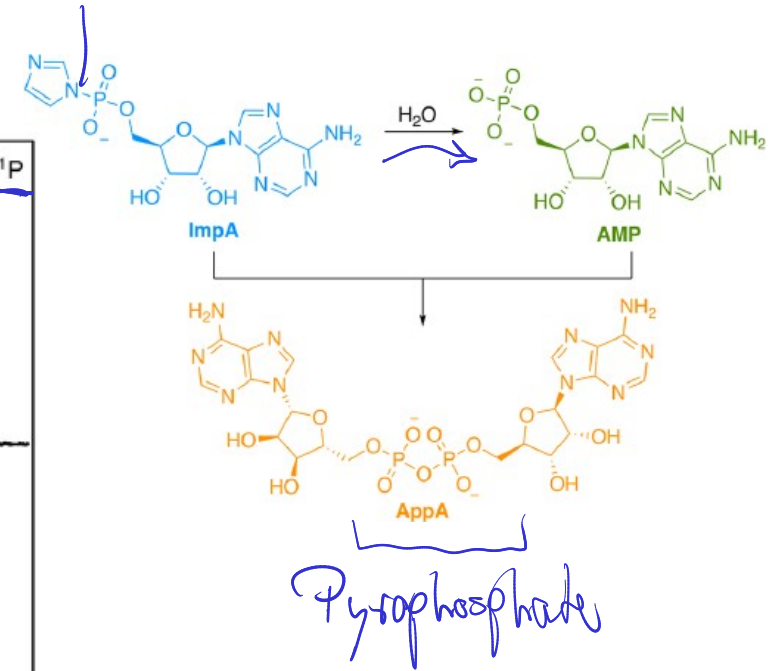
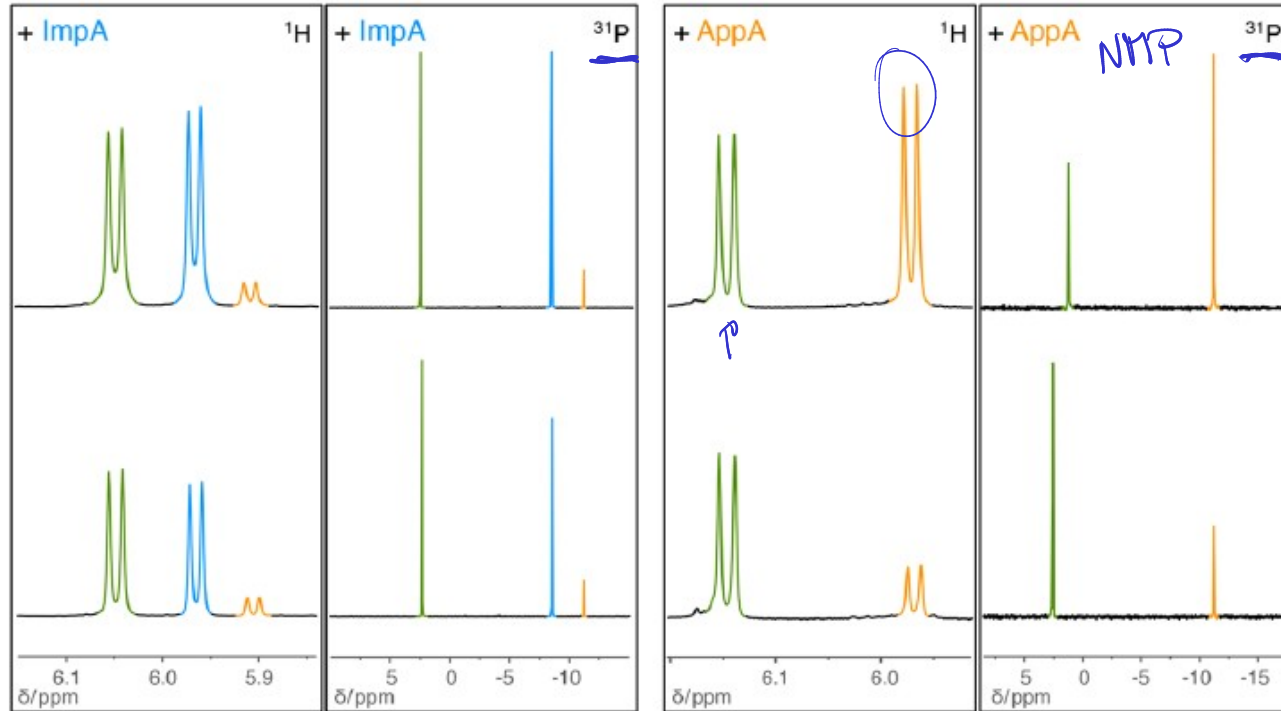
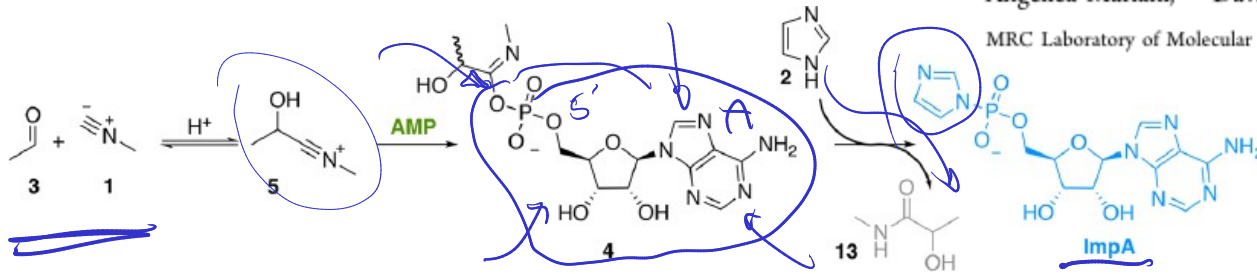
See papers by di Mauro and Judith Sponer

Activation group: in situ possible?

A Light-Releasable Potentially Prebiotic Nucleotide Activating Agent

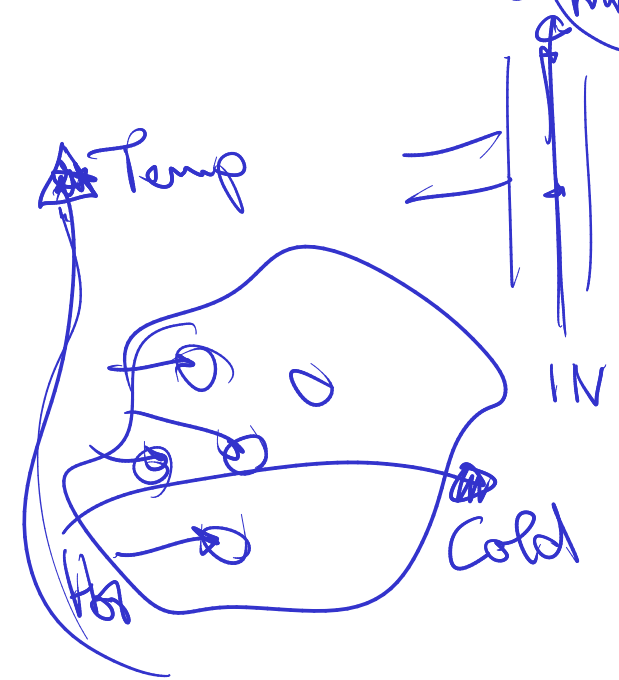
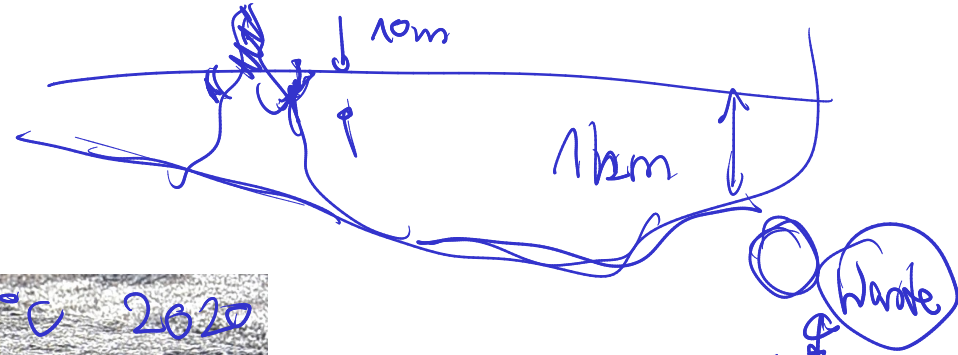
Angelica Mariani,[†] David A. Russell,[†] Thomas Javelle, and John D. Sutherland^{*†}

MRC Laboratory of Molecular Biology, Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge CB2 0QH, U.K.



Accumulation by temperature gradients

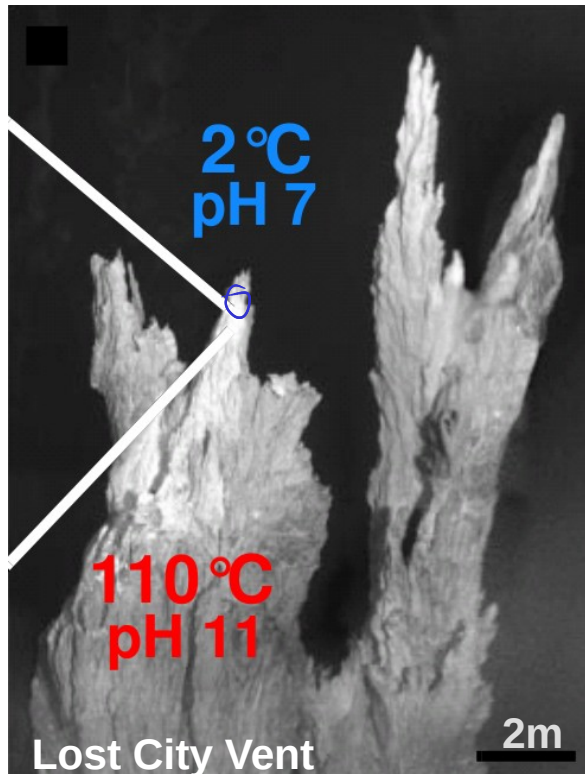
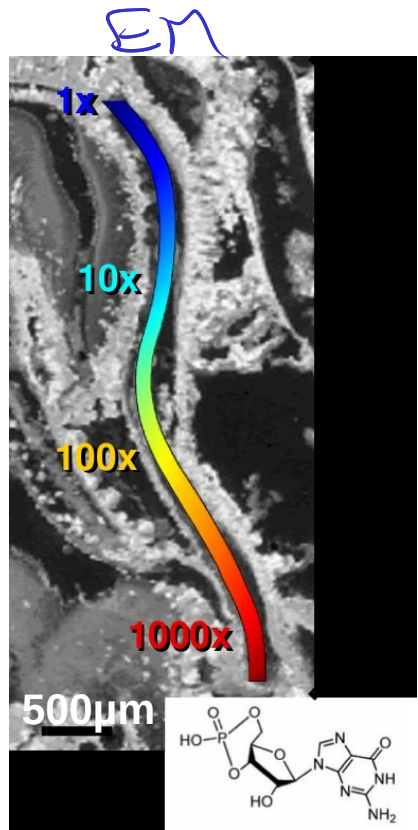
Hot Vapor Settings



Iceland

Accumulation by temperature gradients

Hydrothermal Settings



2007

$$J = -D_T C \nabla T$$

$$-D_T C \nabla C$$

Diffusion

reduced by the elongated structures

even less
Higher Accumulation



1881: Thermogravitational column (Dickel;)

Accumulation by temperature gradients

Cells defined by Pores of Rock

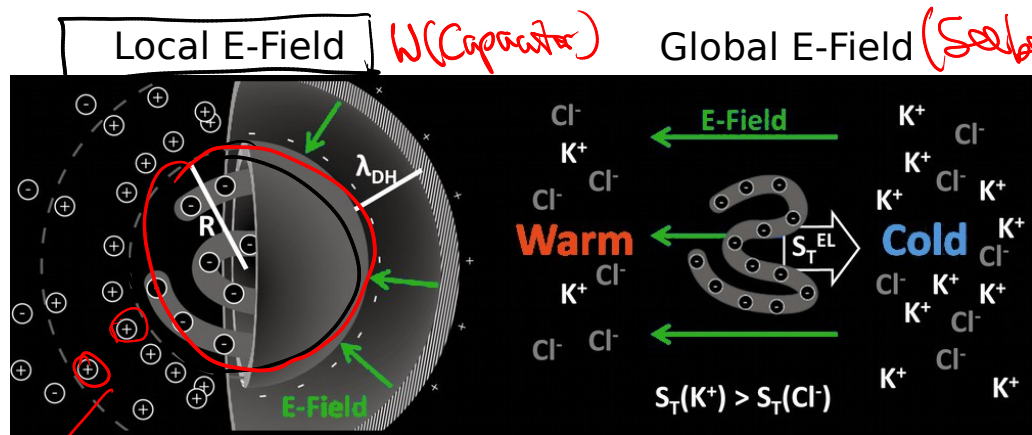


Robert Hooke

Accumulation by temperature gradients

Thermophoresis

Warm \longrightarrow **Cold**

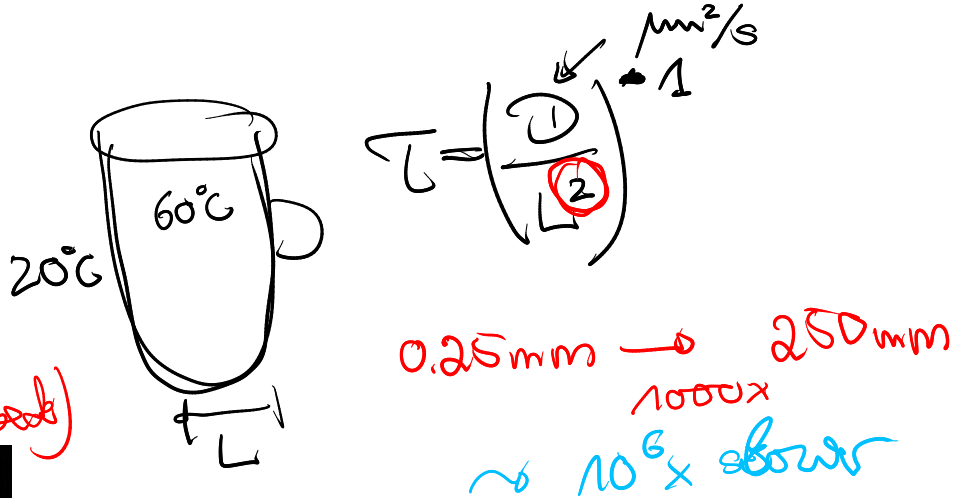


Duhr and Braun, PNAS 103, 19678 (2006)

Reichl, Herzog, Götz, and Braun, PRL 112, 198101 (2014)

Seebeck contribution

$$\frac{S_T^{SCM}}{Z_{eff}^2} = \frac{e^2 R / \lambda_{DH}}{16\pi k_B T^2 \epsilon_r \epsilon_0 (1 + R/\lambda_{DH})^2} \times \left(1 - \frac{\partial \ln \rho(T)}{\partial \ln T} - \frac{\partial \ln \epsilon_r(T)}{\partial \ln T} \left(1 + \frac{2\lambda_{DH}}{R} \right) \right)$$



$$\Delta E = \frac{2W(\text{Capacitor})}{9T} \cdot \Delta T \quad \text{Seebeck coefficient}$$

$$\frac{C_{Cold}}{C_{Warm}} = \exp\left(-\frac{\Delta E}{kT}\right) = \exp\left(\frac{S_T \Delta T}{kT}\right)$$

