

# Improving DNA Detection

## Thermophoresis of DNA

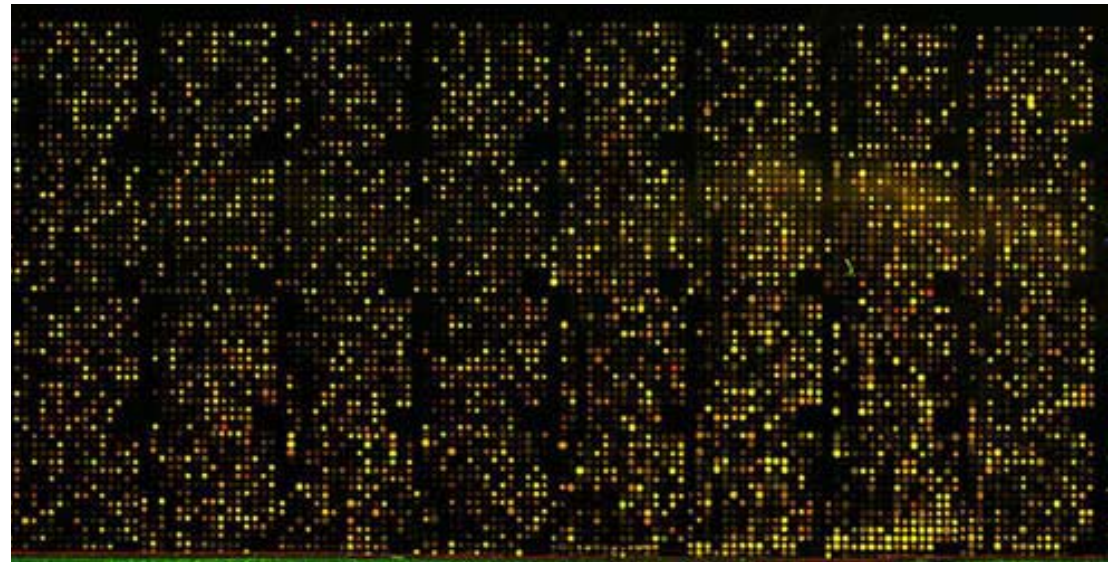
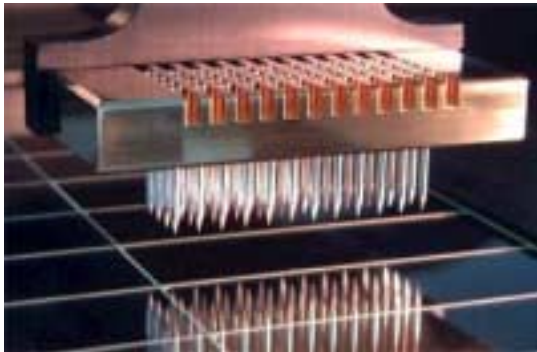
Dieter Braun  
Rockefeller University

## DNA Detection for...

- o Defines a new 'Microscope':  
RNA Profiles of Cells
- o Test for Virus (AIDS...)
- o Selecting medication
- o Test for GMO
- o Criminal investigations

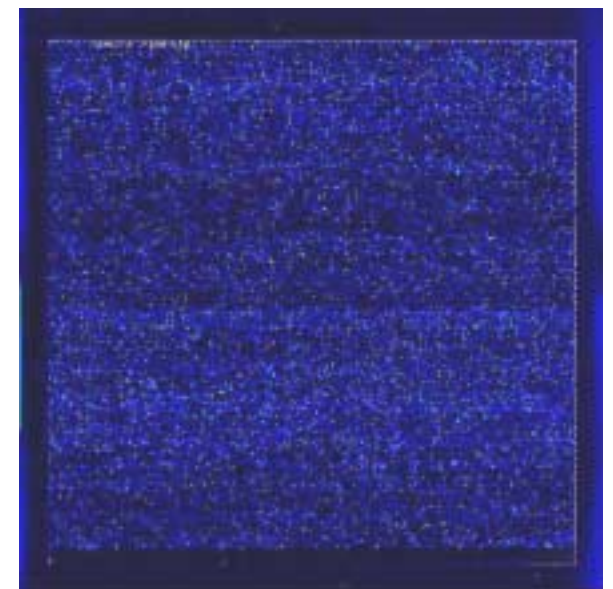
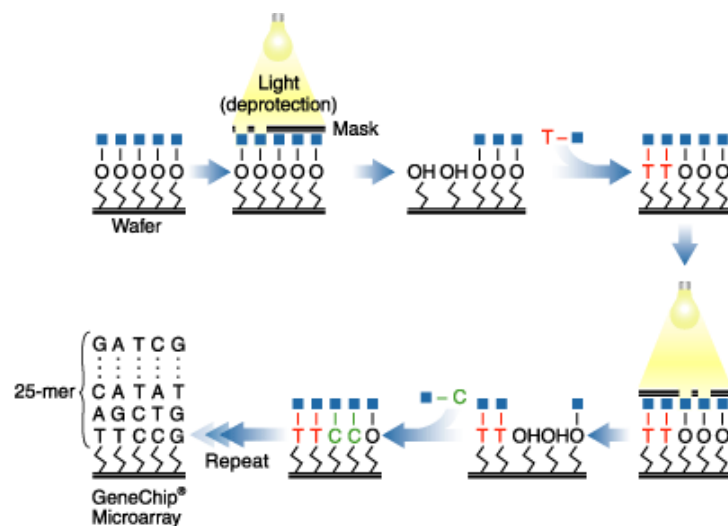
# Highly parallel DNA detection I

## A) Spotted Arrays



Rockefeller

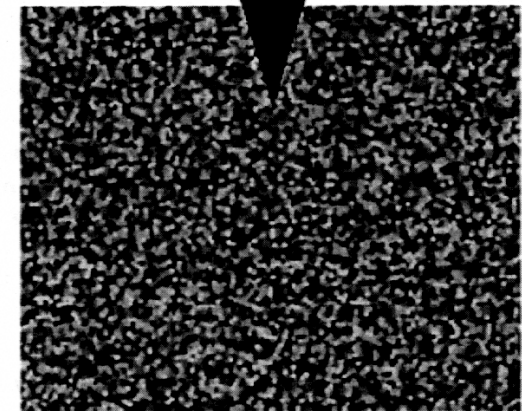
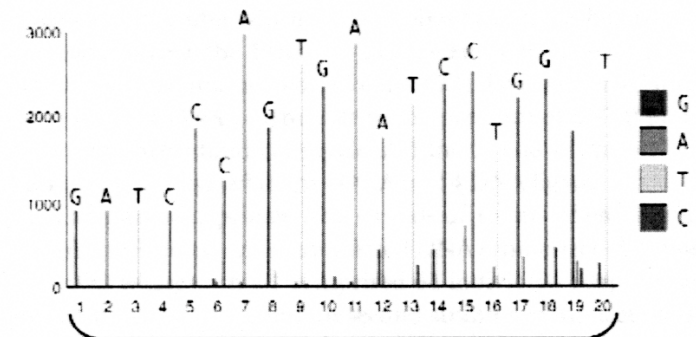
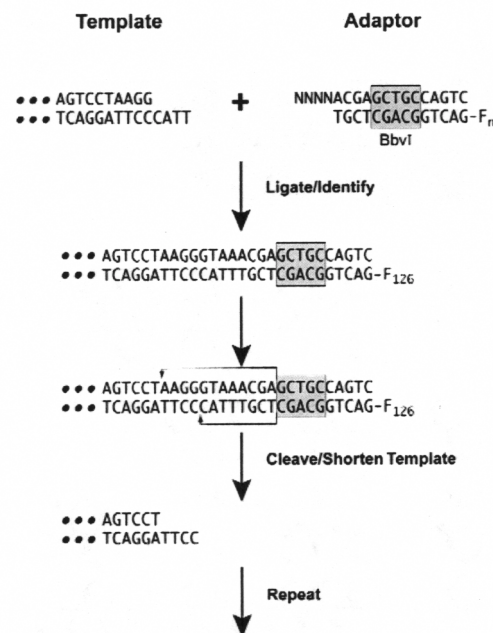
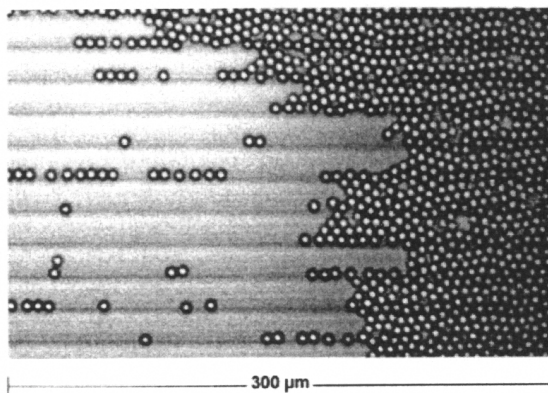
## B) On-Chip Synthesis



Affymetrix

# Highly parallel DNA detection II

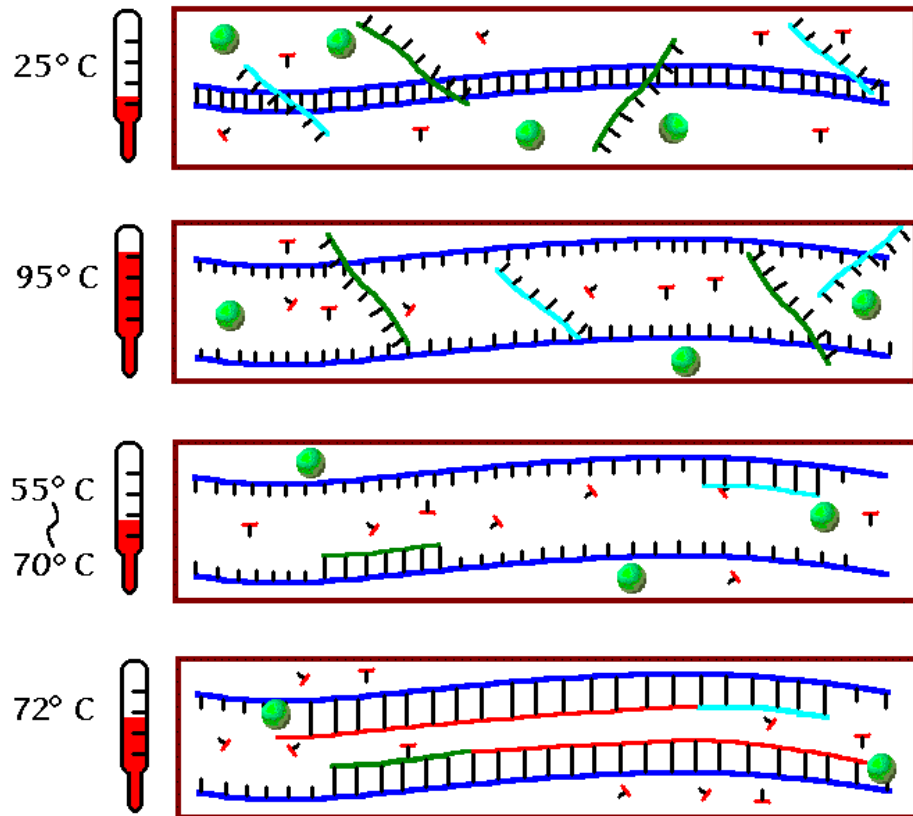
## C) Massive Parallel Signature Sequencing (MPSS)



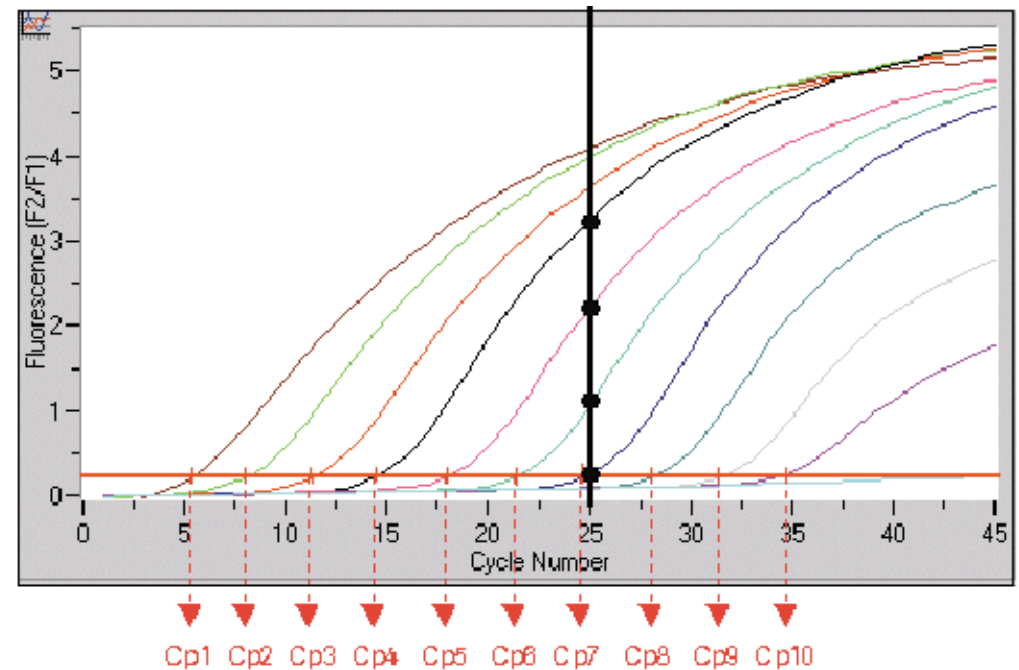
Lynx

+ Searching for unknown sequences

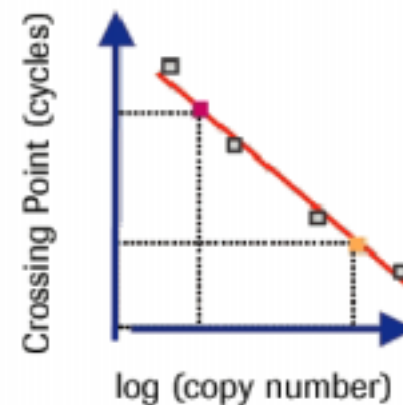
# Detecting DNA with Polymerase Chain Reaction



