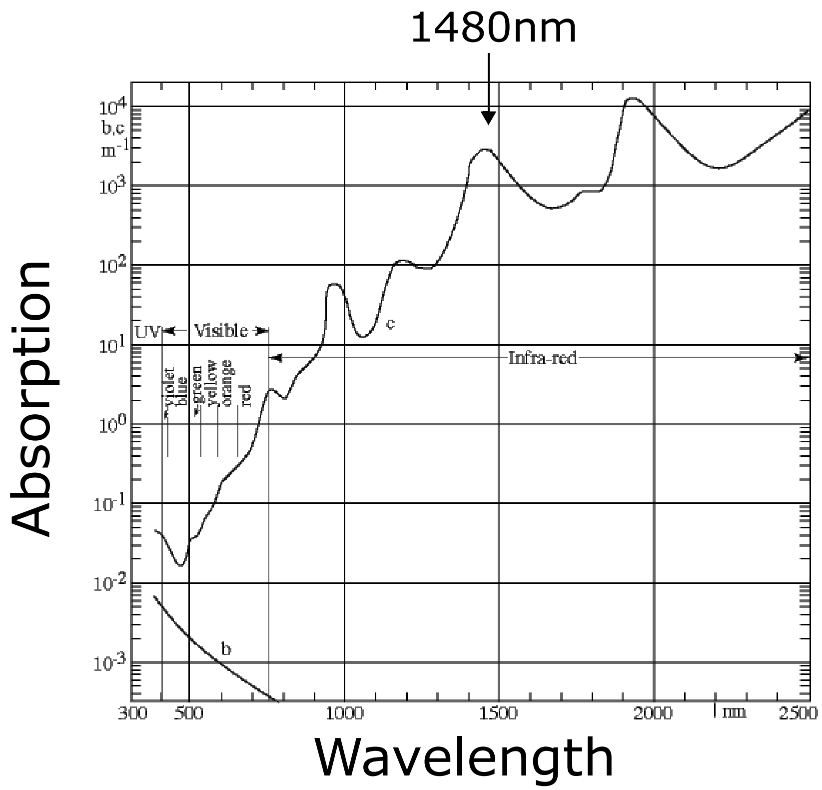
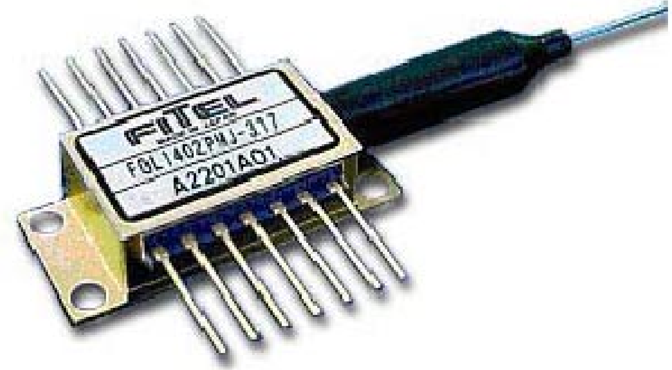
# Trapping and Replicating DNA by Constant Heating