Velocity of particles \Rightarrow NanoTemper

$$j = -D \nabla c - D_T c \cdot \nabla T \stackrel{s.s.}{=} 0$$

$$v = -\frac{D_T}{D} \nabla T$$

IR $S_T = \frac{D_T}{D} \left[\frac{1}{k} \right]$

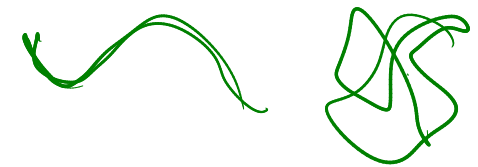
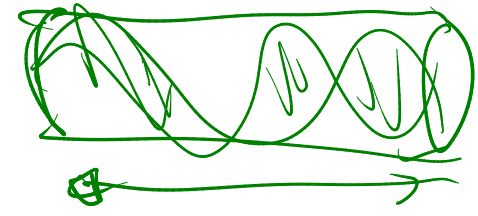
Accumulation by temperature gradients

Thermophoresis

Warm \rightarrow **Cold**

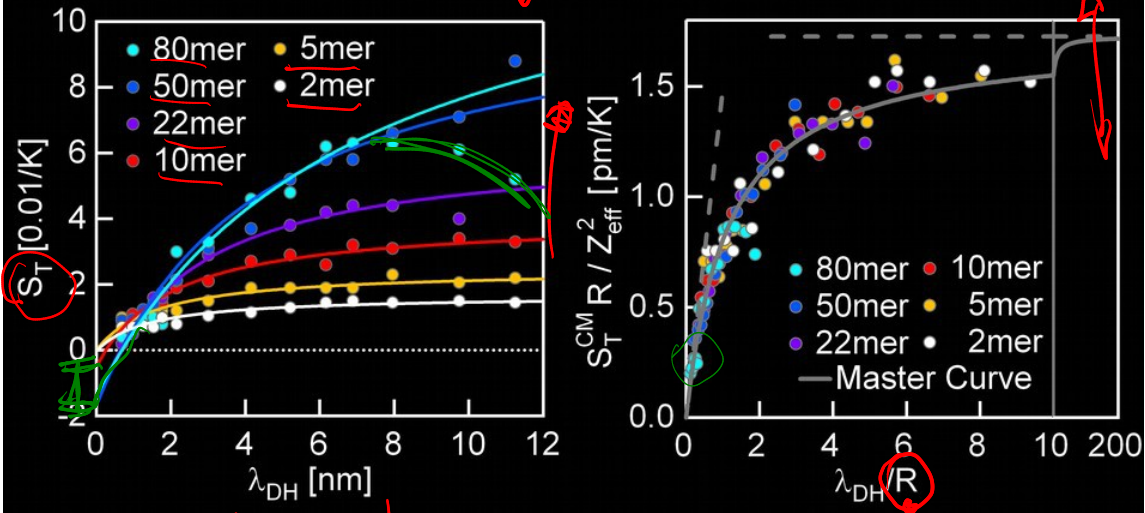
500mM

low ion concentration (mM)



R: Hydrodynamic radius

$$D = \frac{kT}{6\pi\eta R} f(T)$$



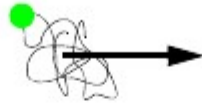
$$\frac{S_T^{CM} R}{Z_{eff}^2} = \frac{e^2 R / \lambda_{DH}}{16\pi k_B T^2 \epsilon_r \epsilon_0 (1 + R / \lambda_{DH})^2} \times \left(1 - \frac{\partial \ln \rho(T)}{\partial \ln T} - \frac{\partial \ln \epsilon_r(T)}{\partial \ln T} \left(1 + \frac{\lambda_{DH}}{R} \right) \right)$$

50% 50%

Accumulation by temperature gradients

Thermophoresis of DNA

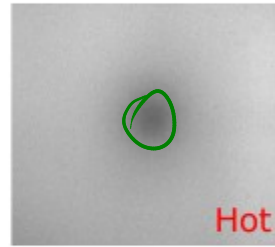
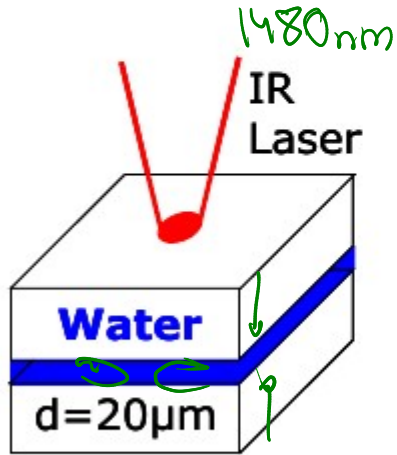
Warm



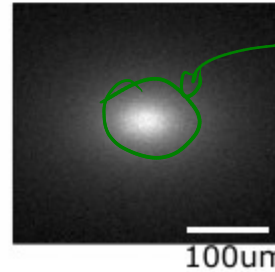
Cold

$$v = -D_T \nabla T$$

$$j = -D \nabla c - D_T c \nabla T$$



Temperature
Image
(z-average)



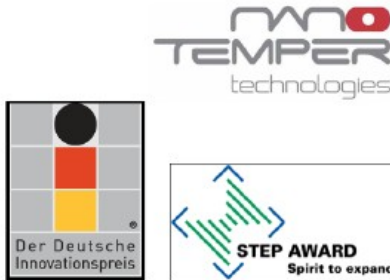
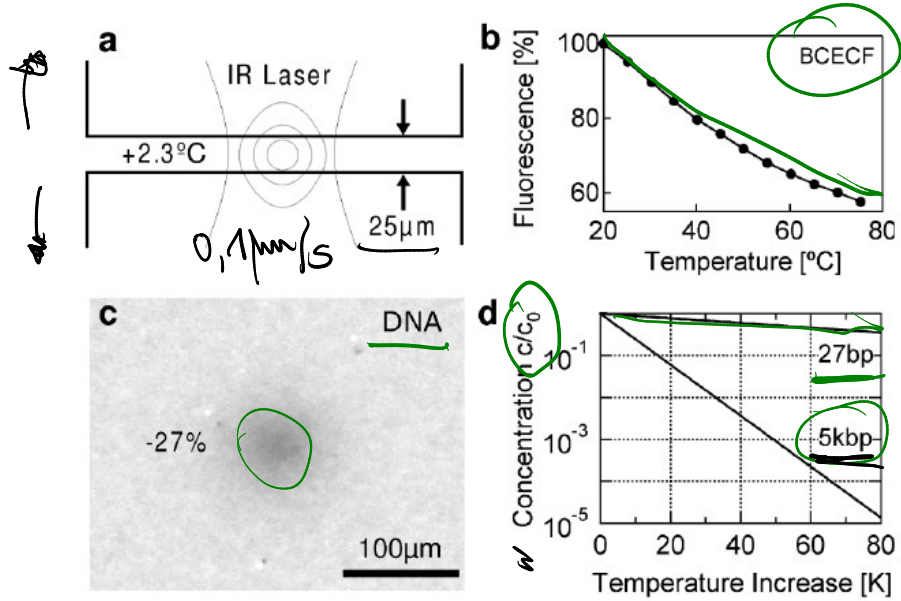
10K

Trapping of DNA by Thermophoretic Depletion and Convection

Dieter Braun* and Albert Libchaber

Center for Studies in Physics and Biology, Rockefeller University, New York, New York 10021

(Received 2 May 2002; published 14 October 2002)



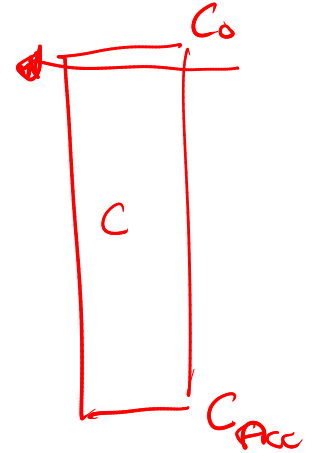
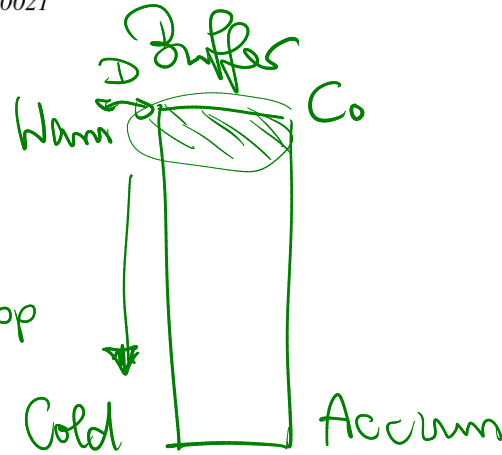
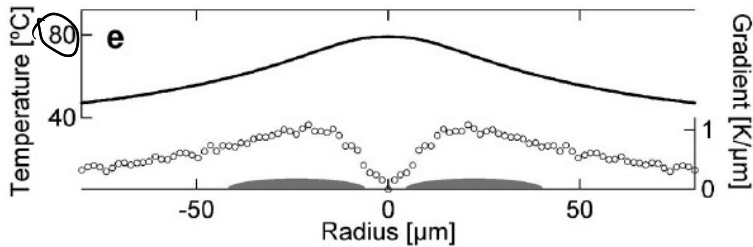
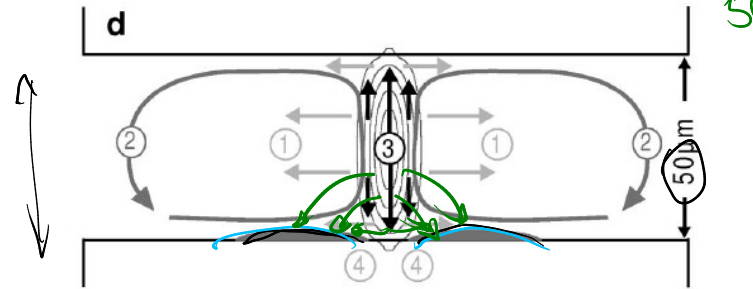
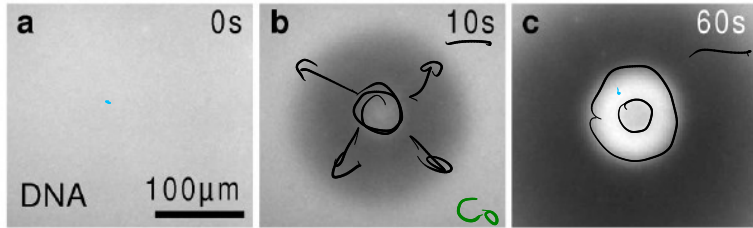
Accumulation by temperature gradients

Trapping of DNA by Thermophoretic Depletion and Convection

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Single Nucleotides
777

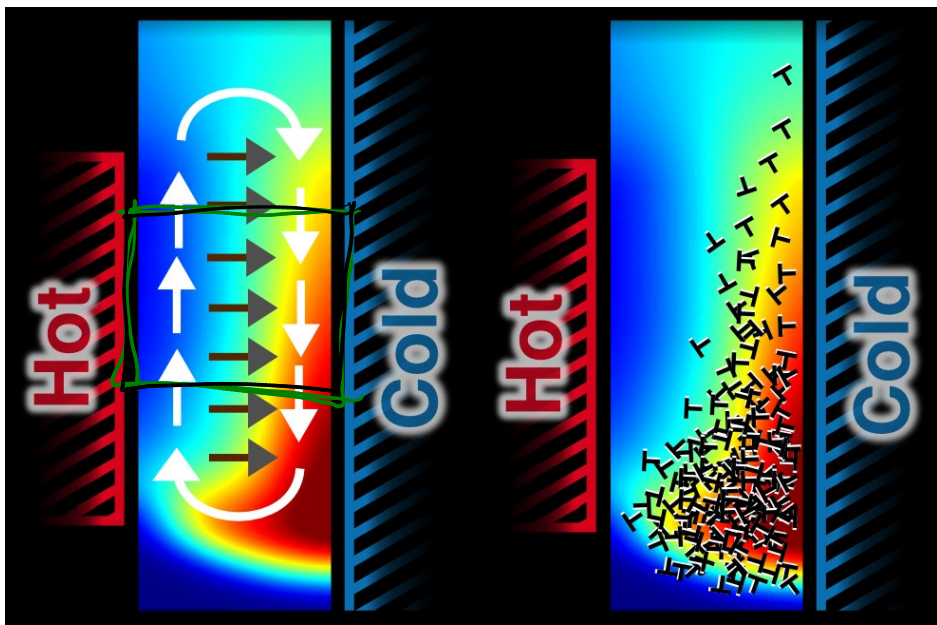
• Dry 20mM

$$C_{Acc} = 10^{10} \cdot C_0$$

$$\int C_0 = \text{const.}$$

Accumulation by temperature gradients

Accumulation by heat flow



Convection
Thermophoresis

PRL 2002, PNAS
2007, NanoLetters
2009, PRL 2010,
APL 2015, PCCP
2016

$L = 15\text{mm}$ to
 $\approx c/c_0 = 10$

$d = 150\mu\text{m}$

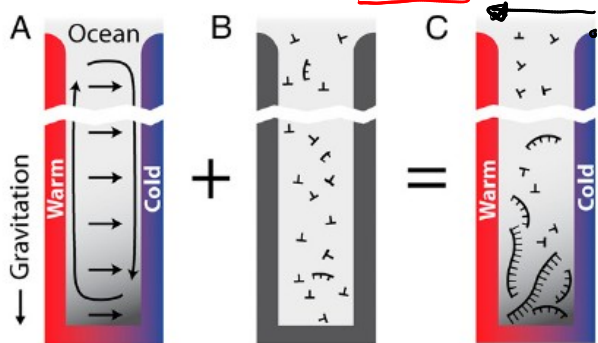
2x
2x
2x
Cold
Height
 c/c_0
Too fast flow
- d too large
- D too small
(molecules is too large)
 $C = c_0 \exp(-S_T d / T)$
 $C = c_0 \exp(+S_T L / d T)$
0.42

10x Simulation with Comsol

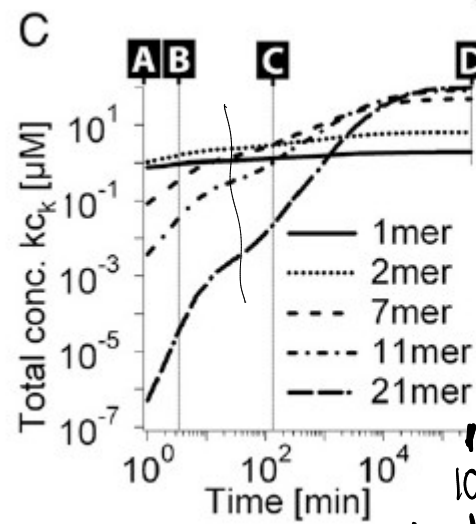
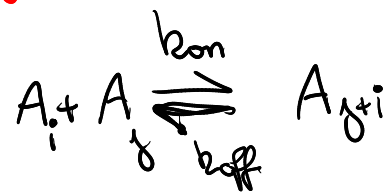
Accumulation and Polymerization