## Online Detection of Product



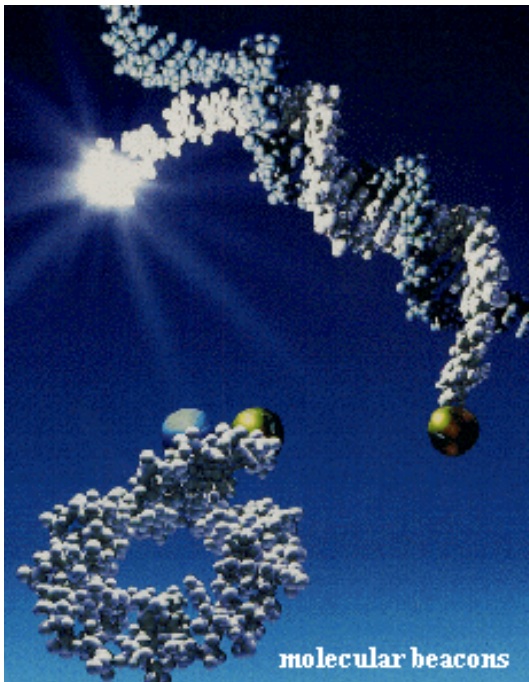
## Standard Curve



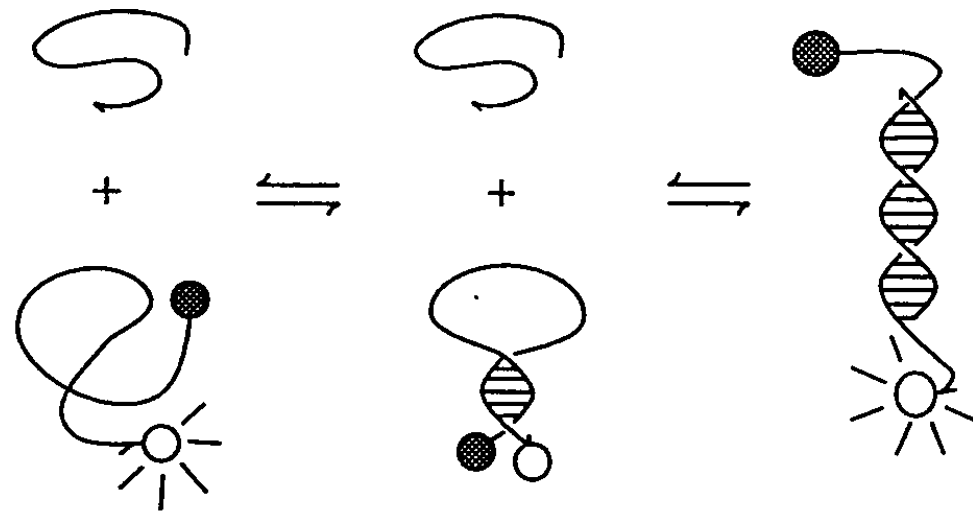
(c) Roche



# Beacon-Approach: Unstained Target

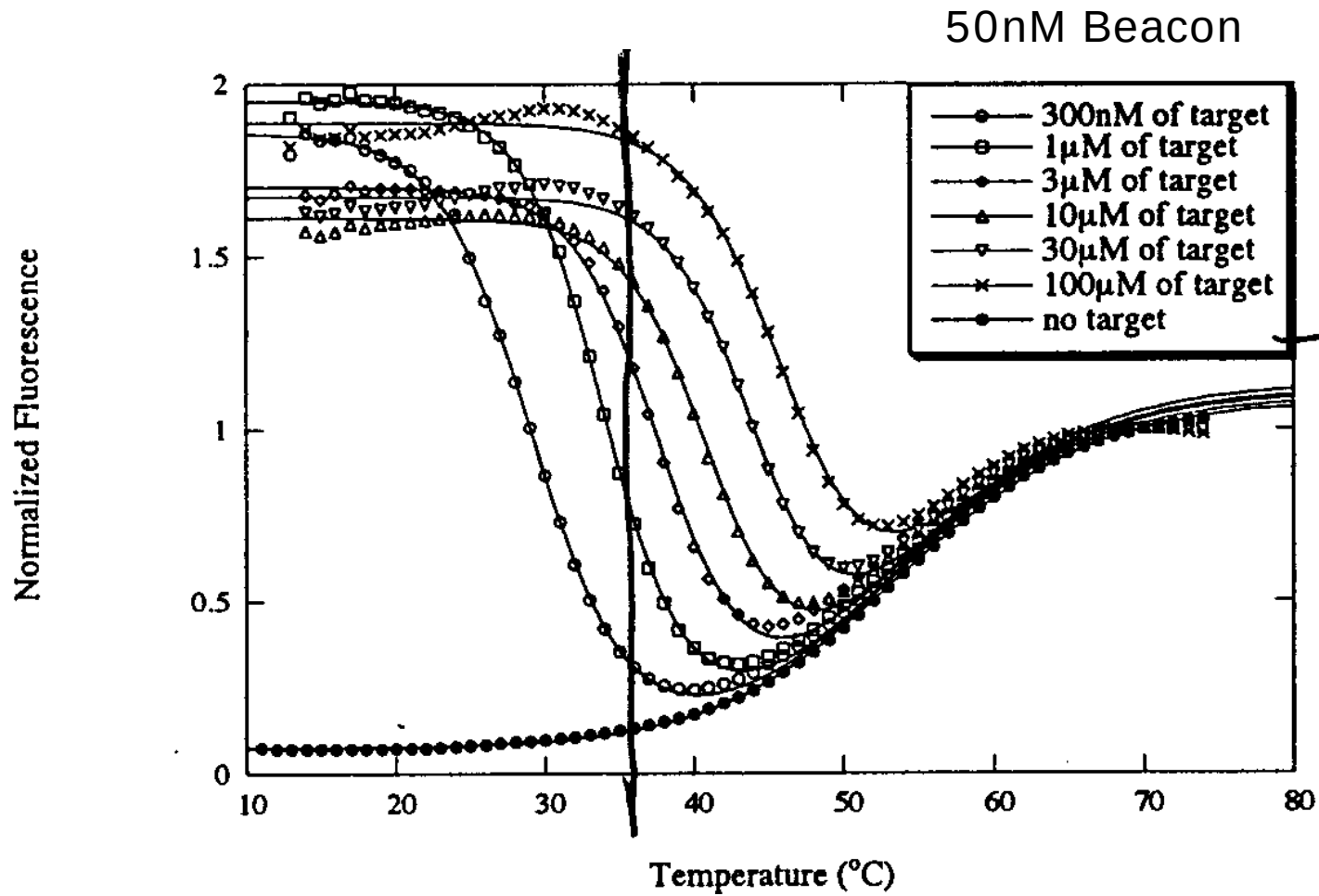


Tyagi & Kramer



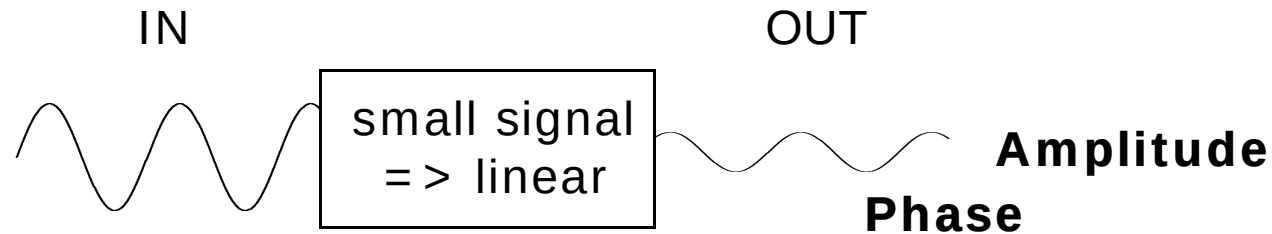
/56-FAM/  
CTCTTCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAATGAAGAG  
/3DAb/

# Detection of DNA with Beacons

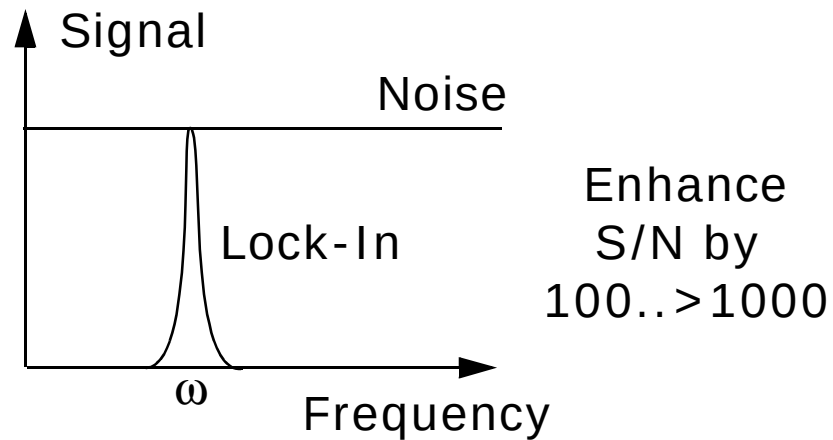


G. Bonnet

# Lock-In approach to kinetics

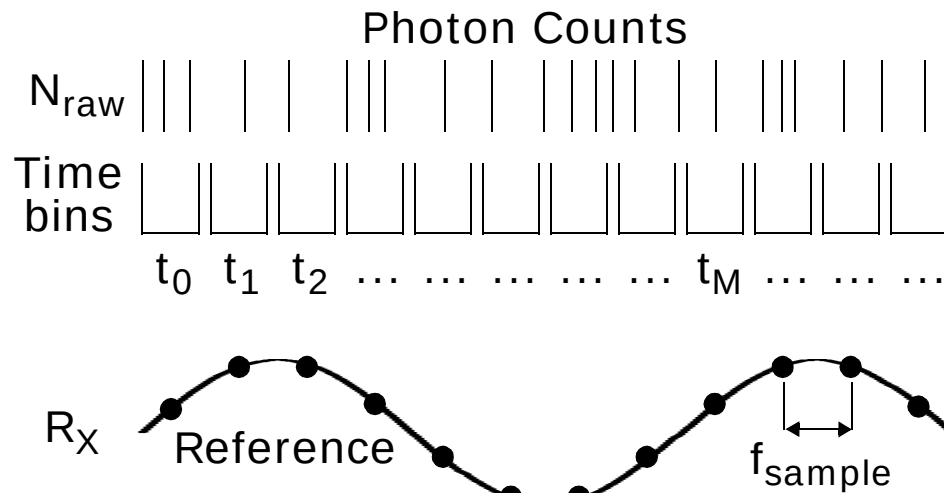


## Noise reduction

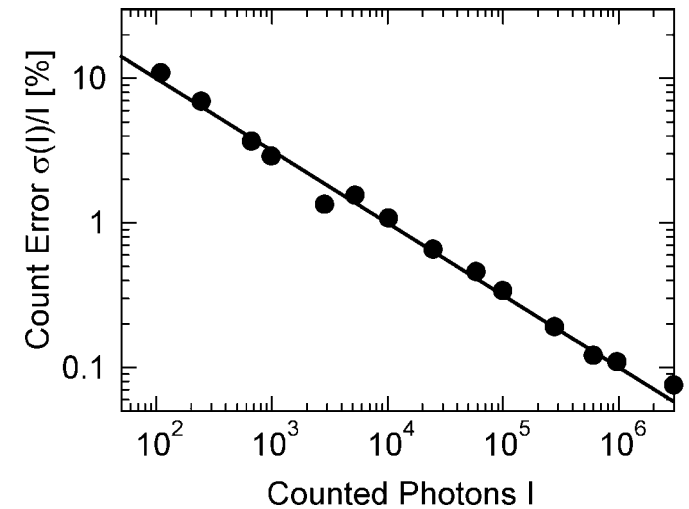




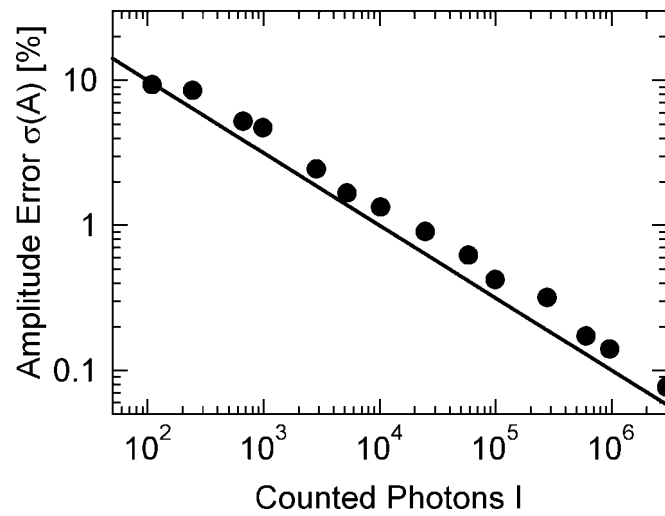
# Single Photon Lock-In



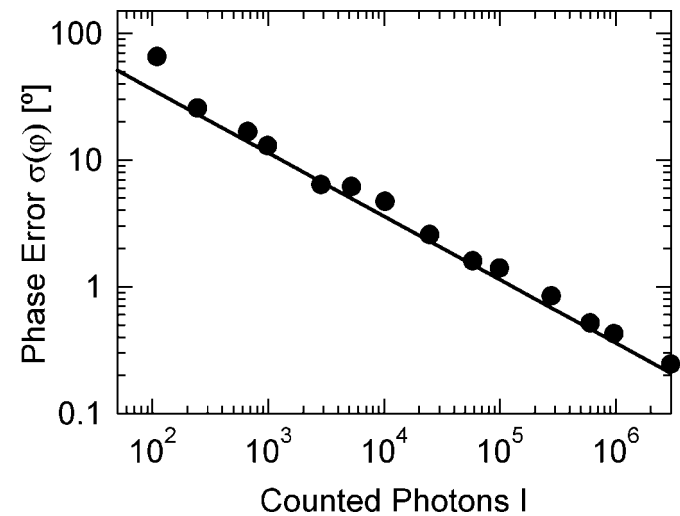
$$\text{Error(Photons)} = 100\% / \sqrt{\text{Photons}}$$