Escalation of polymerization in a thermal gradient

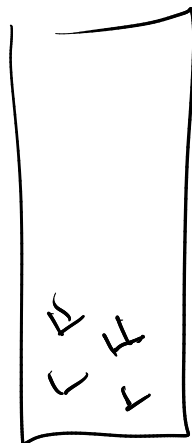
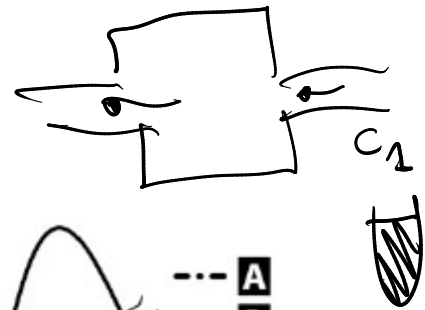
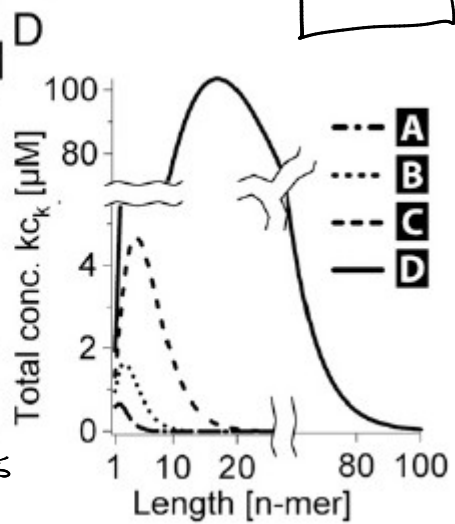
Christof B. Mast^{a,1}, Severin Schink^{b,1}, Ulrich Gerland^b, and Dieter Braun^{a,2}



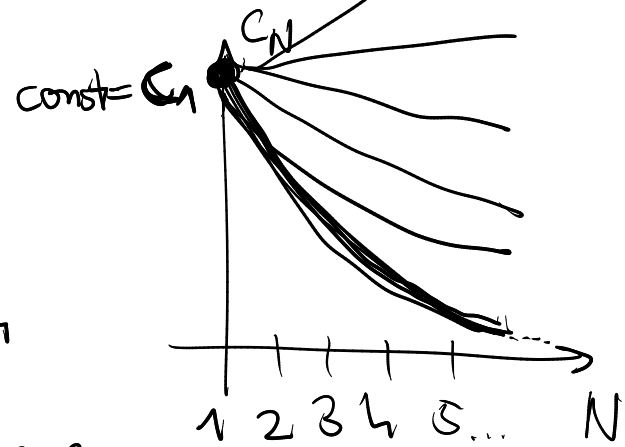
FRET → State of polymerization
80mer
25mer
"Monomer"



70 days



$$C_{tot} = \sum_{i=1}^{\infty} C_i$$

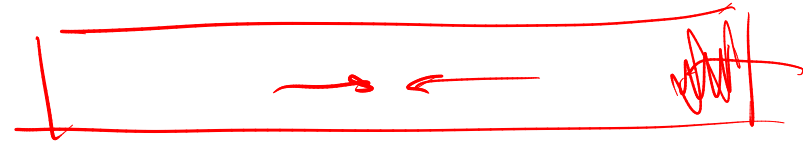
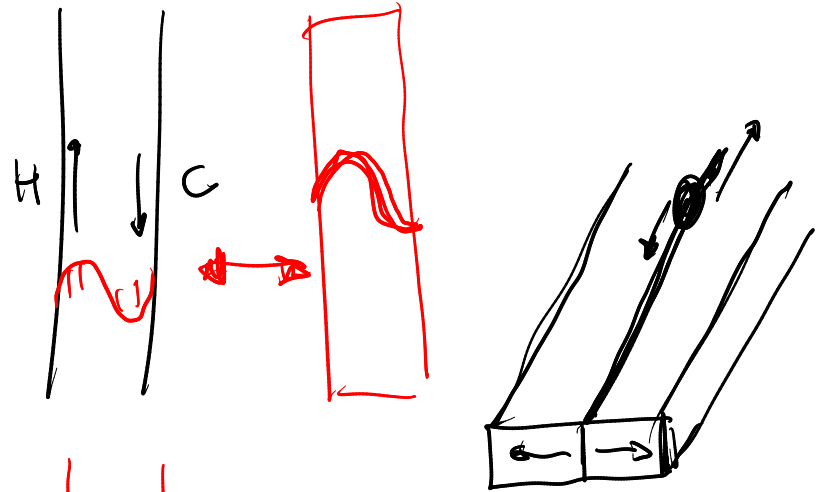
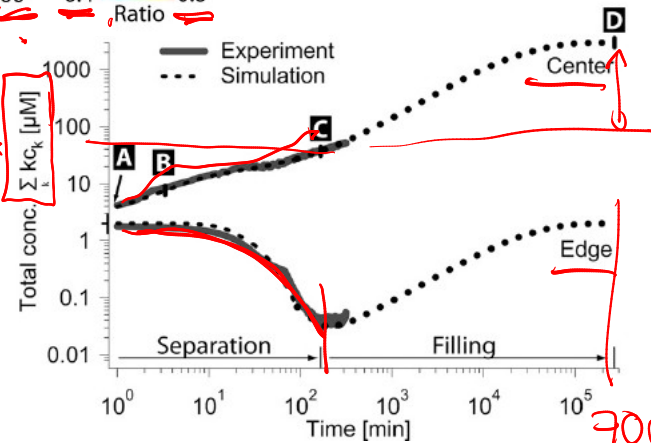
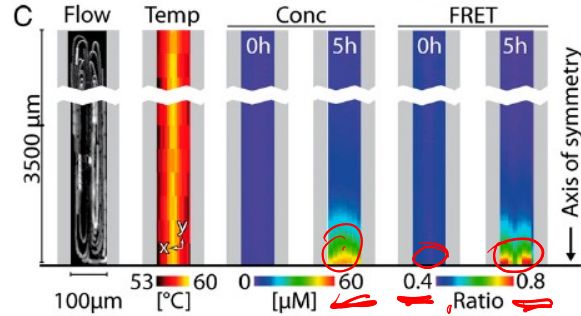
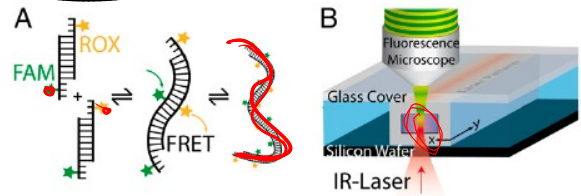


$\sigma_T \sim \sqrt{N}$
 ↑
 Length of Polymer

Accumulation and Polymerization

Escalation of polymerization in a thermal gradient

Christof B. Mast^{a,1}, Severin Schink^{b,1}, Ulrich Gerland^b, and Dieter Braun^{a,2}



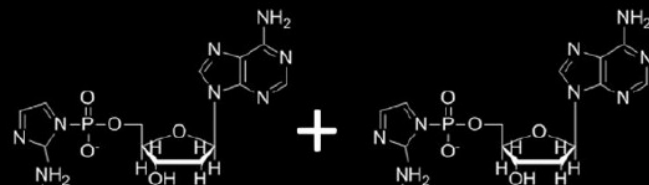
700d

Accumulation and Polymerization

Back @ 8.45



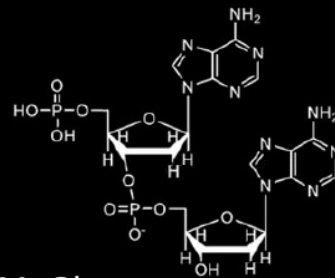
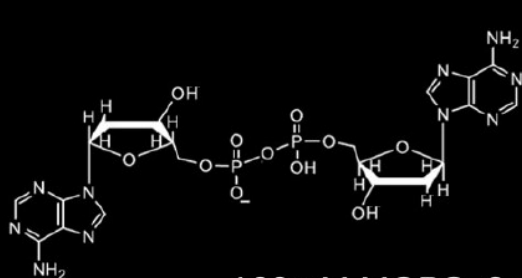
Christina Dirscherl



Less Concentration

Pyrophosphate Oligomers

Linear Oligomers



100mM MOPS, 2mM MgCl₂
150 / 15 / 1.5mM Amino-ImpdA
pH 6.5 (NaOH), Time = 24h
a) Isothermal 8 / 20 / 30°C
b) Trap with T = 8 - 30°C

Initial Steady state

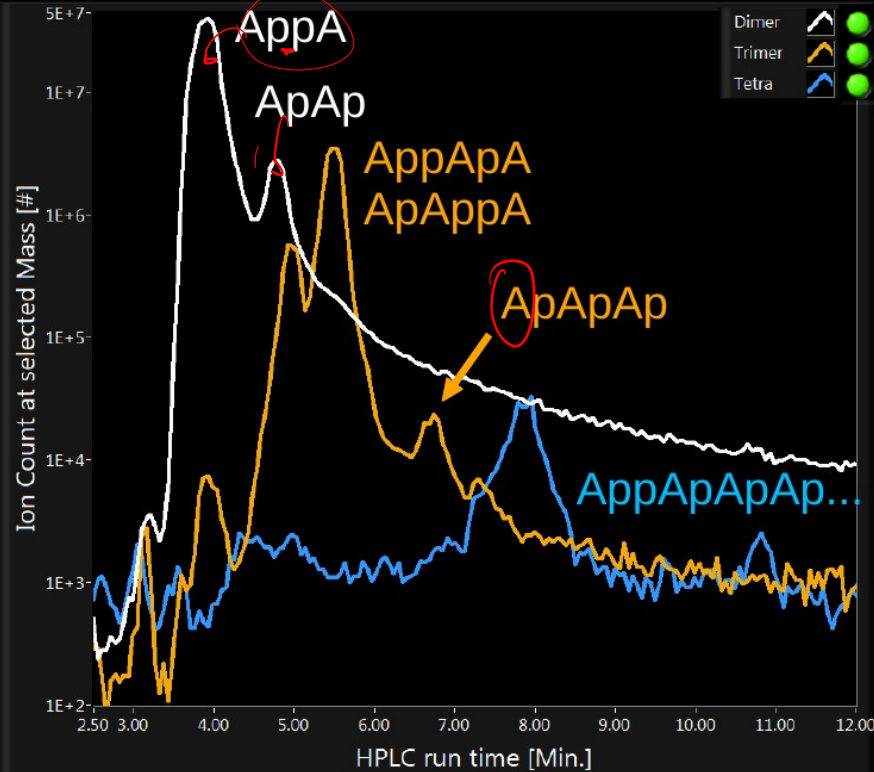
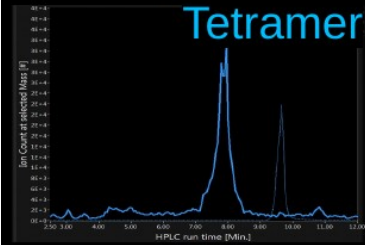
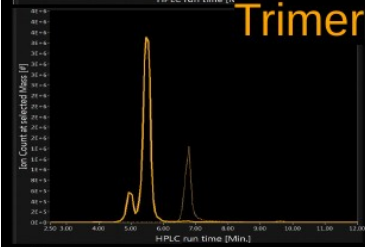
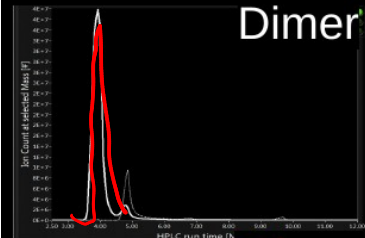


Accumulation and Polymerization

Boosting polymerization by thermal trap

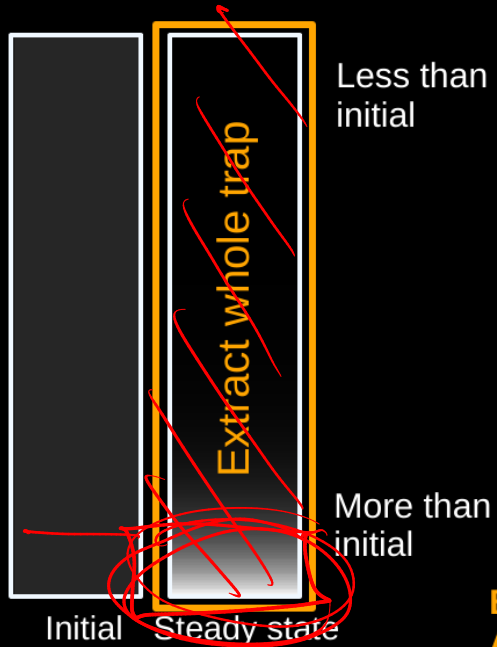
Detection in HPLC-ESI-TOF

Ion pairing reverse phase HPLC
(H₂O, Methanol, TEA, HFIP)