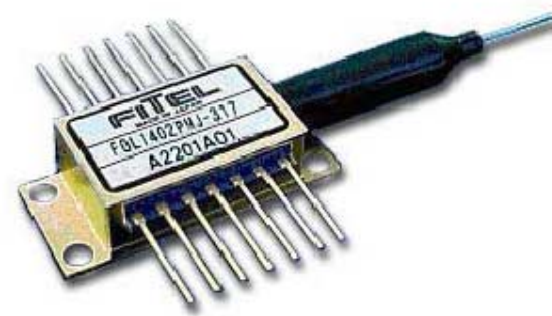
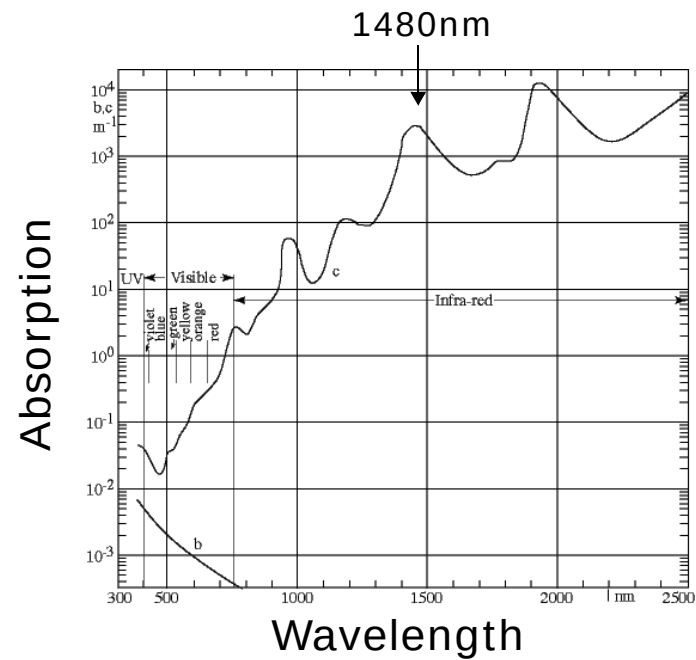
$$\text{Error(Amplitude)} = 100\% / \sqrt{\text{Photons}}$$



$$\text{Error(Phase)} = 360^\circ / \sqrt{\text{Photons}}$$



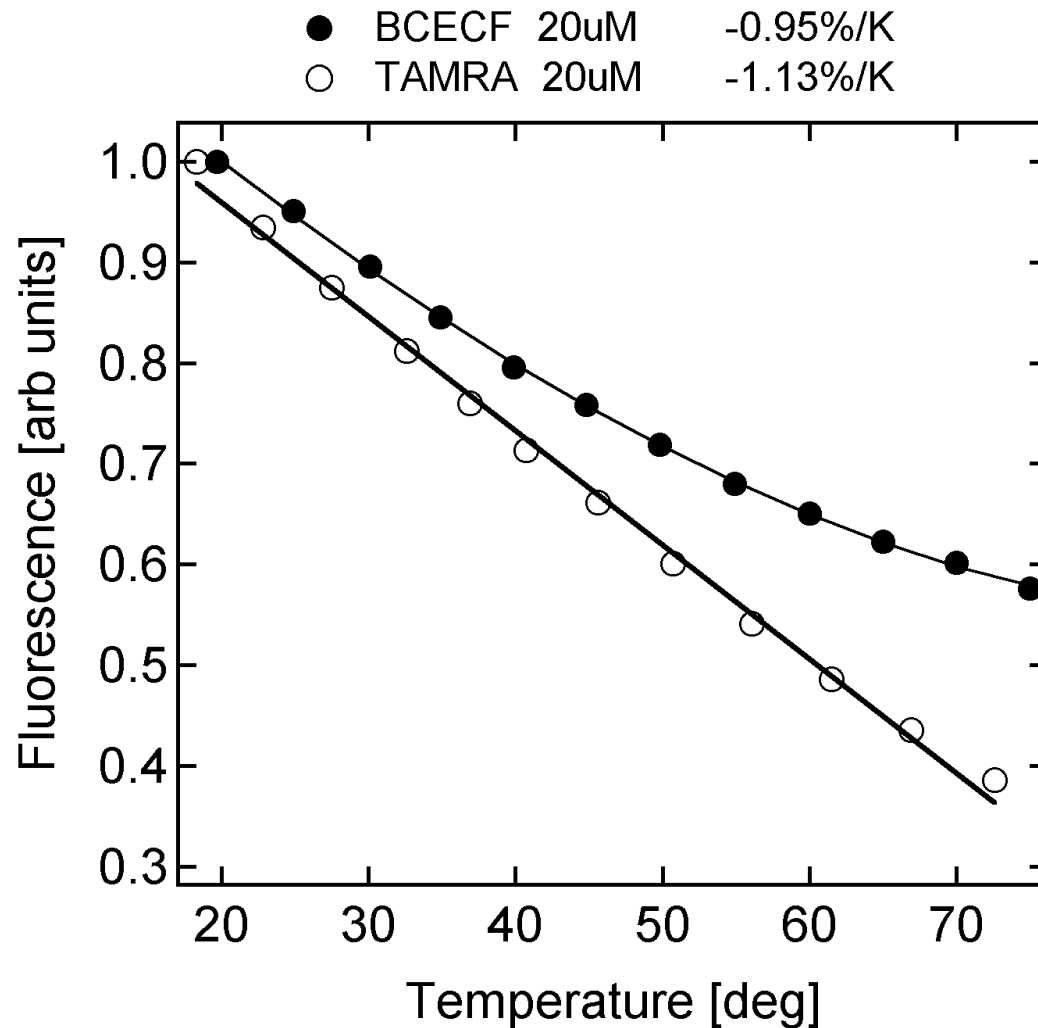
# Infrared heating



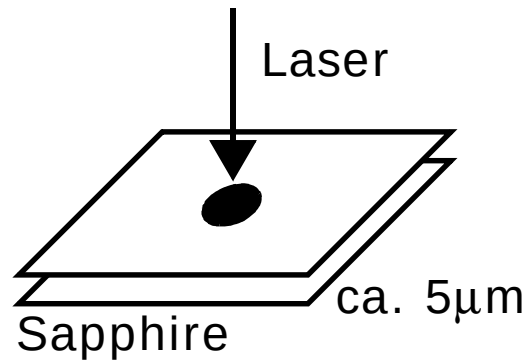
1480nm, 100mW

# Dye Molecules as a Thermometer

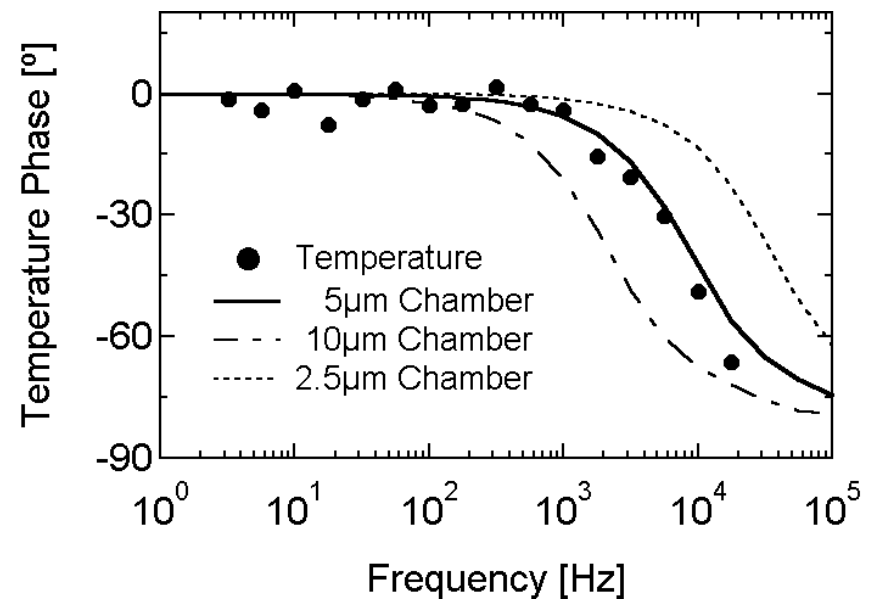
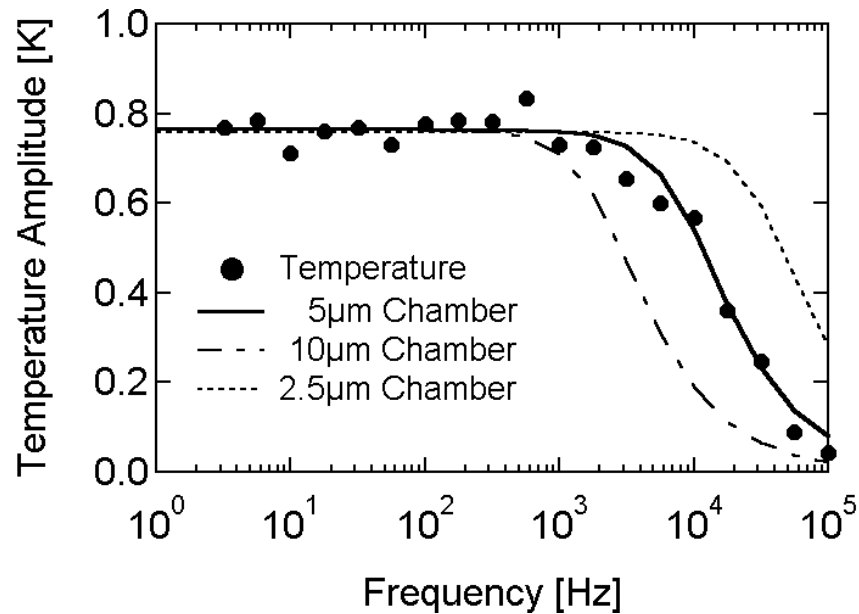
Temperature  $\rightarrow$  pH of TRIS  $\rightarrow$  pH Probe



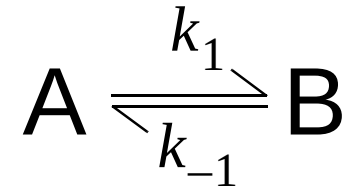
# How to apply Temperature Oscillations



Report Temperature  
by Fluorescence using  
Single Photon Lock-In



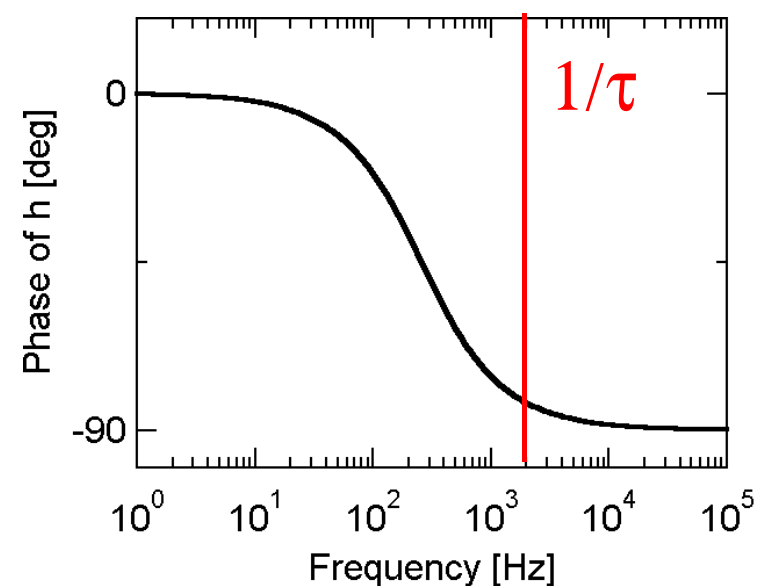
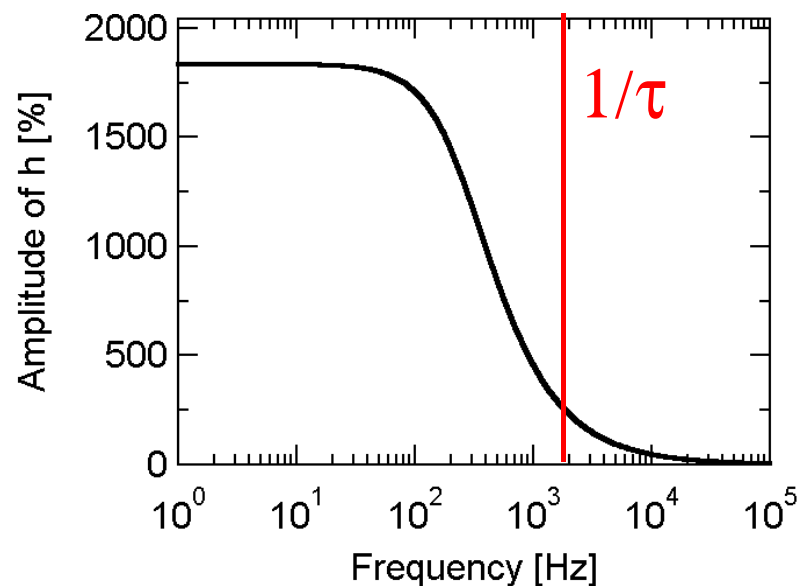
# Transfer function of a reaction



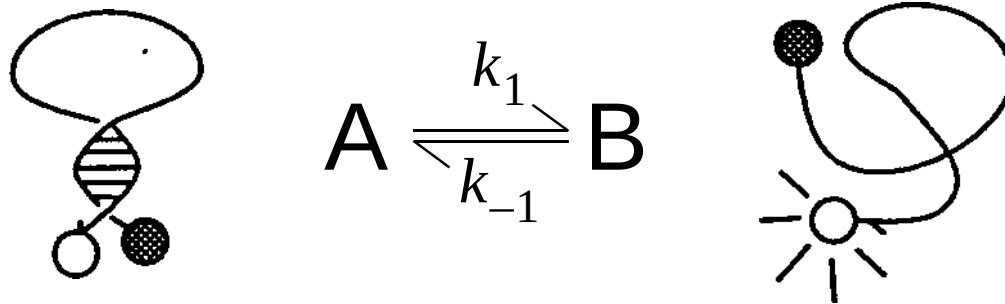
Temperature Oscillation  $\Delta T/T$

$$\frac{\Delta[B]}{[B]} = \underbrace{-\frac{\Delta H}{RT} \frac{1}{1+K}}_{h(\omega)} \frac{1}{1+i\omega\tau} \frac{\Delta T}{T}$$

$$\tau = \frac{1}{k_1 + k_{-1}}$$



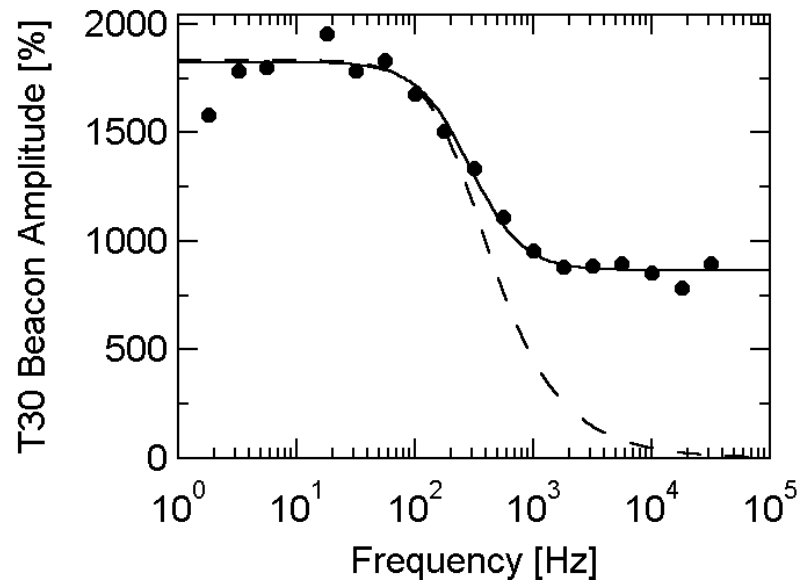
# Speed of opening/closing of DNA hairpins



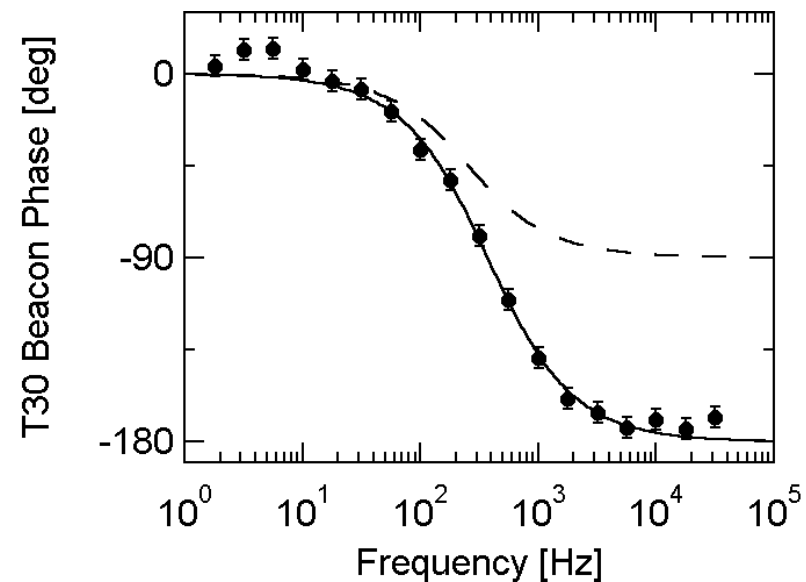
/56-FAM/

CTCTTCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAATGAAGAG

/3DAb/

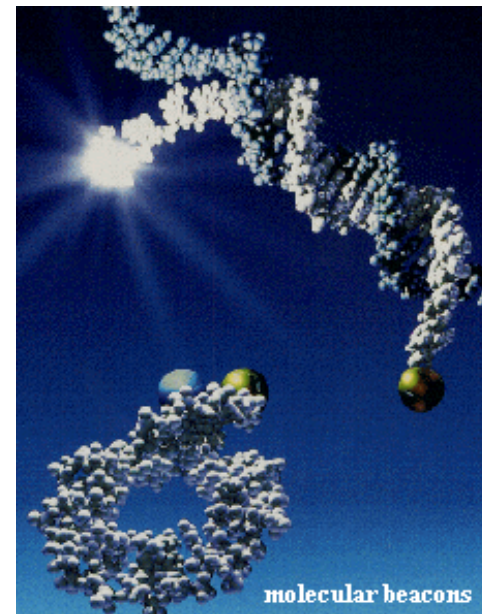
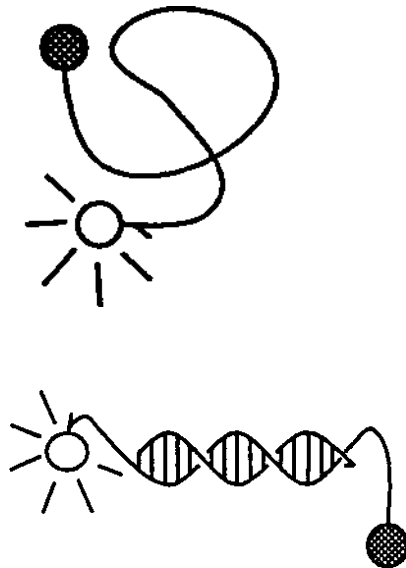
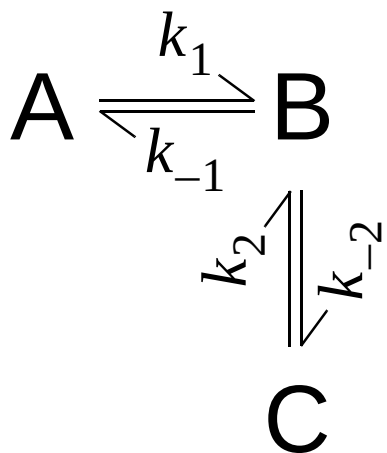


$$\tau = 617 \pm 37 \mu\text{s}$$



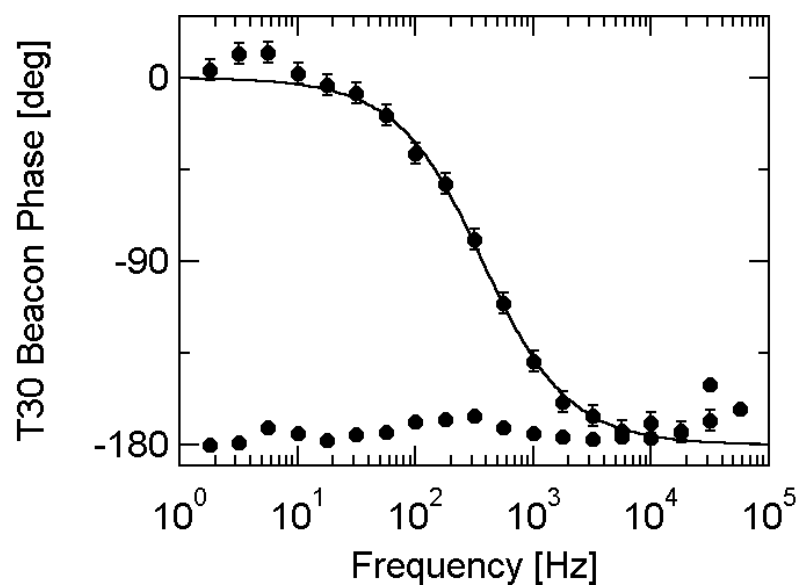
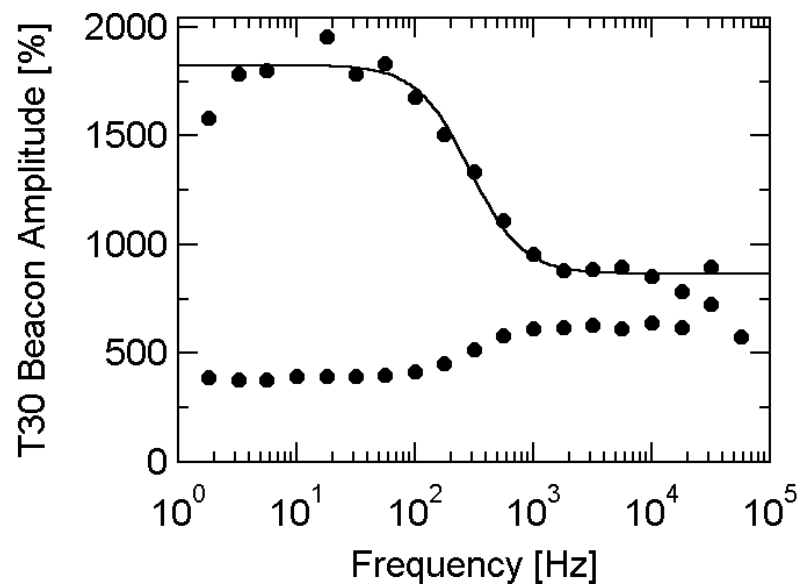
$$\frac{\Delta T}{T} \rightarrow \frac{\Delta[B]}{[B]} \rightarrow \frac{\Delta F}{F}$$

# With Target DNA



[Target] : [Bacon] = 1 : 1

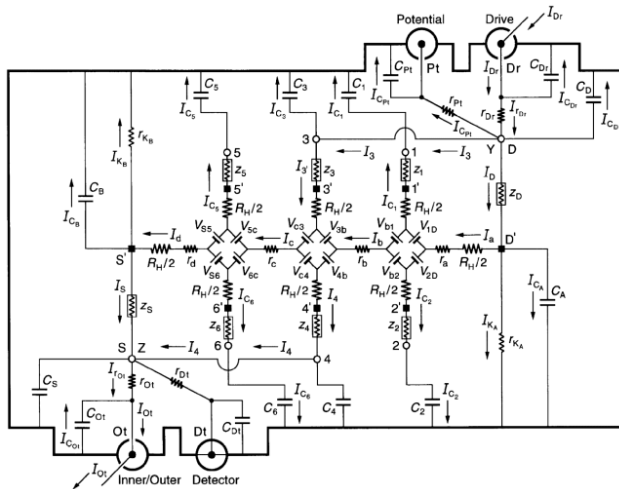
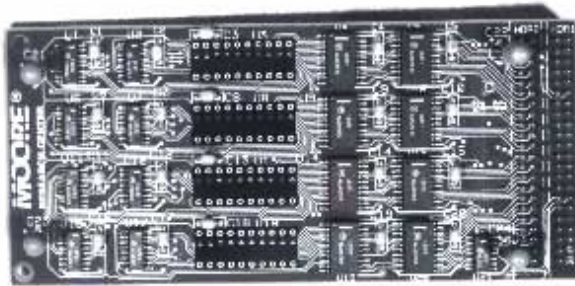
Tyagi