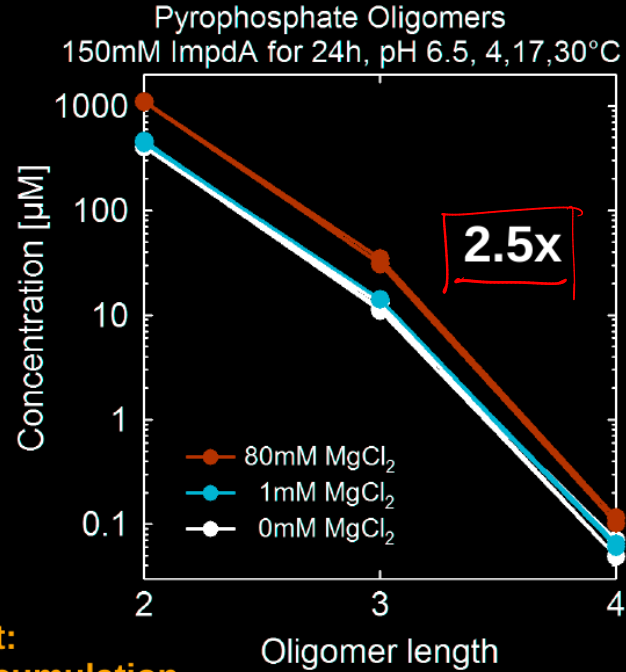


Accumulation and Polymerization

Boosting polymerization by thermal trap

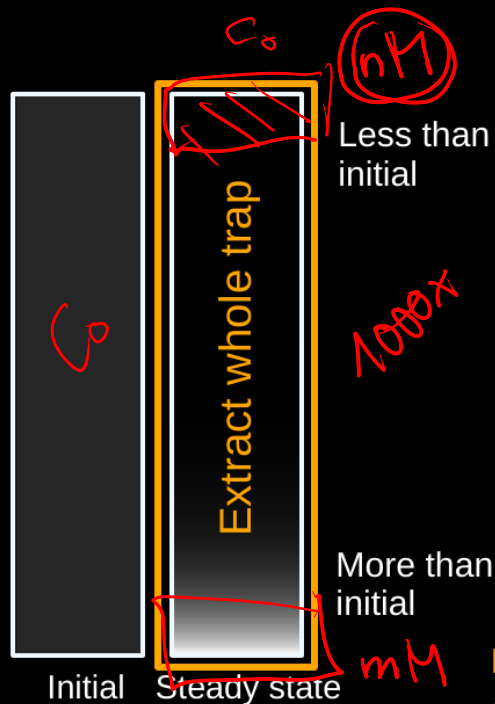


But:
Accumulation.
of ImpA and Mg

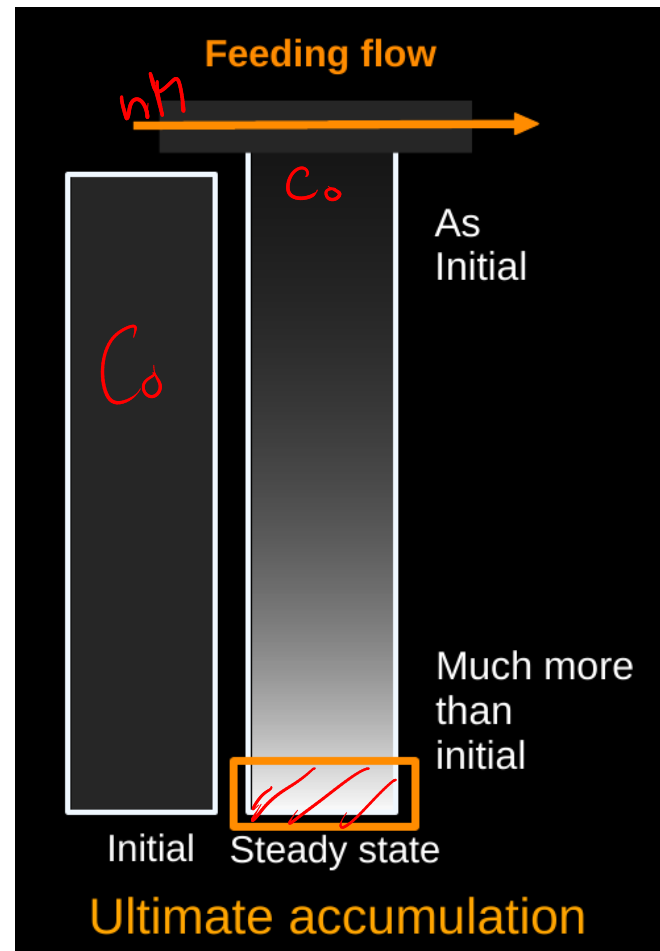
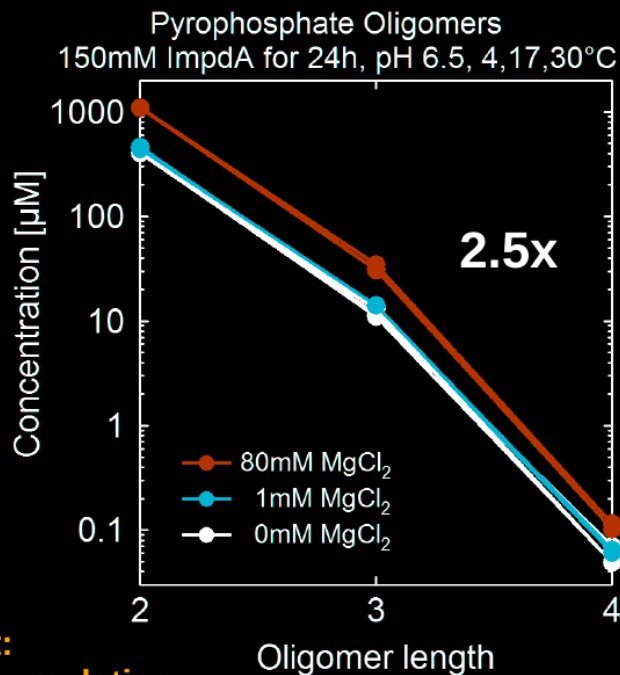


Accumulation and Polymerization

Boosting polymerization by thermal trap



But:
Accumulation.
of ImpA and Mg

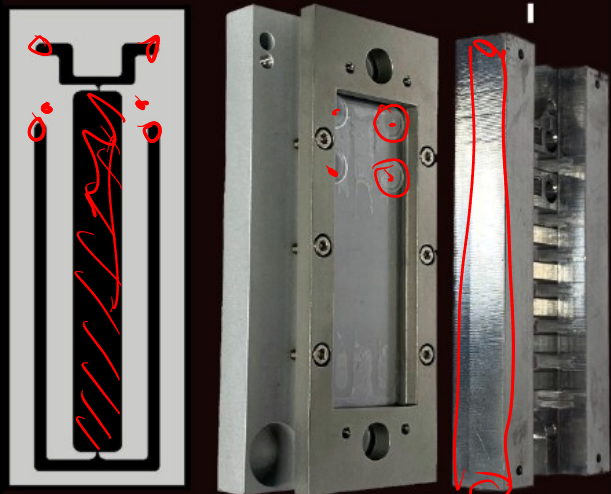


Accumulation and Polymerization



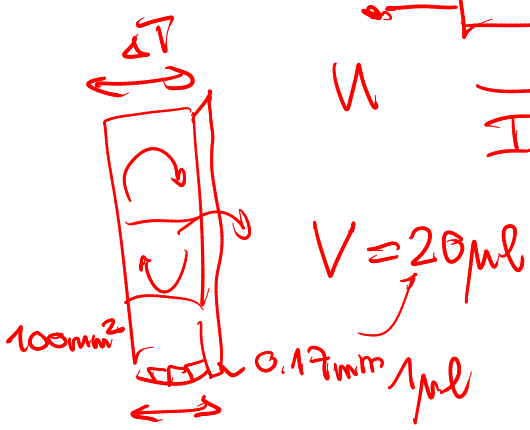
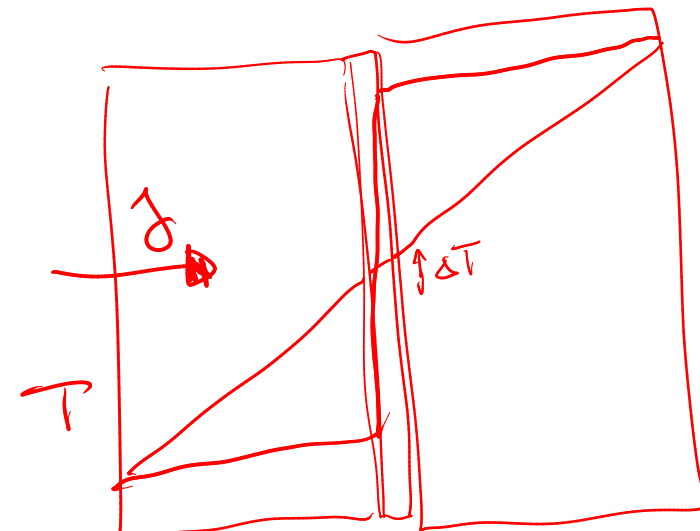
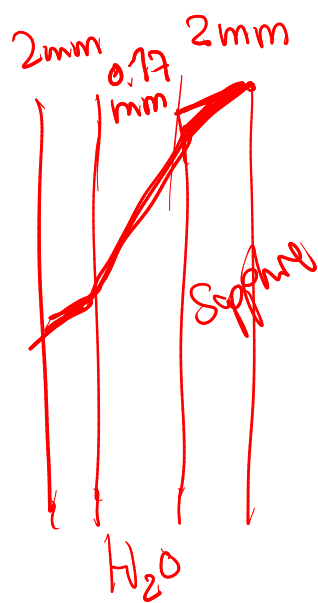
Christof Mast

Teflon cooled microfluidics electr. heater



Teflon foil microfluidics
 Thickness 120...500 μm
 $V = 10..50\mu\text{l}$, $p < 20\text{atm}$

10 mm



Accumulation and Polymerization



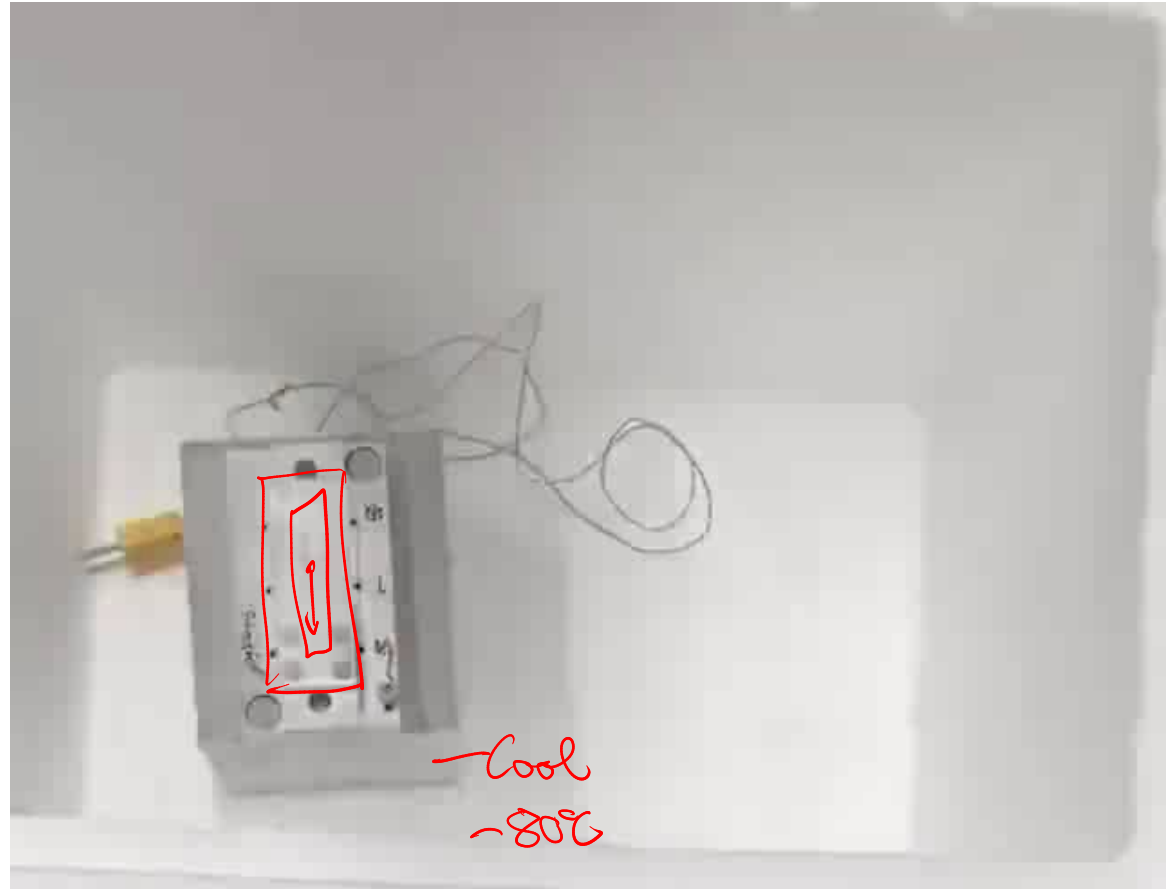
Christof
Mast

cooled
microfluidics electr.
heater



Teflon foil microfluidics
Thickness 120...500 μ m
 $V = 10..50\mu$ l, $p < 20$ atm