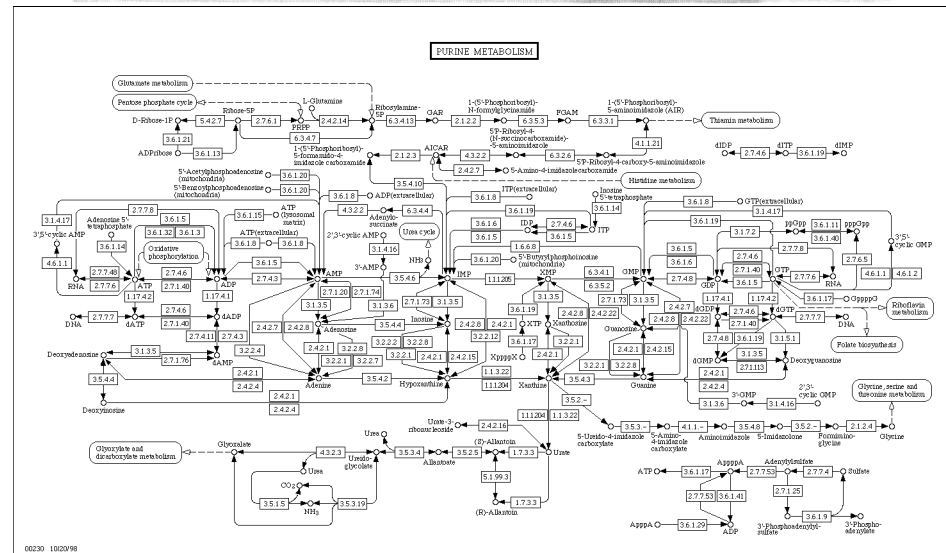
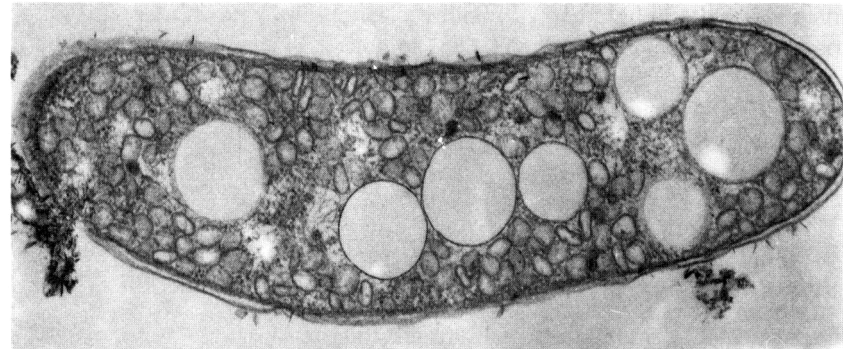
# Motivation II: Kinetics within cells

## Electric Network



Lock-In

## Biochemical Network



Lock-In ?

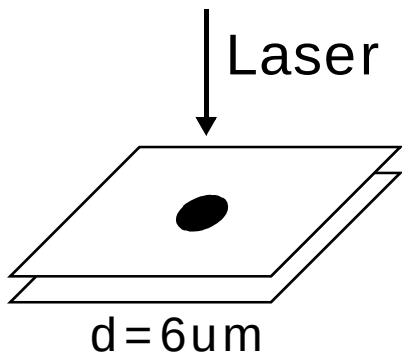
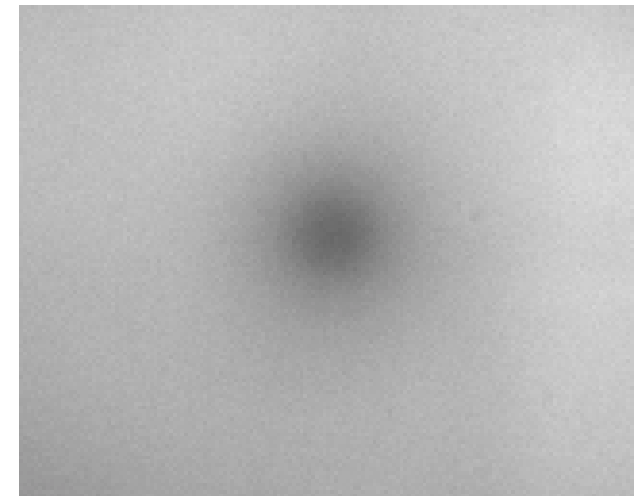
Moving DNA by Temperature  
Trapping DNA by Temperature

# Imaging Temperature

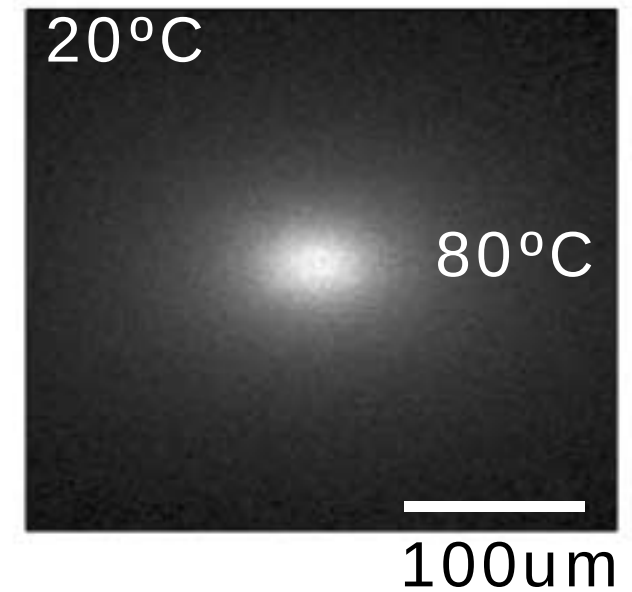
Laser off: cold



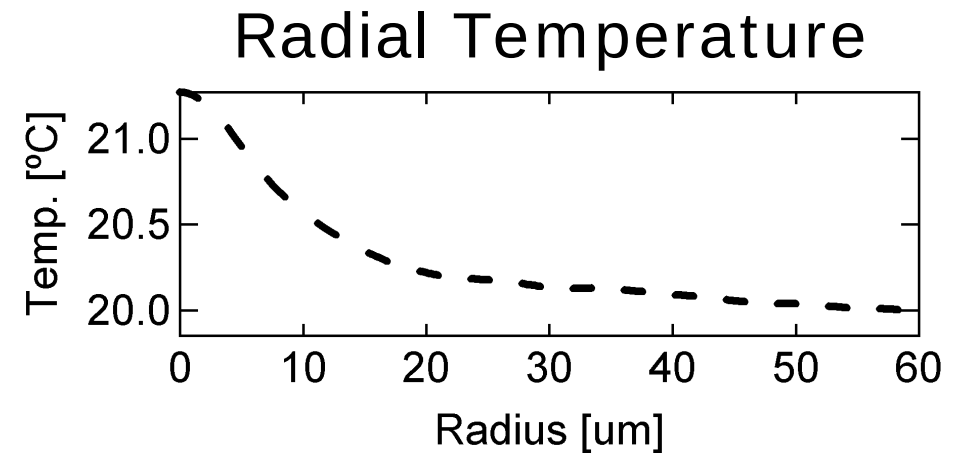
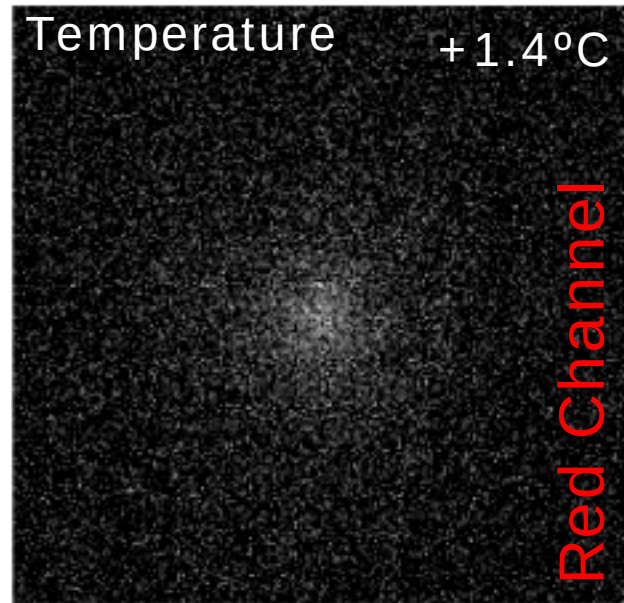
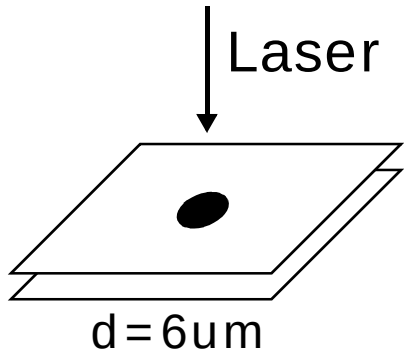
Laser on: hot



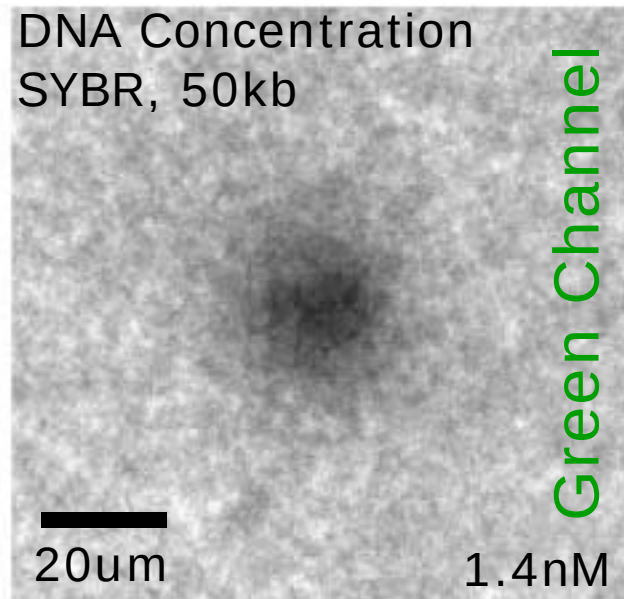
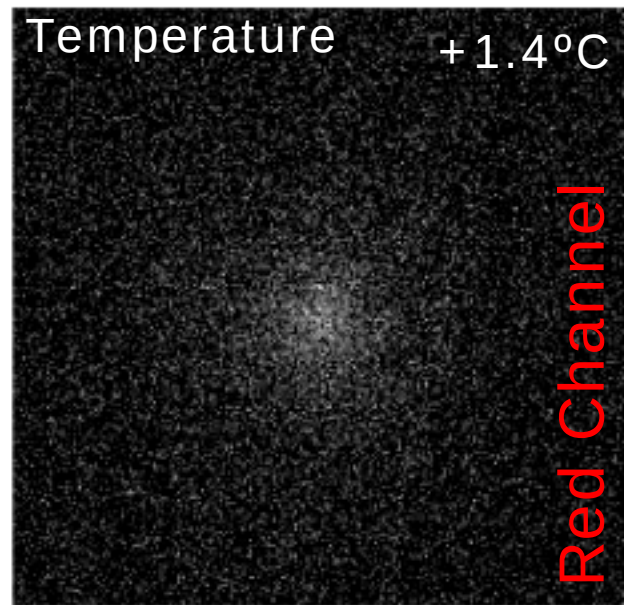
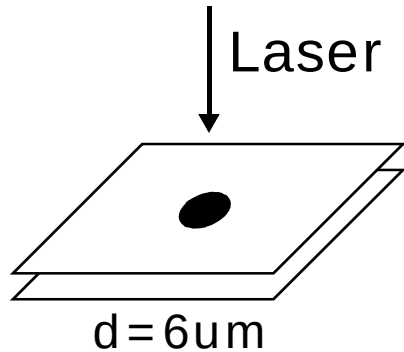
Temperature  
Image



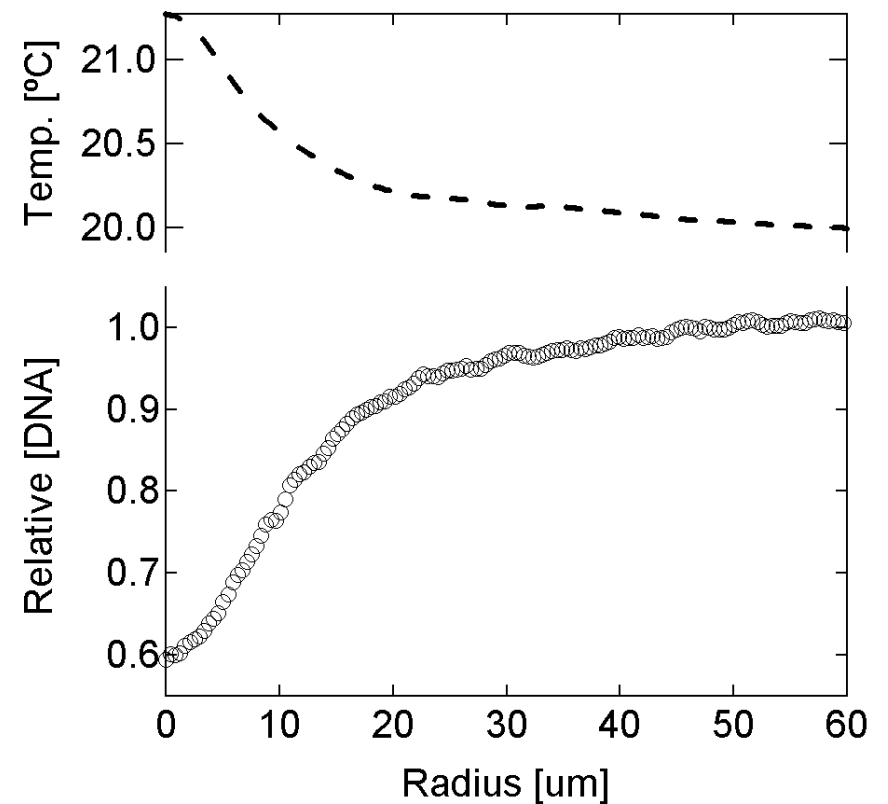
# Local, mild heating



# Depletion of DNA from heat



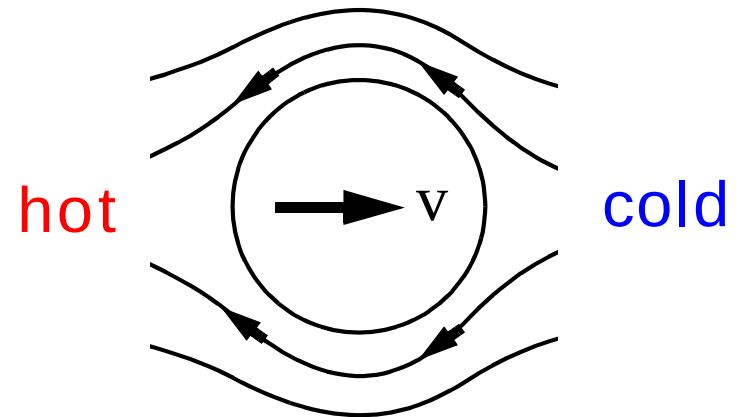
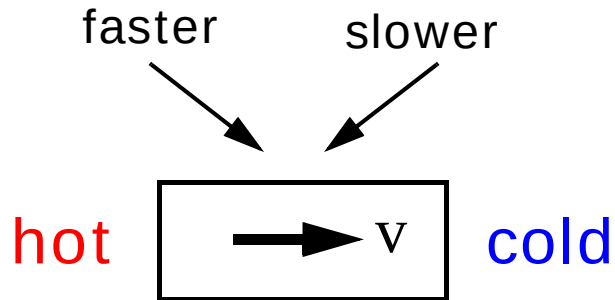
## Radial Distribution



## Exclude Artefacts

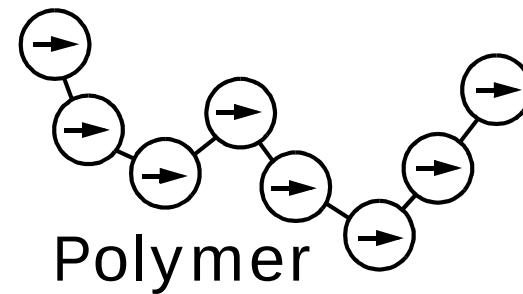
- no optical trapping
- no temp. dep. of DNA stain

# Thermophoresis - Theory



Maxwell Force

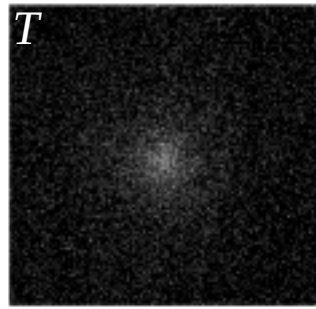
$$v = \frac{3\eta}{4\rho} \frac{\nabla T}{T}$$



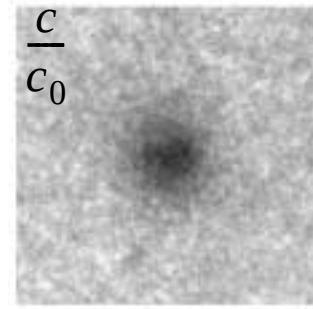
1. Fick' Law

$$j = -D\nabla c + D_T c(1-c)\nabla T \stackrel{!}{=} 0 \longrightarrow \frac{c}{c_0} = e^{-\frac{D_T}{D}(T-T_0)}$$

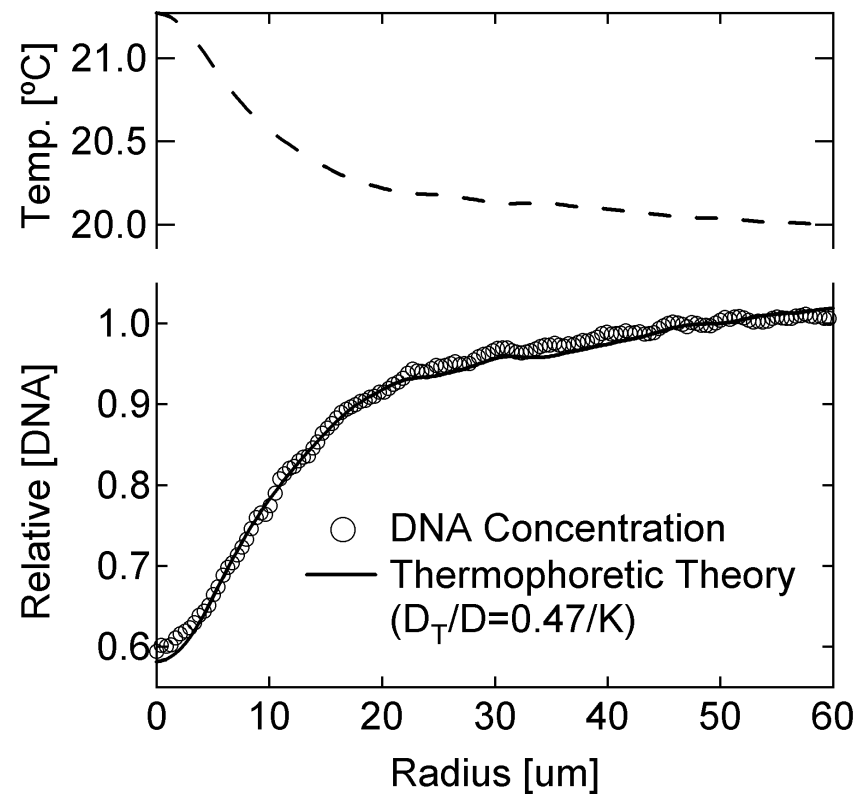
# Thermophoresis of DNA - Fit



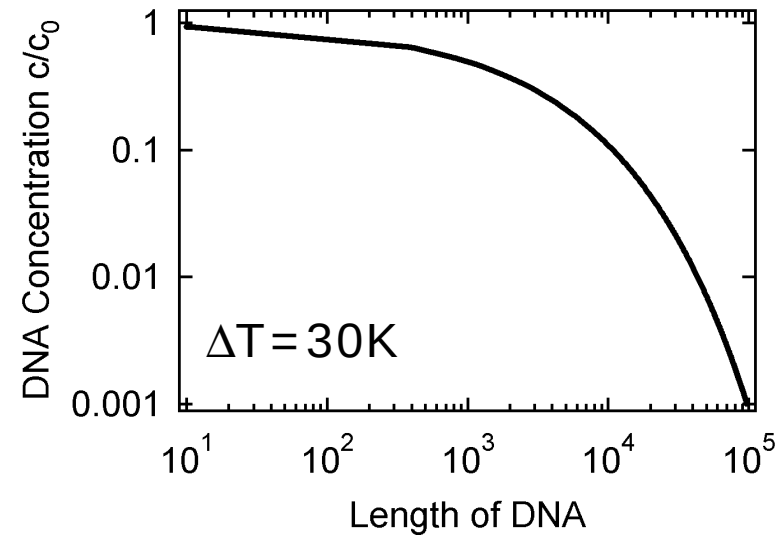
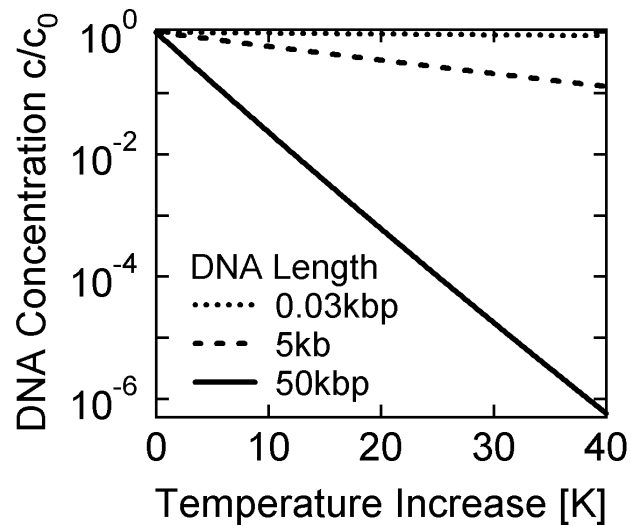
$$\frac{c}{c_0} = e^{-\frac{D_T}{D}(T - T_0)}$$



Fit  
 $\frac{D_T}{D}$

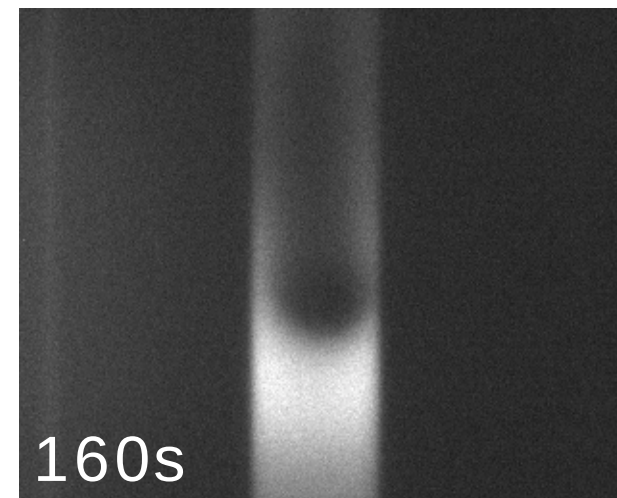
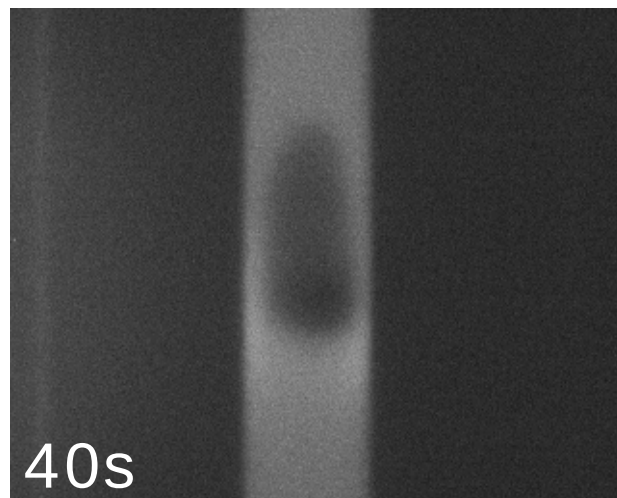
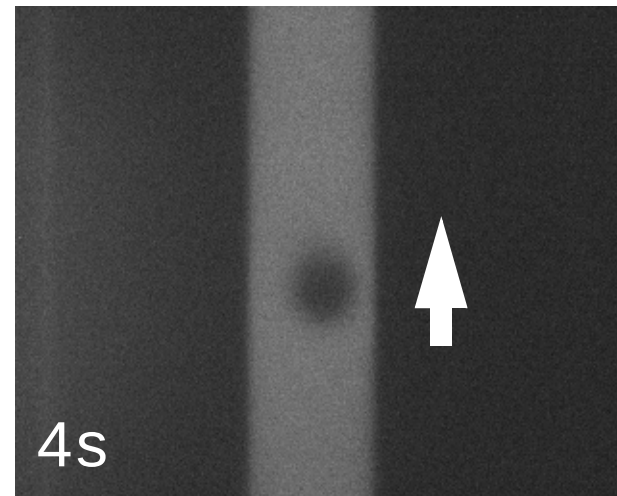
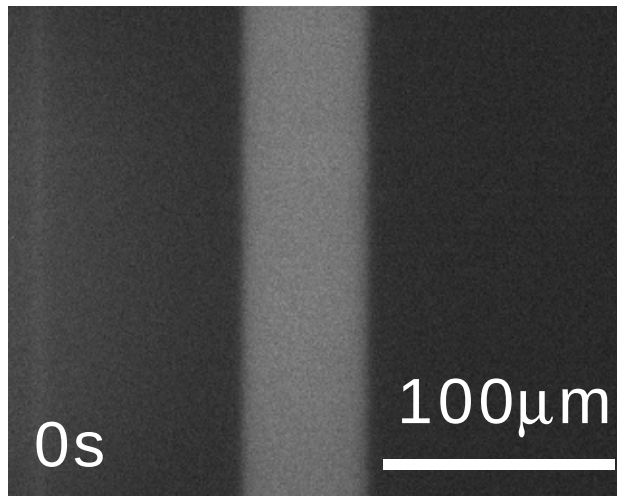