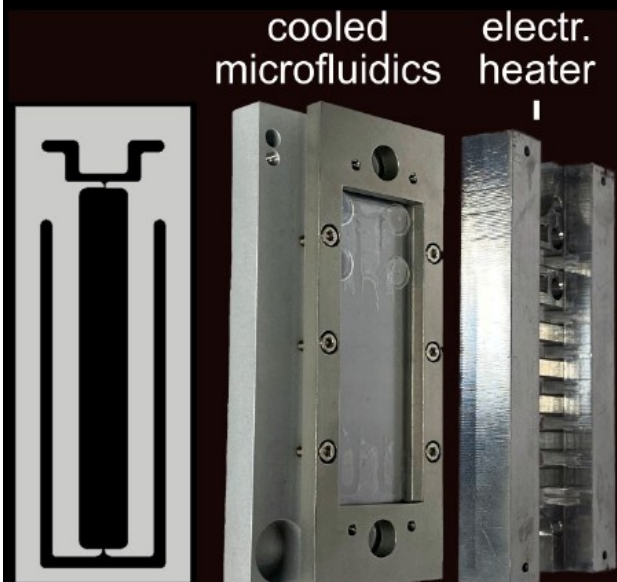
10 mm



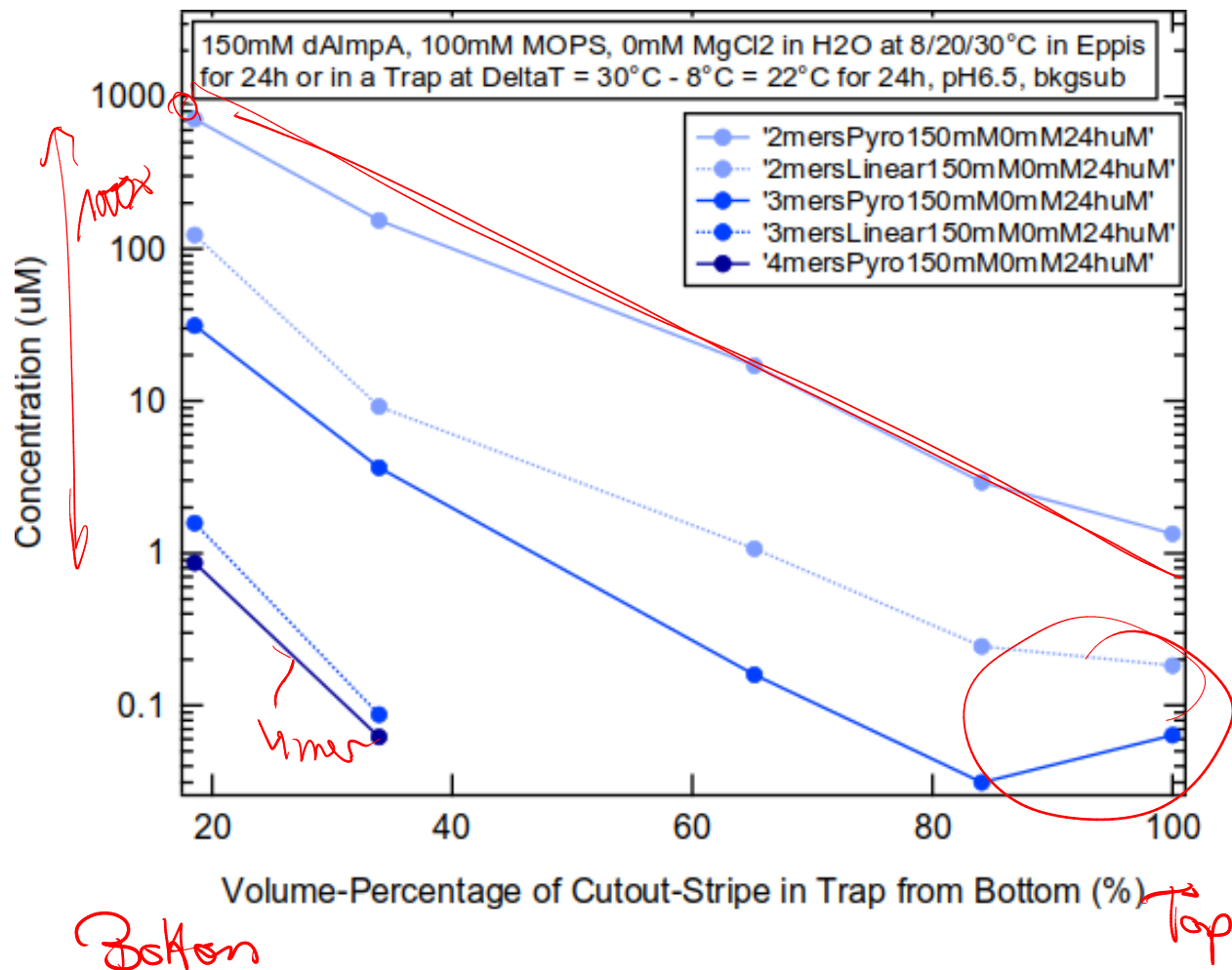
Accumulation and Polymerization



Christof Mast



Teflon foil microfluidics
Thickness 120...500 μ m
V = 10..50 μ l, p < 20atm



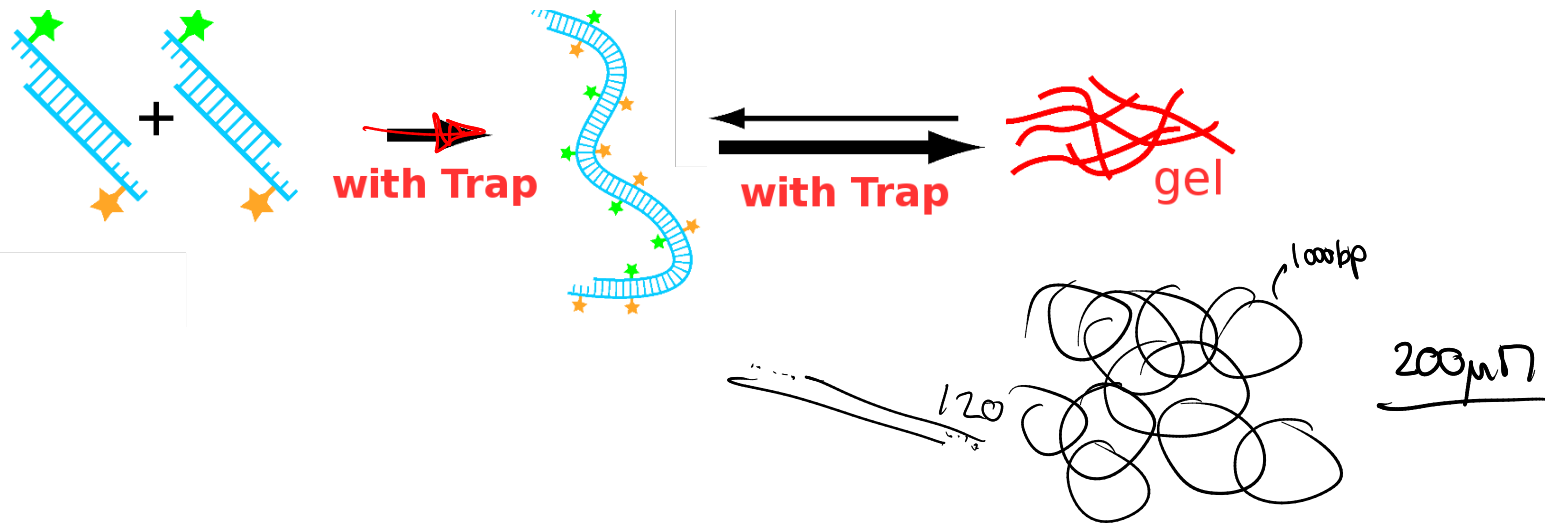
Accumulation and Polymerization leads to gels

 **DNA Hydrogels** Hot Paper

International Edition: DOI: 10.1002/anie.201601886
German Edition: DOI: 10.1002/ange.201601886

Heat-Flow-Driven Oligonucleotide Gelation Separates Single-Base Differences

Matthias Morasch, Dieter Braun, and Christof B. Mast*



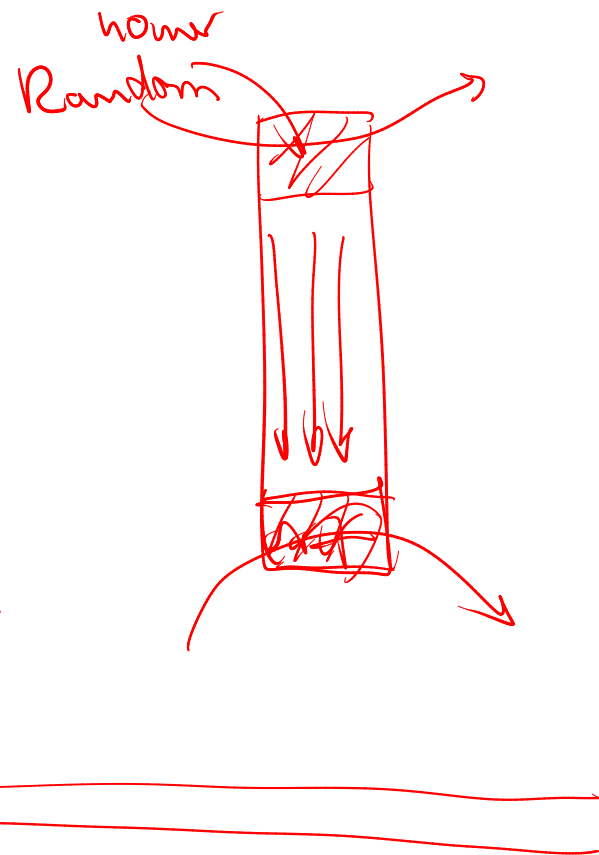
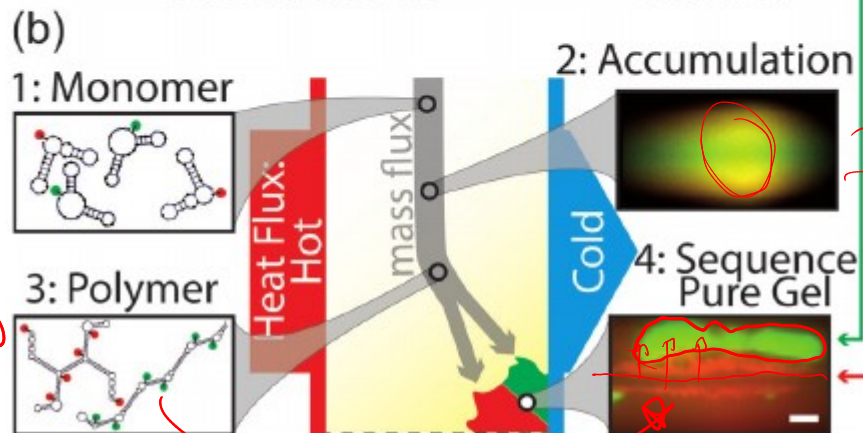
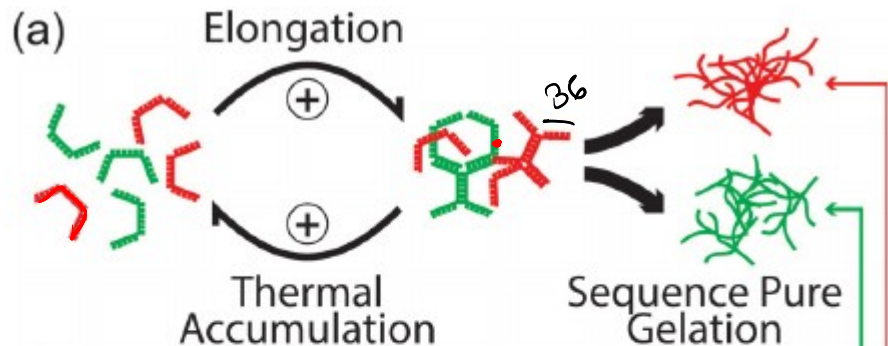
Accumulation and Polymerization leads to gels

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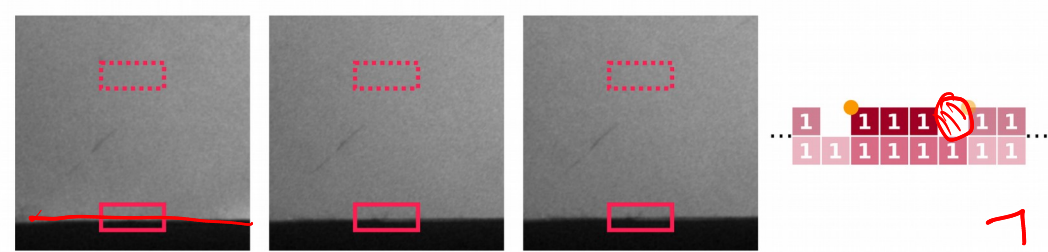
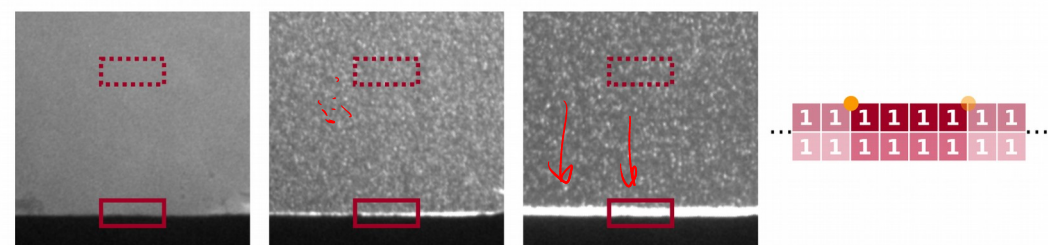
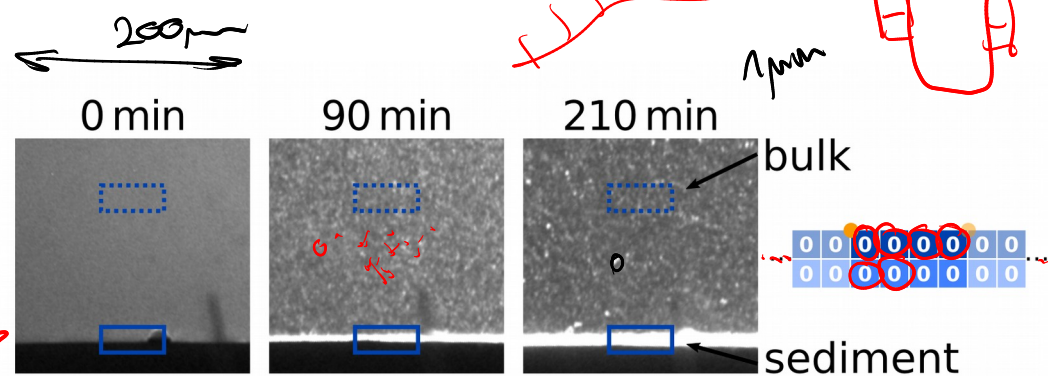
Heat-Flow-Driven Oligonucleotide Gelation Separates Single-Base Differences

Matthias Morasch, Dieter Braun, and Christof B. Mast*



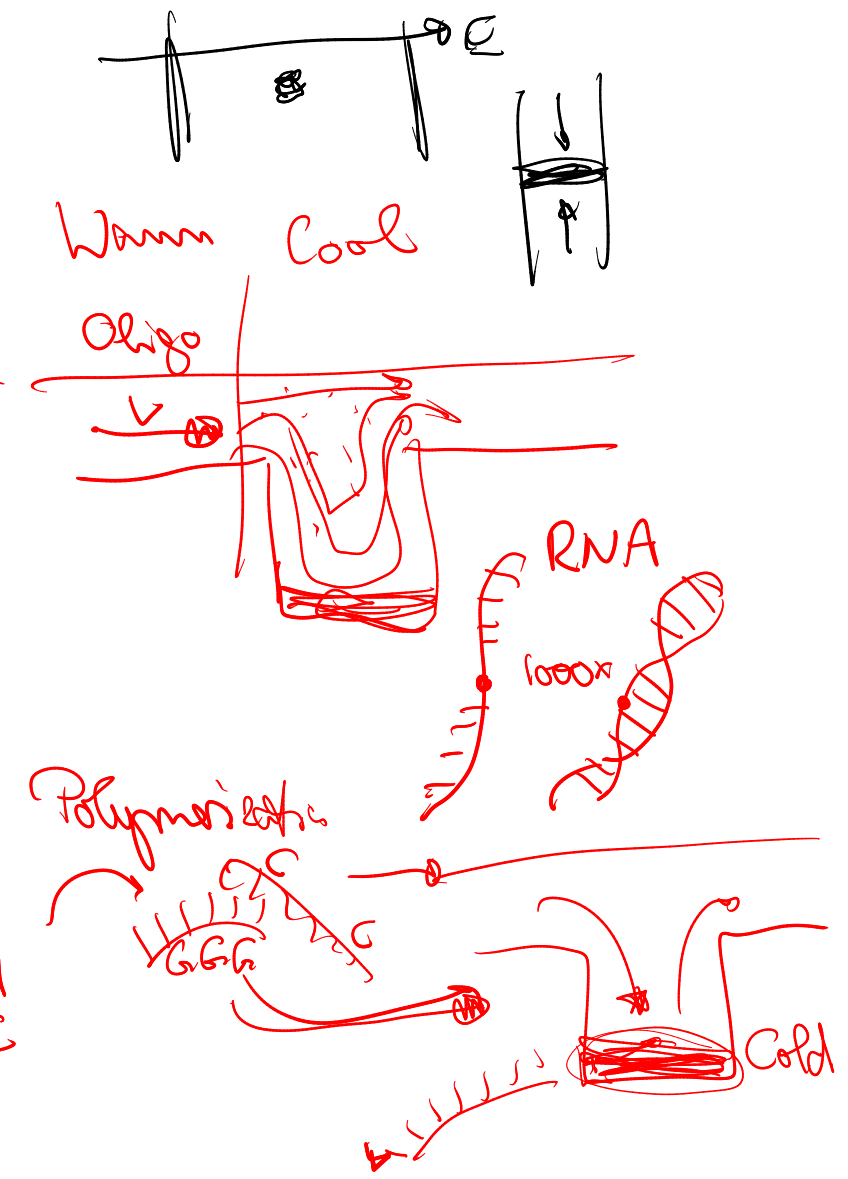
Gelation and sedimentation

a

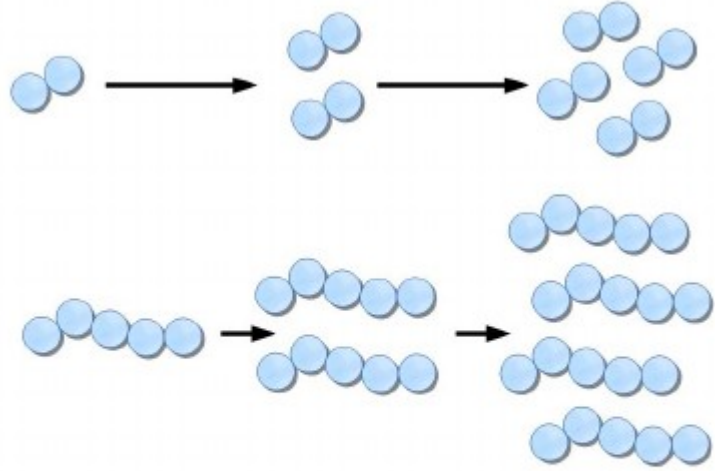


$2^{12} = 4096$

77
G,C

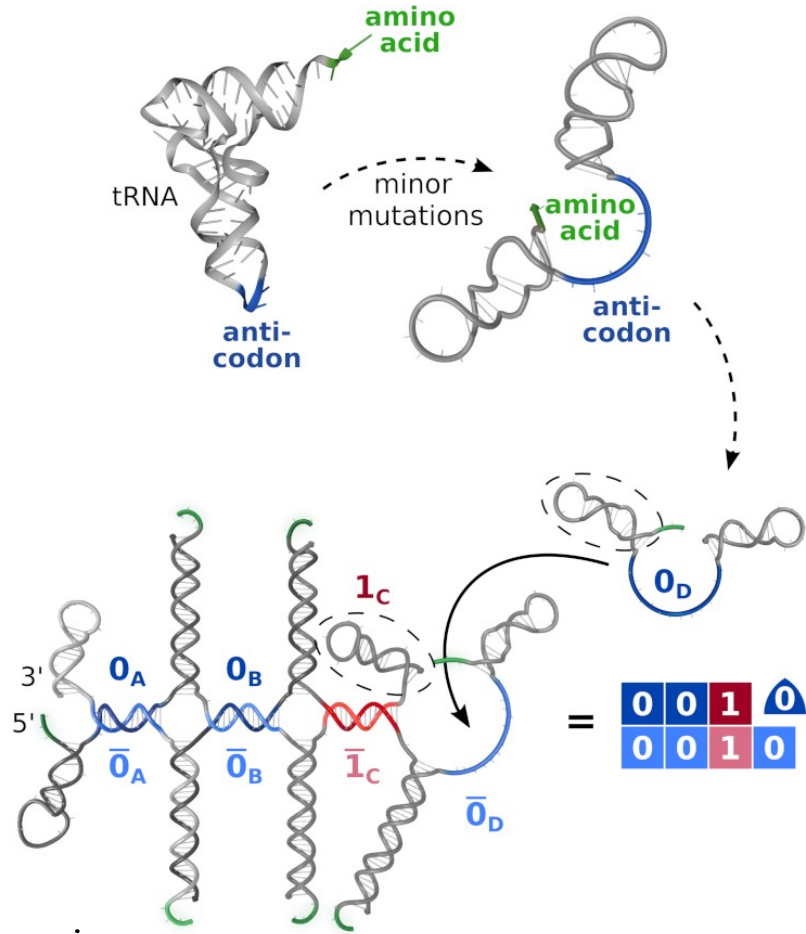


Replication driven by temperature gradients

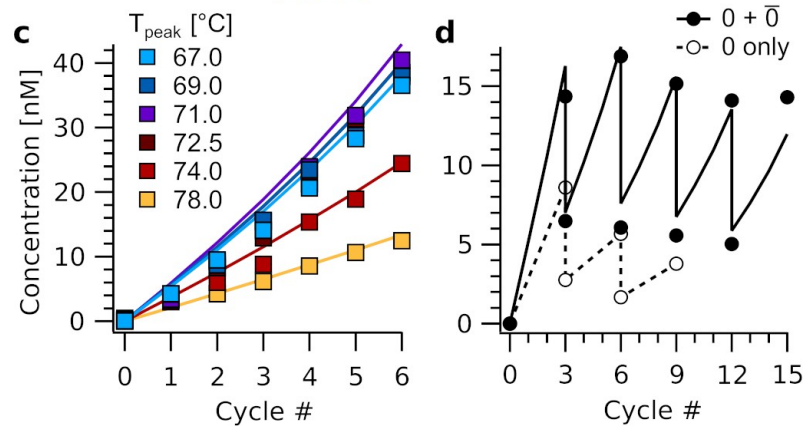
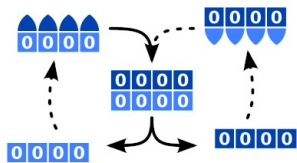
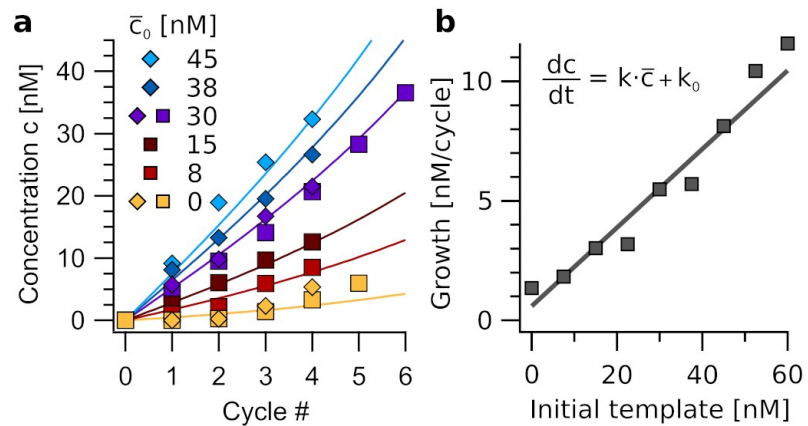


**Replication
by Convection**

Replication driven by temperature gradients

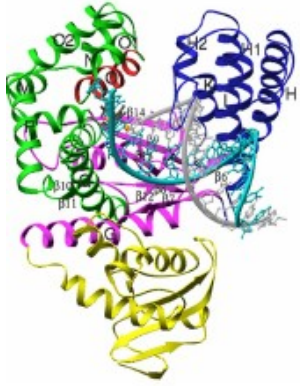


Replication driven by temperature gradients

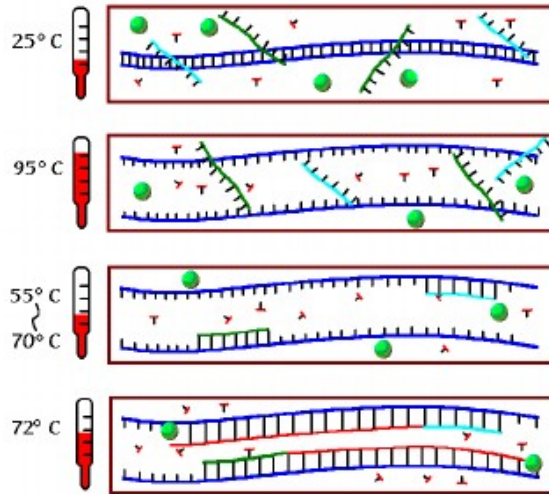


Replication driven by temperature gradients

Polymerase Chain Reaction (PCR)

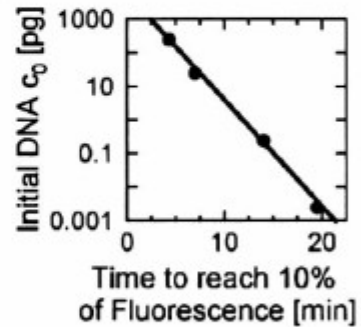
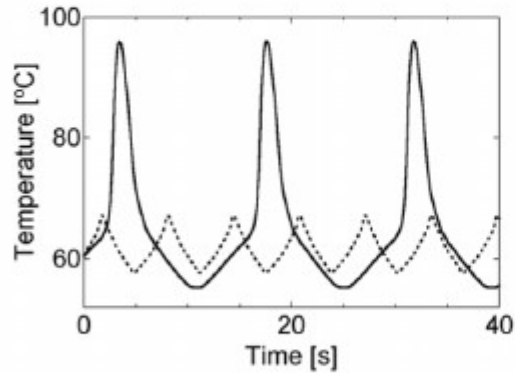
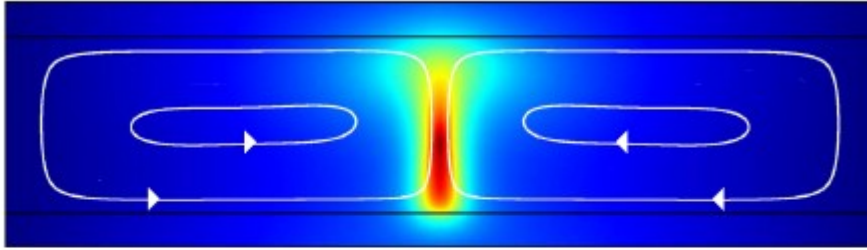


Taq Polymerase



Replication driven by temperature gradients

Replication by Convection (PCR)



Length independent Replication
(80-2000 base pairs)

Braun, Goddard & Libchaber, PRL 91, 158103 (2003)

Replication only by RNA

to be submitted to PRL

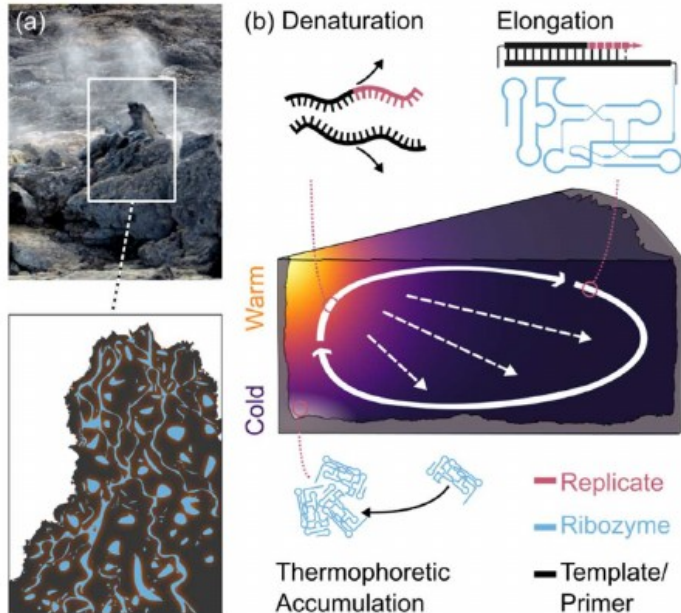
A THERMAL HABITAT FOR RNA AMPLIFICATION AND ACCUMULATION

Lorenz M. R. Keil^{a#}, Annalena Salditt^{a#}, David P. Horning^{b#},
Christof B. Mast^a, Gerald F. Joyce^b & Dieter Braun^{a*}

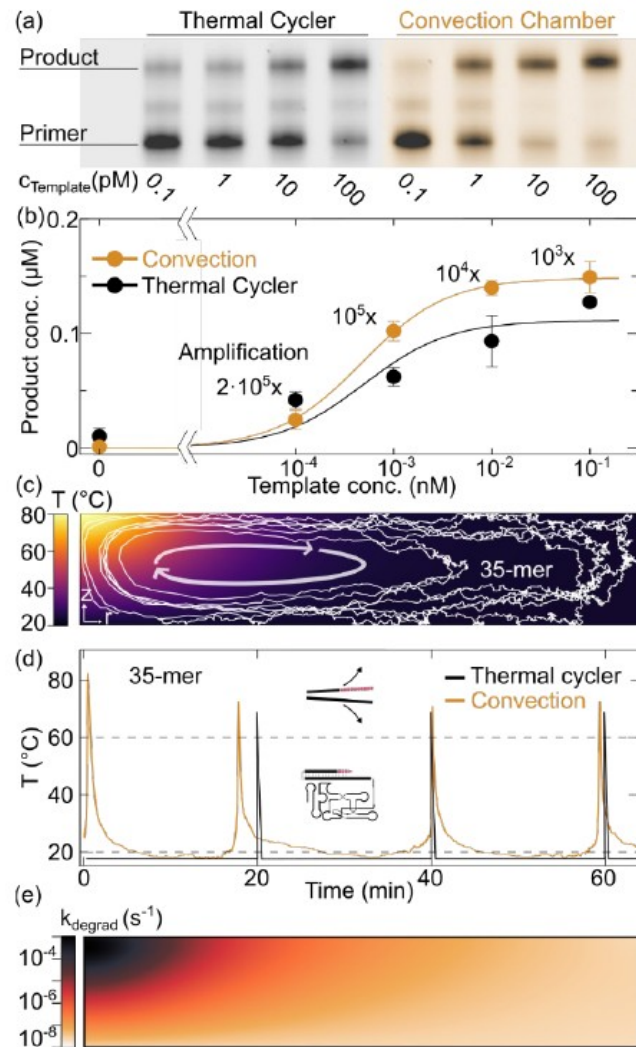
Affiliations: ^aSystems Biophysics, Physics Department, Center for Nanoscience,
Ludwig-Maximilians-Universität München, 80799 Munich, Germany
^bThe Salk Institute, 10010 N. Torrey Pines Road, La Jolla, CA 92037

* Corresponding author. Email: dieter.braun@lmu.de; Phone: +49-89-2180-1484

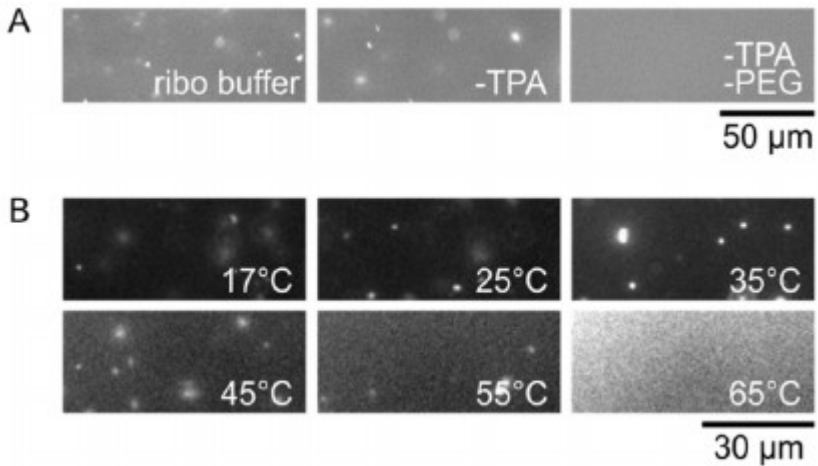
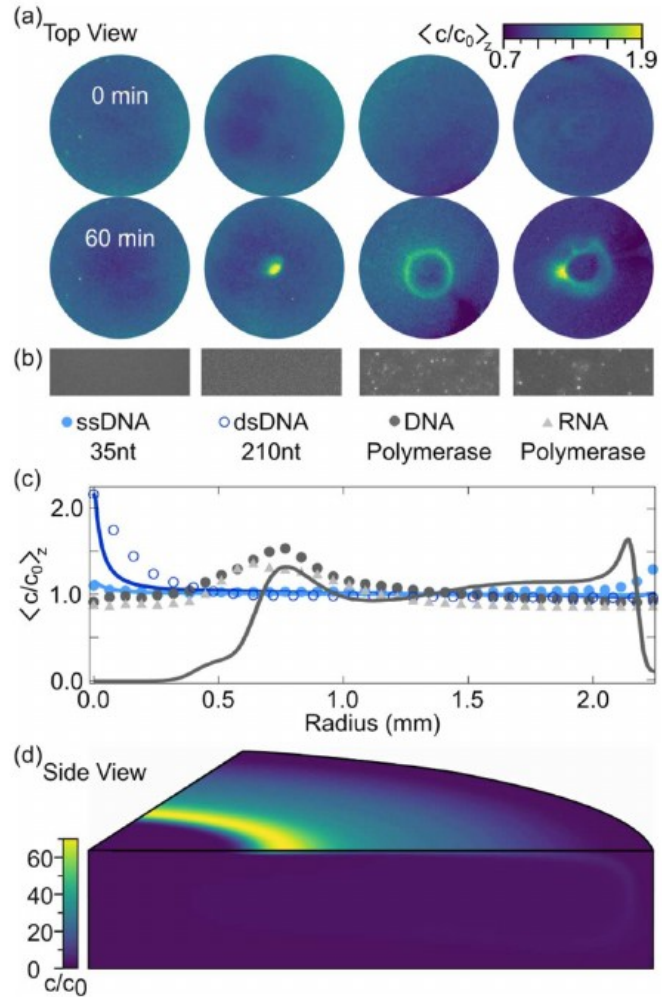
Contributed equally