# Thermophoresis of DNA





# Thermophoresis against microfluidic flow

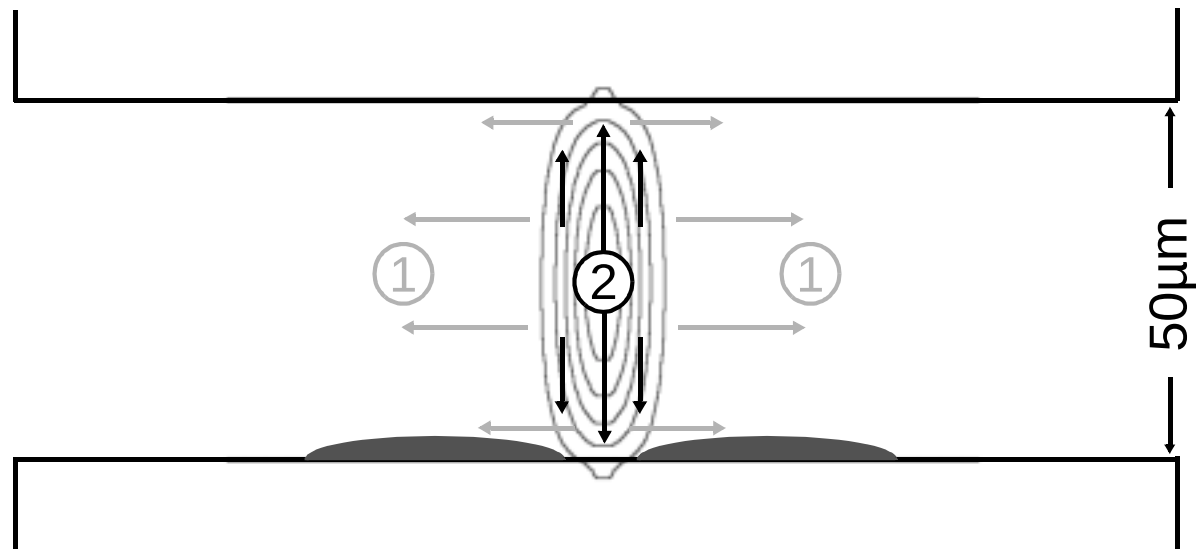
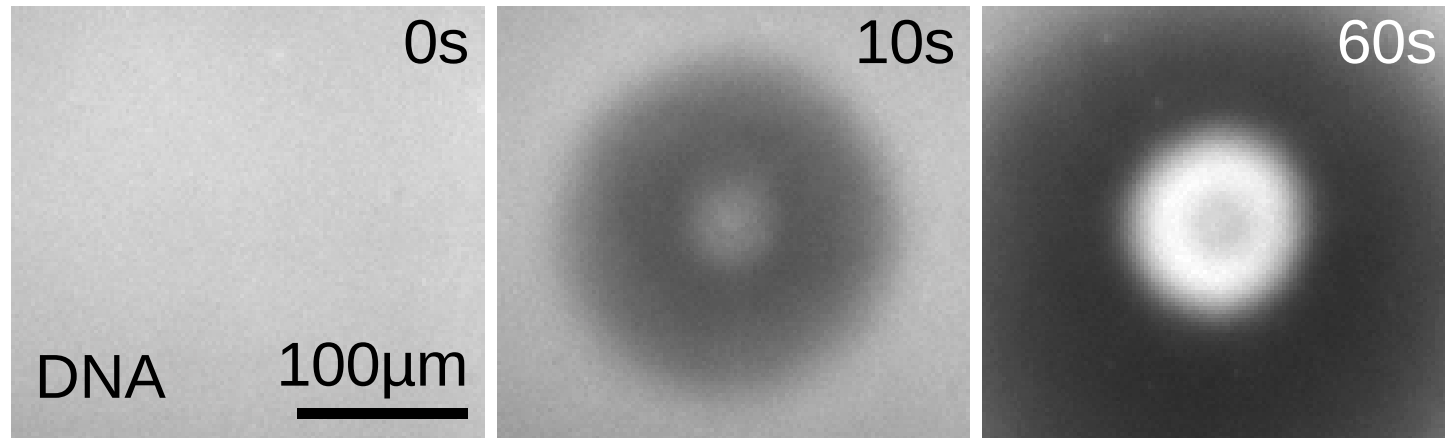


# Trapping DNA by Temperature

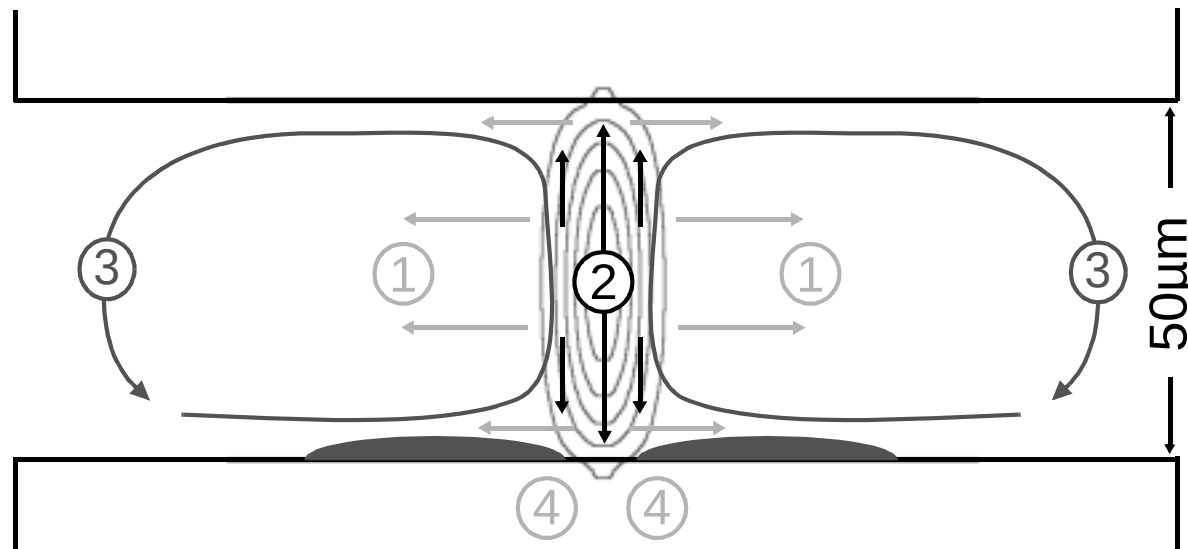
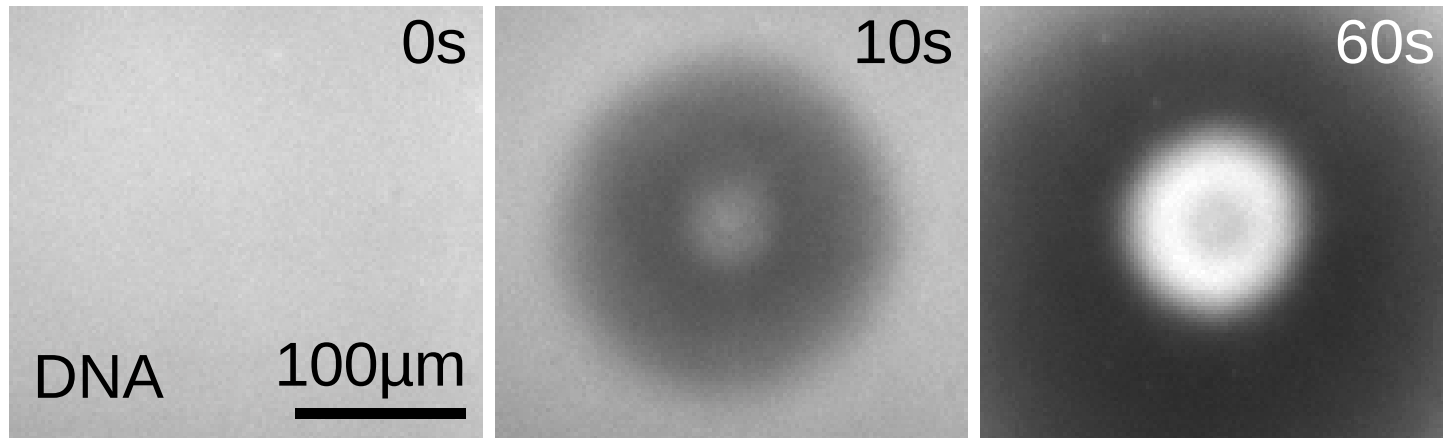
## Rendering Depletion into Attraction