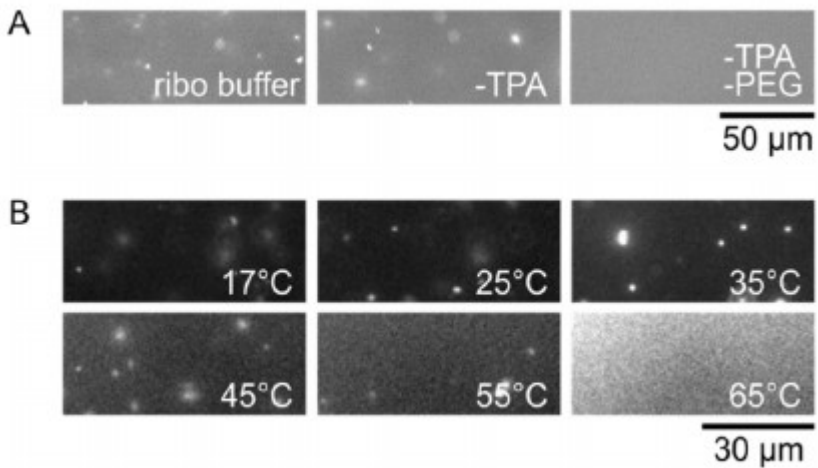
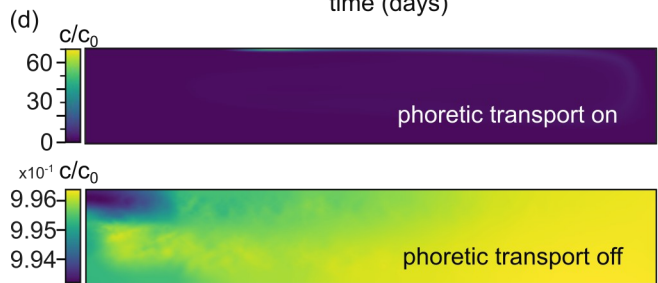
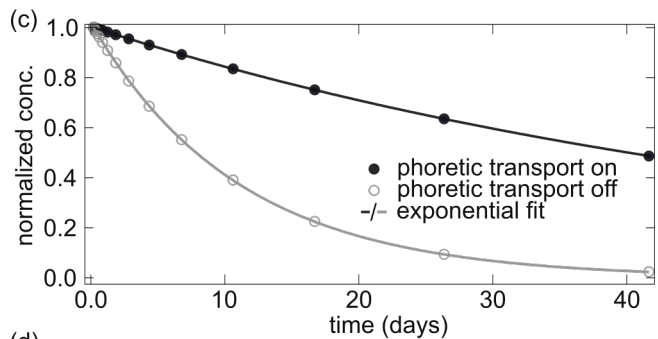
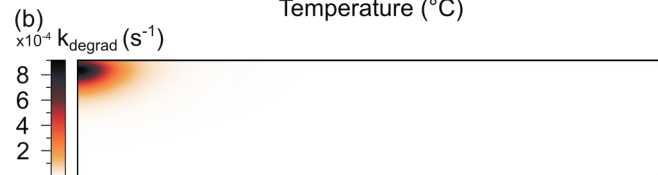
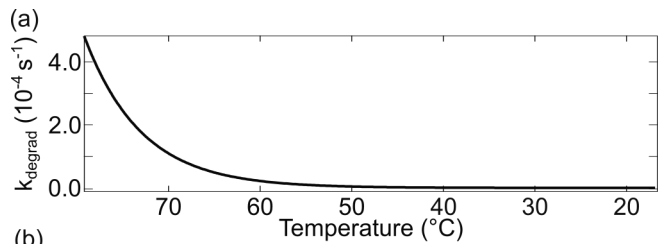
Replication only by RNA



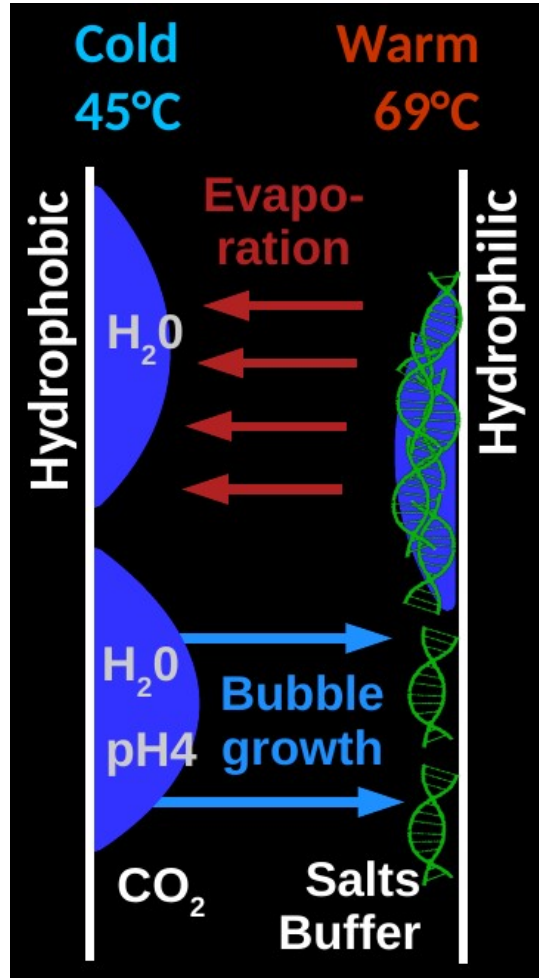
Replication only by RNA



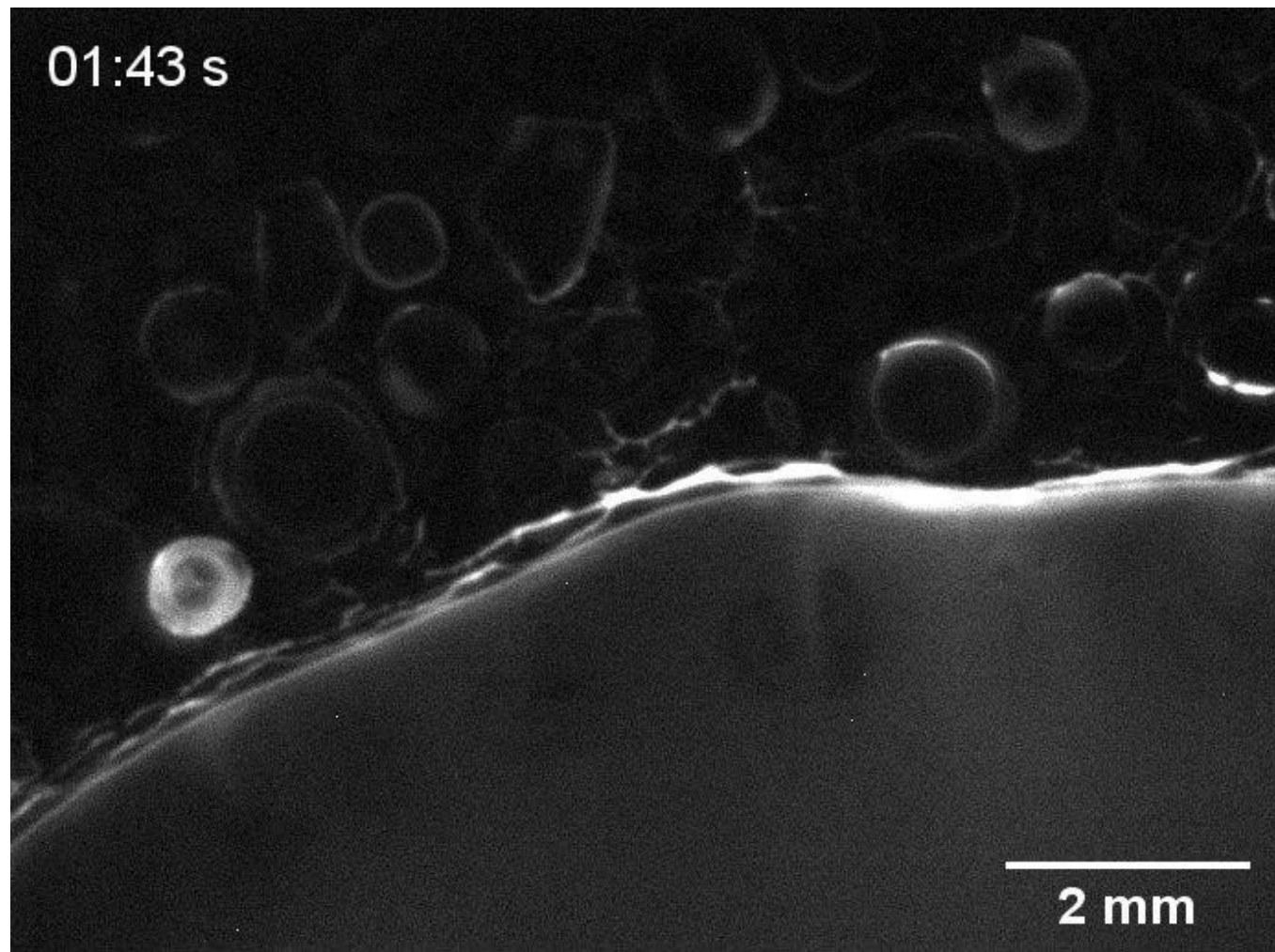
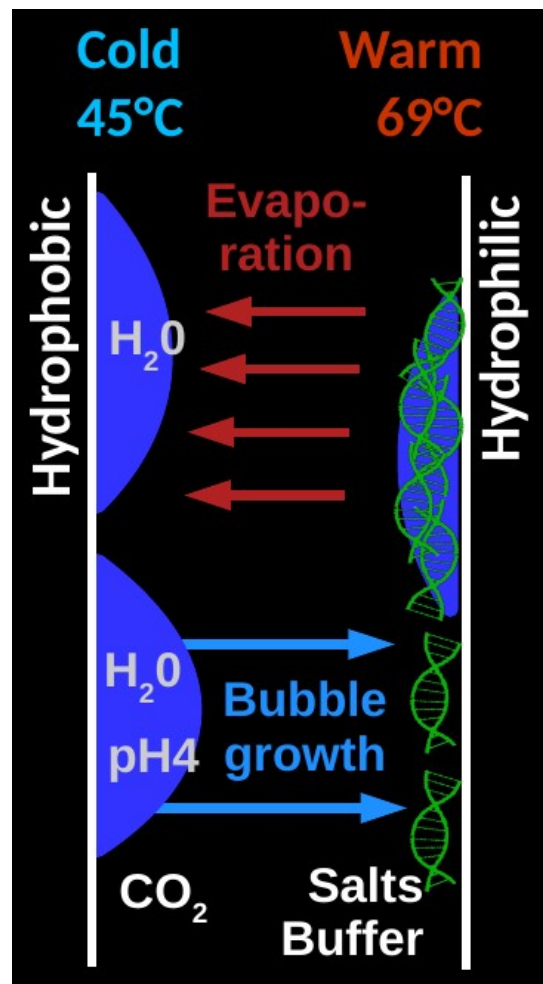
Protection by accumulation



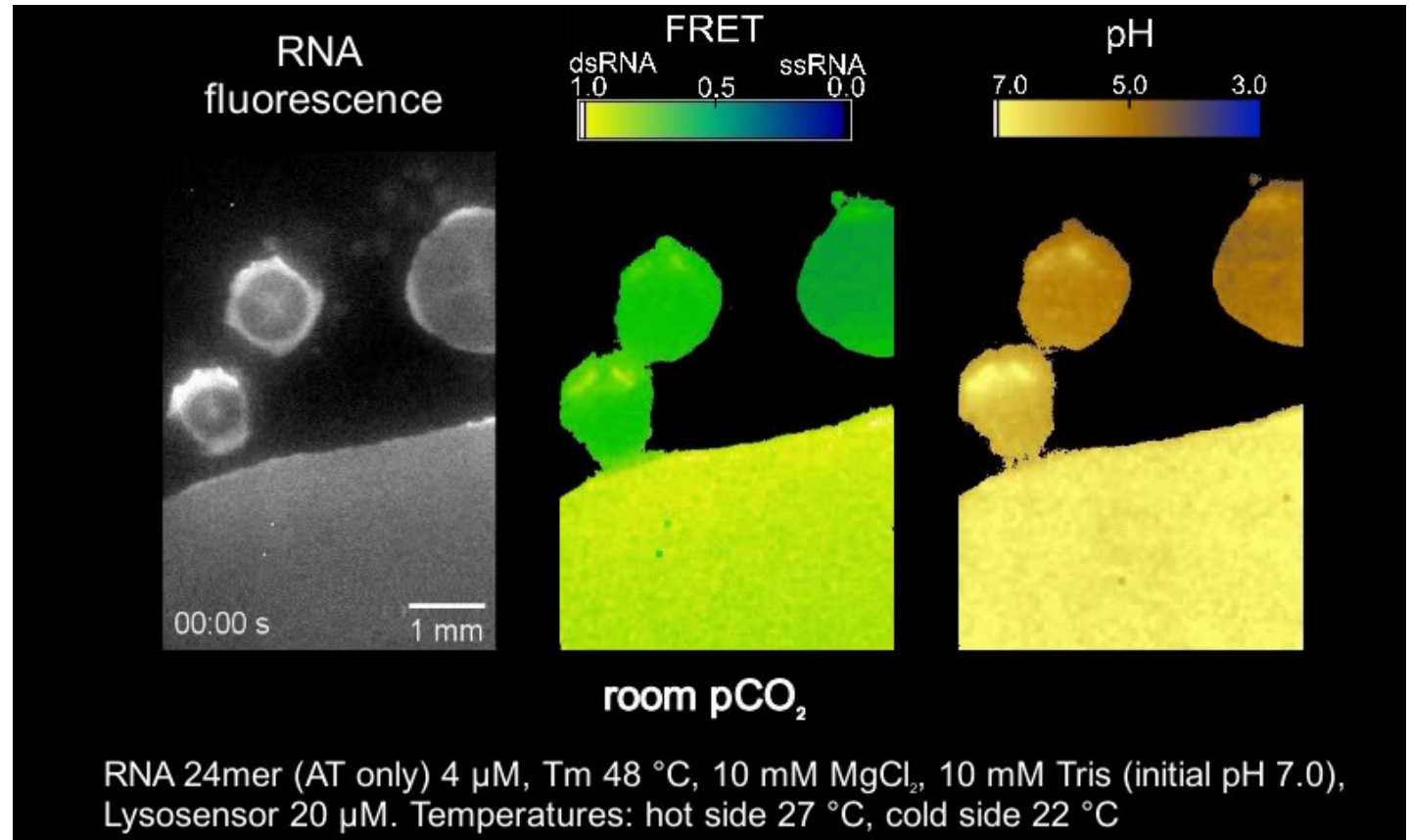
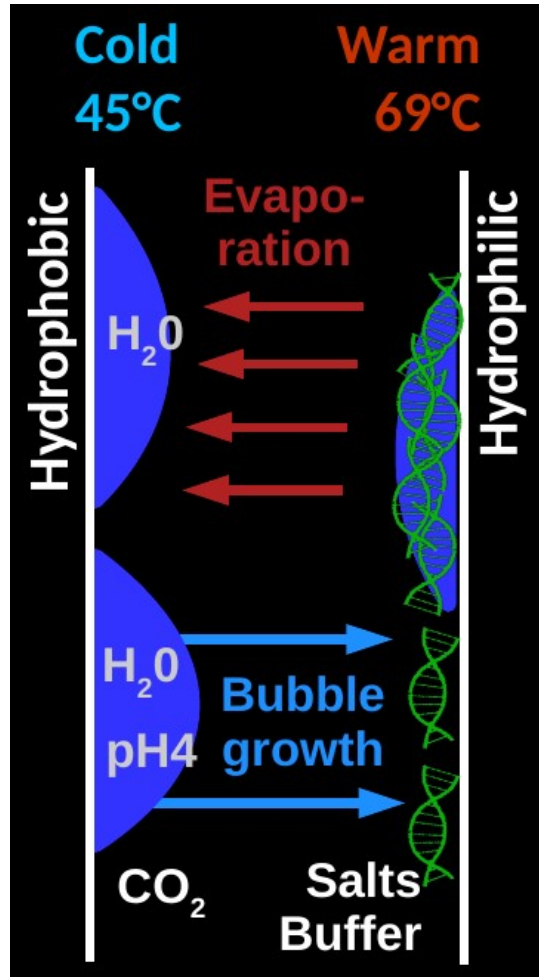
Fog PCR