Braun & Libchaber, Phys. Rev. Lett., in press

# Trapping DNA by Temperature

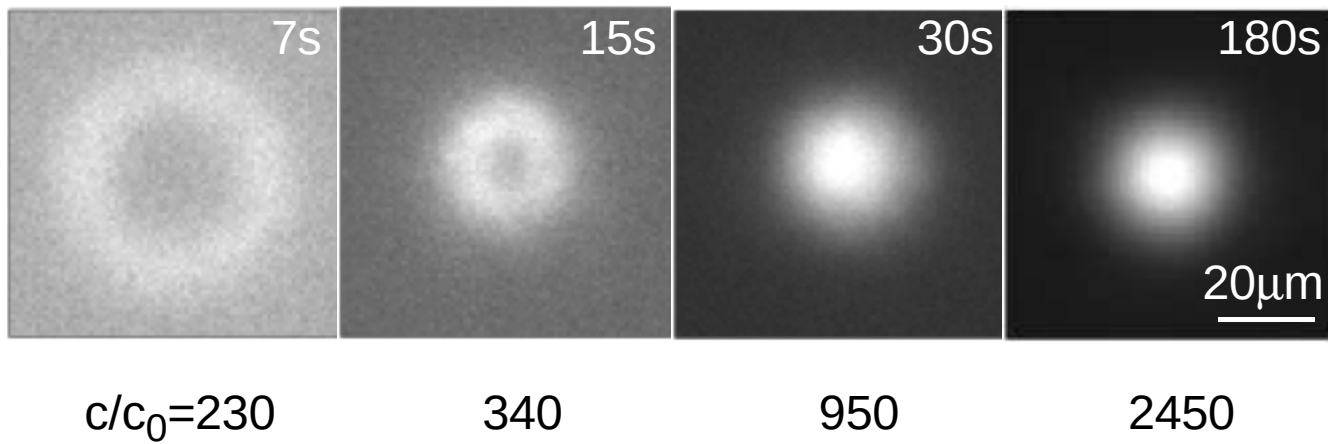


# Trapping DNA by Temperature

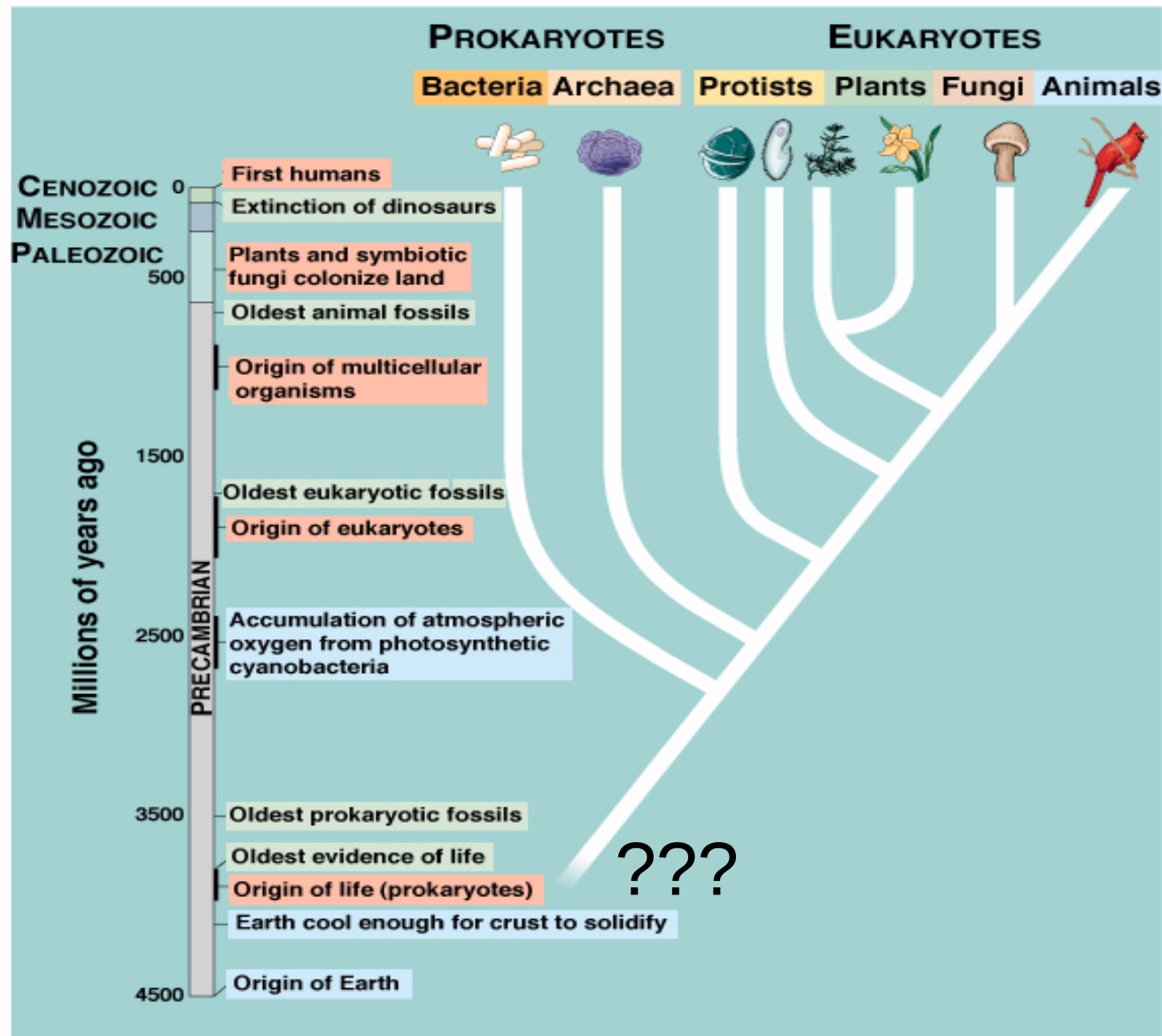


Concentration increase approx. 60-fold

# Strong accumulation

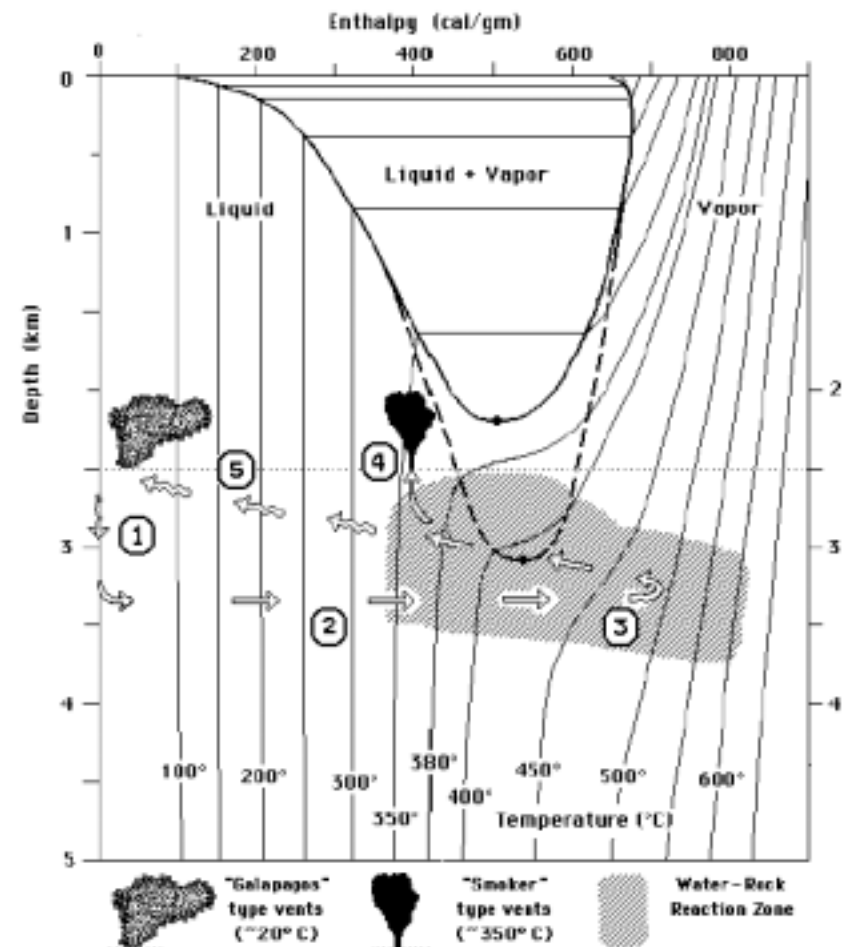
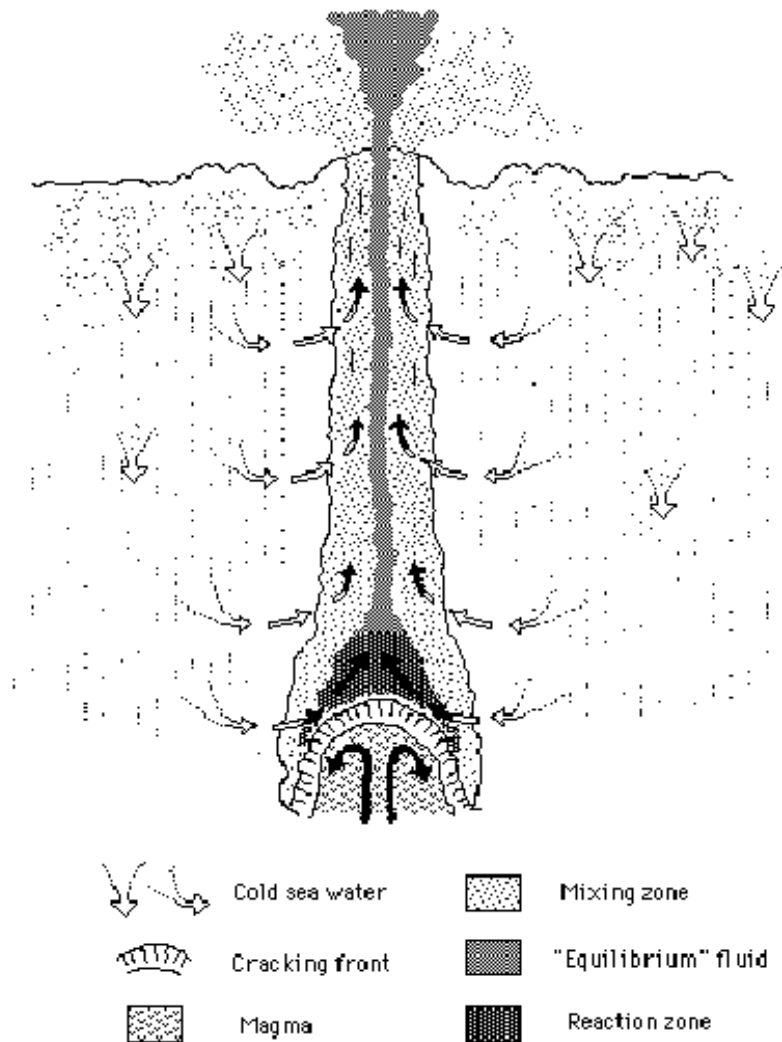


# Origin of Life: Role of thermophoresis?



# Thermophoretic trapping in sea floor?

## Hydrothermal vents



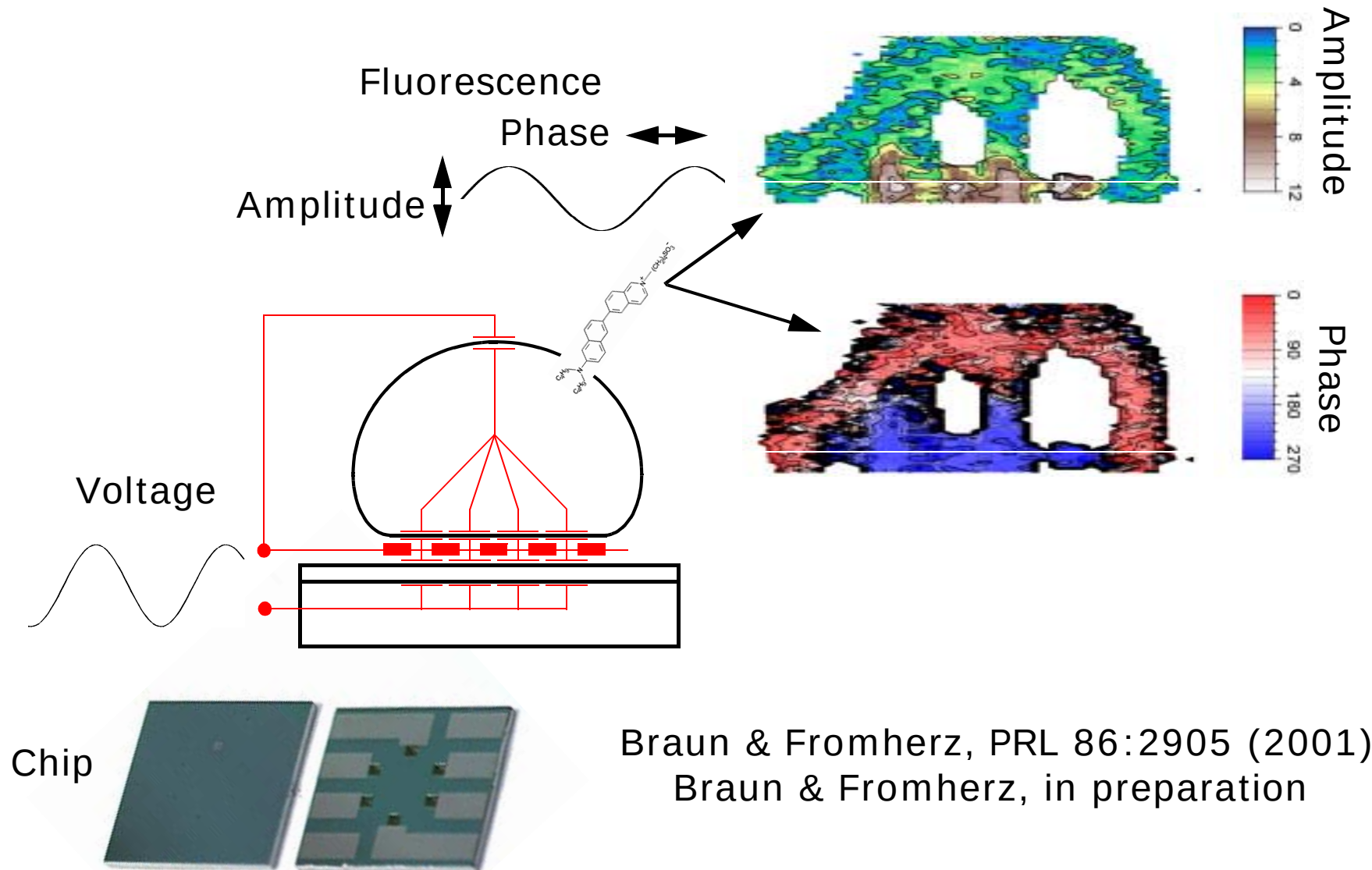
# Acknowledgements

Libchaber Lab

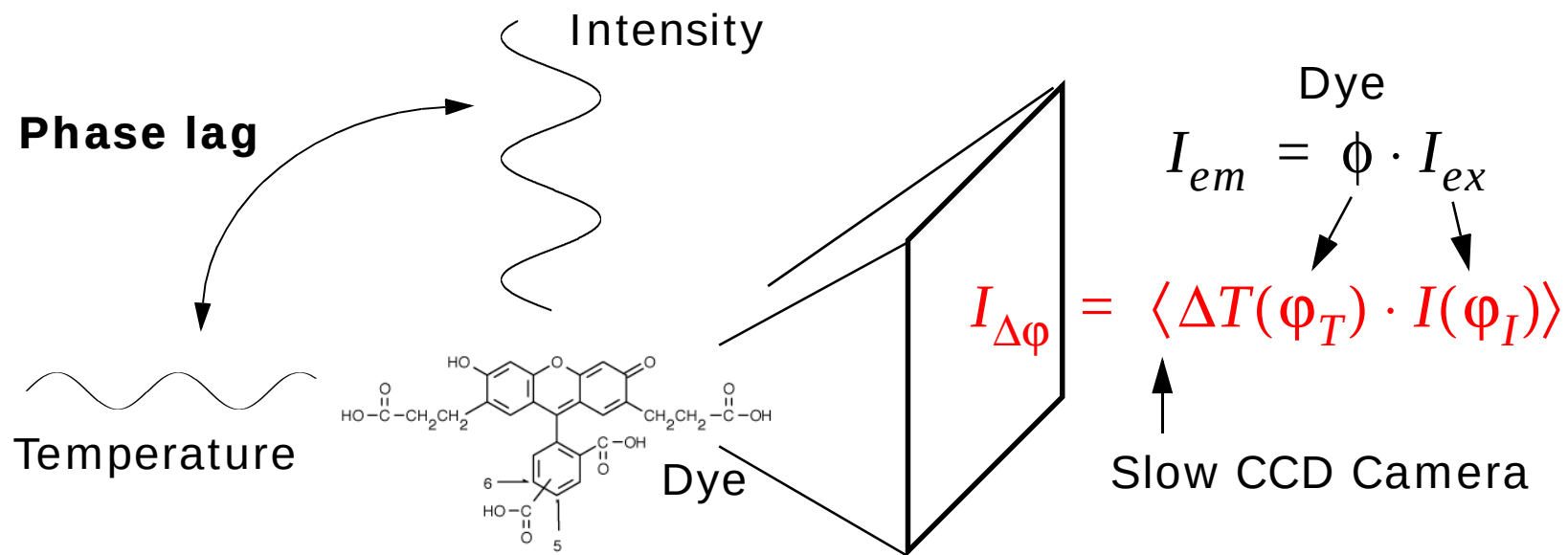
Emmy Noether Scholarship, DFG



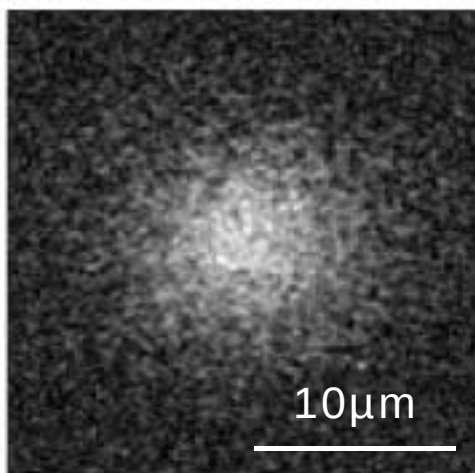
# Lock-In Imaging of Neural Stimulation



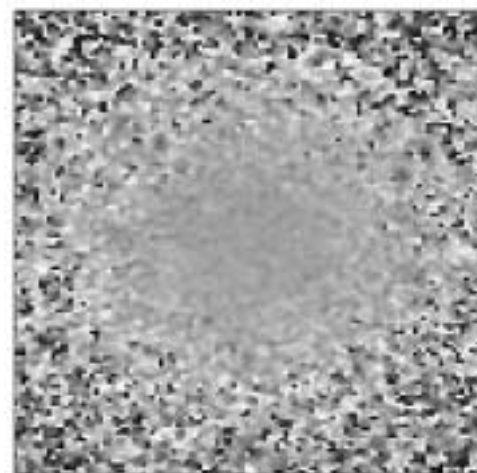
# 2D-CCD Molecular Lock-In



Amplitude Image



Phase Image



f = 1kHz  
CCD 4s