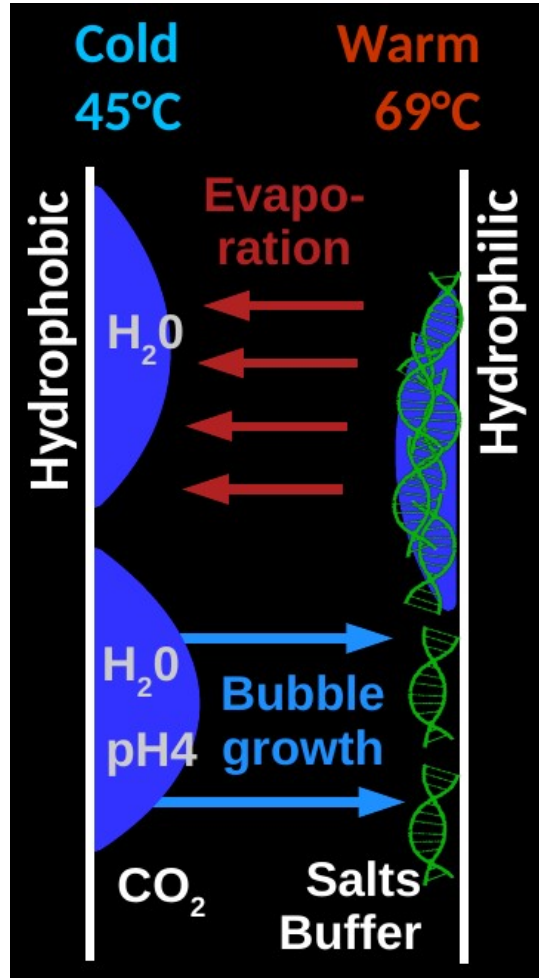
Fog PCR



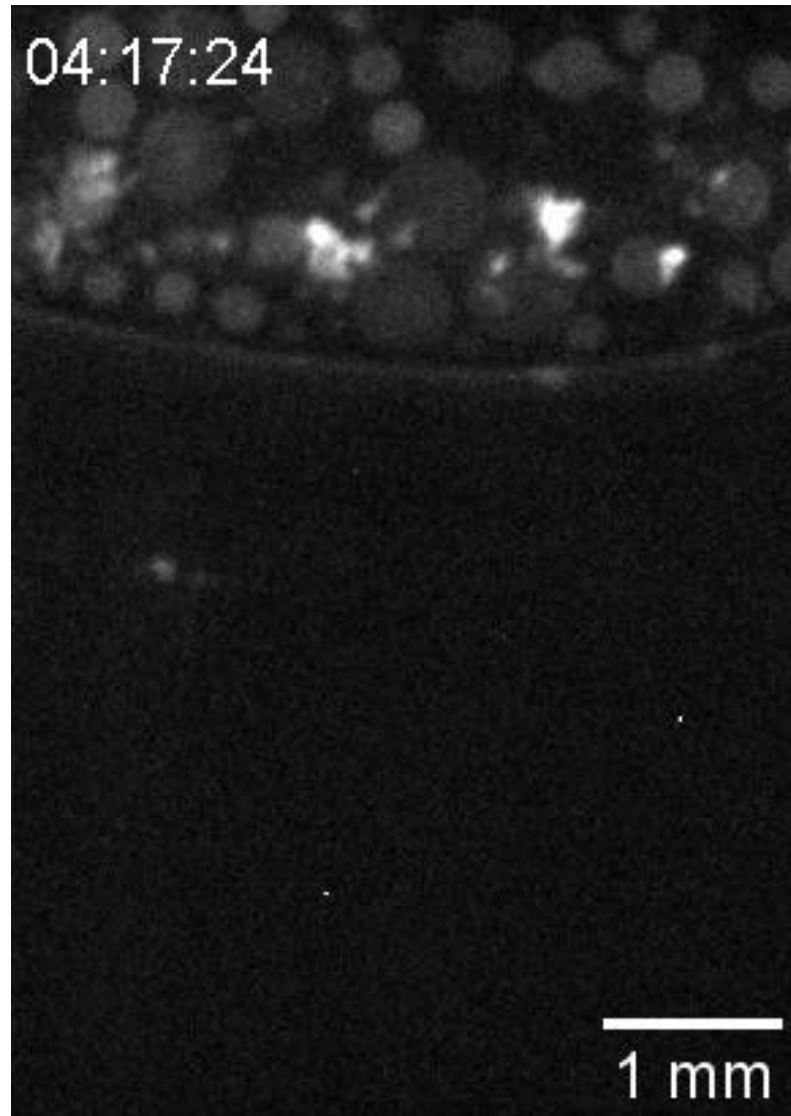
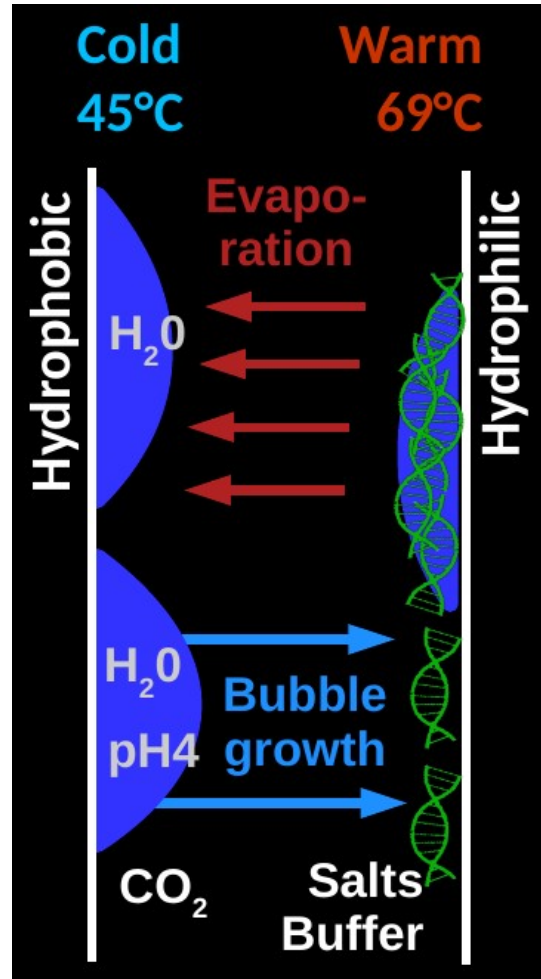
Fog PCR



Fog PCR



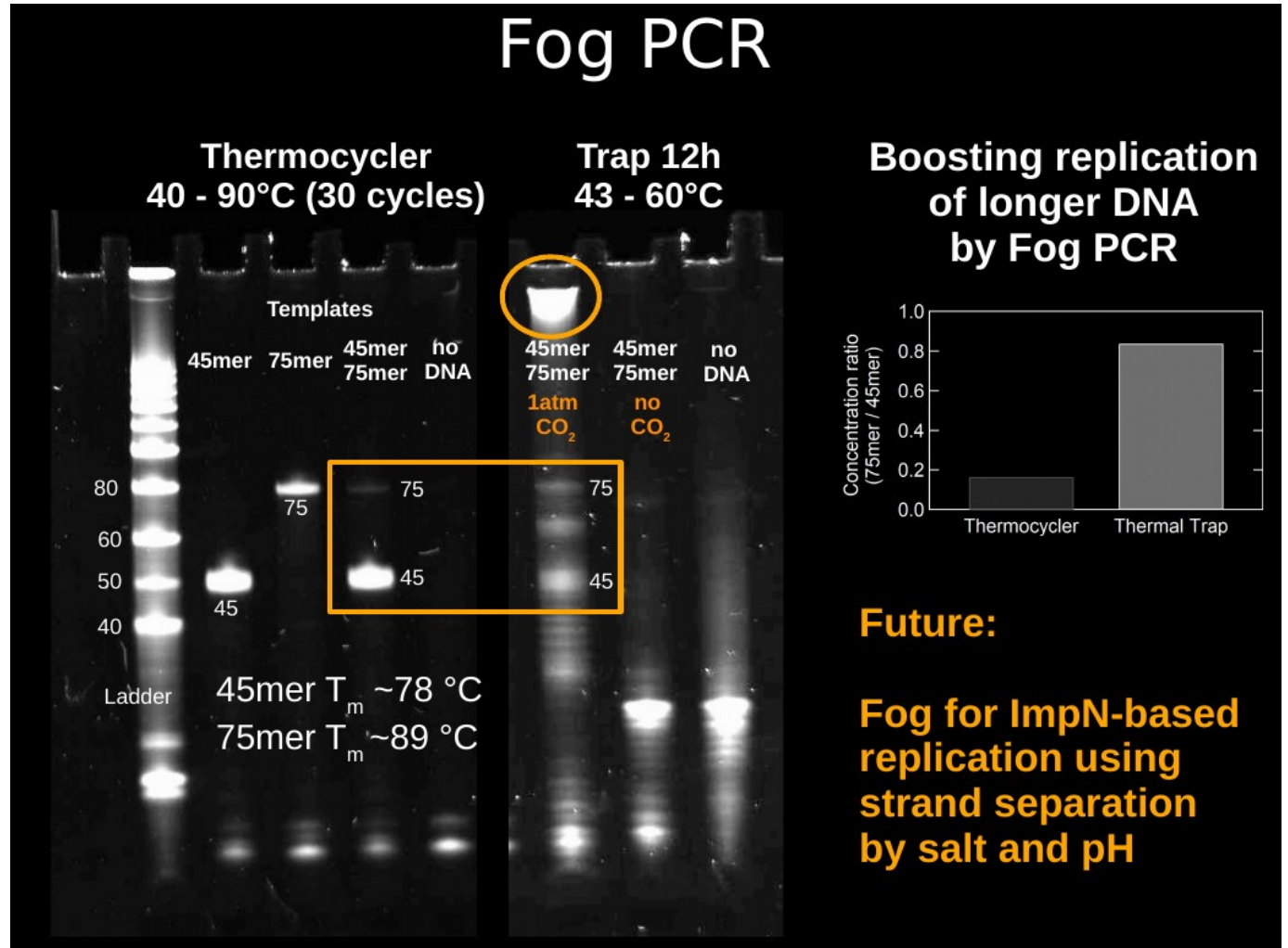
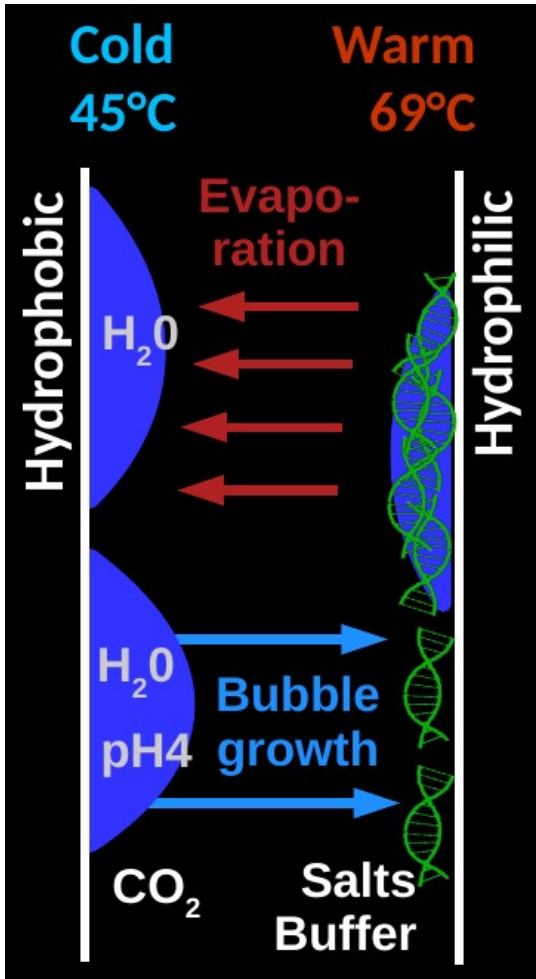
Fog PCR



Alan
Ianeselli

T gradient:
45 °C - 69 °C
51mer $T_m = 83$ °C
1 bar CO₂
1 nM template DNA
0.5 μM primers
Taq polymerase
1.5 mM MgCl₂
0.1% BSA
2x SYBR Green

Fog PCR



Polymerization boost by Thermophoretic Trap

- Accumulation PRL 2002
- Click together the accumulation in comsol
- Sidepoint: NanoTemper
- PNAS paper accumulation
- Szostak vesicle formation paper
- PNAS polymerization
- Simons update polymerization
- Gel formation Angewandte
- Gel formation and sedimentation (tRNA)

Replication

- tRNA-based replication
- Convection PCR
- Ribo-PCR
- NatChem2015: replication and selection
- Alan results
- Water-Air interface Natchem 2018
- Overview over non-equilibrium (rep from last).

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