Dieter Braun
Rockefeller University

# Infrared heating

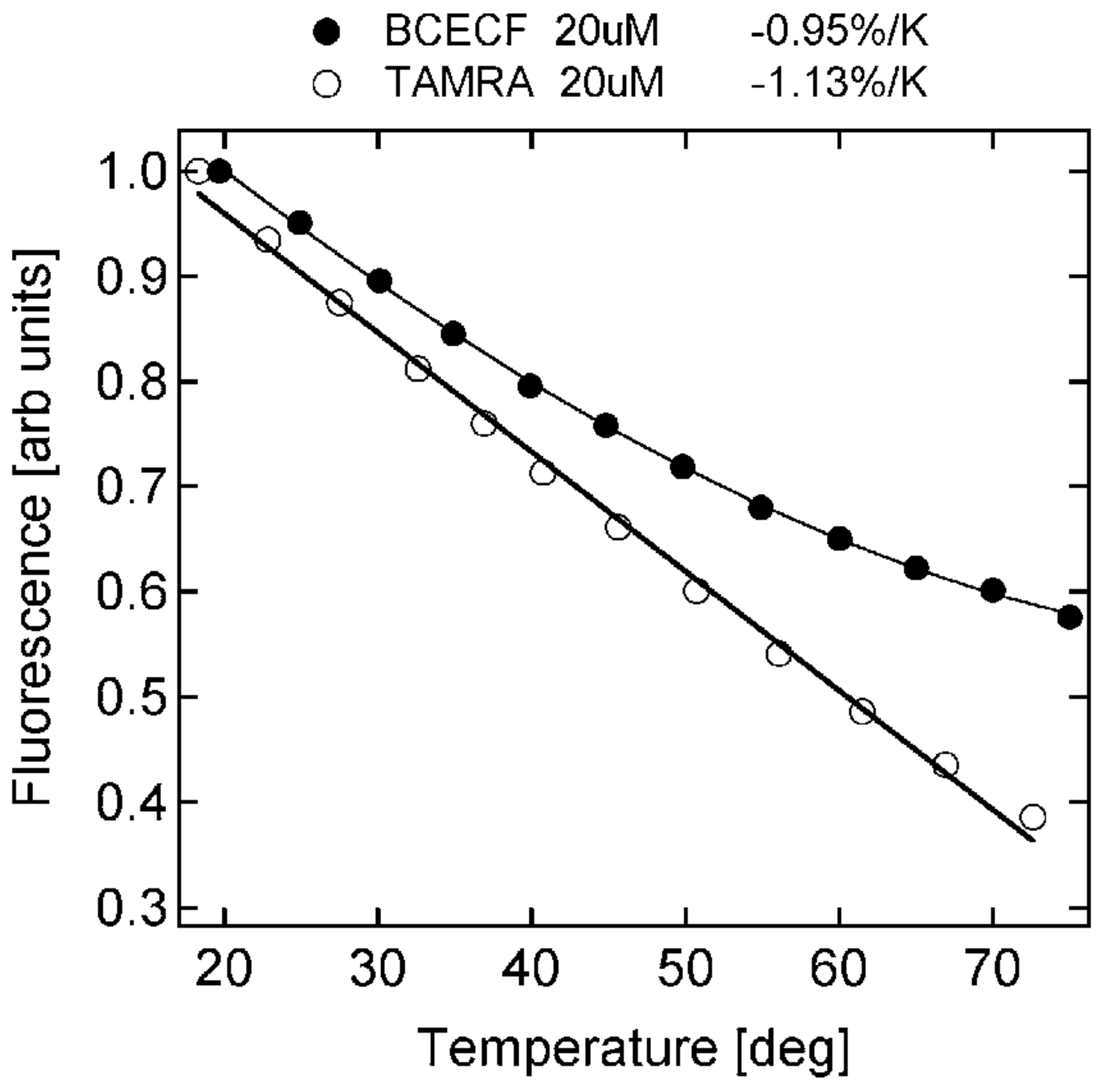


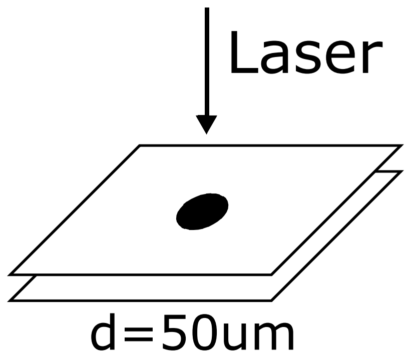

1480nm, 100mW

# Using Dye Molecules as Thermometer

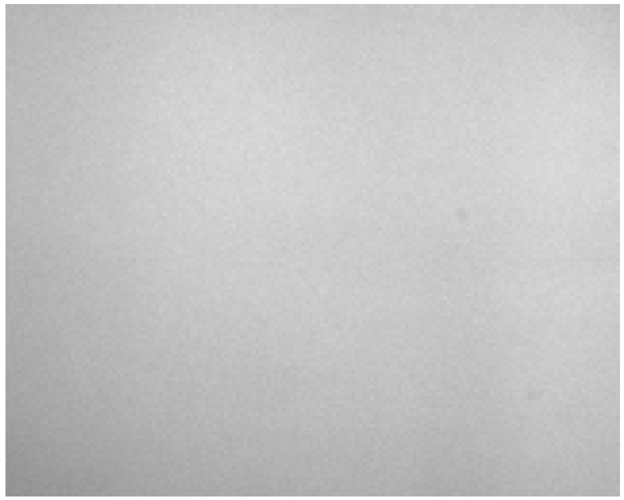
Temperature -> pH of TRIS -> pH Probe



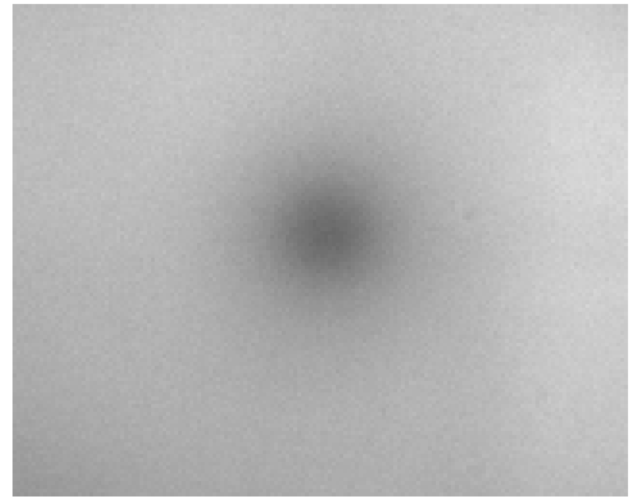
# Imaging Temperature



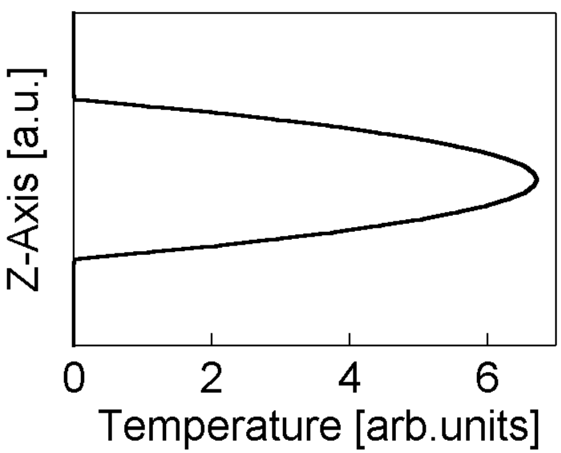

Laser off: cold



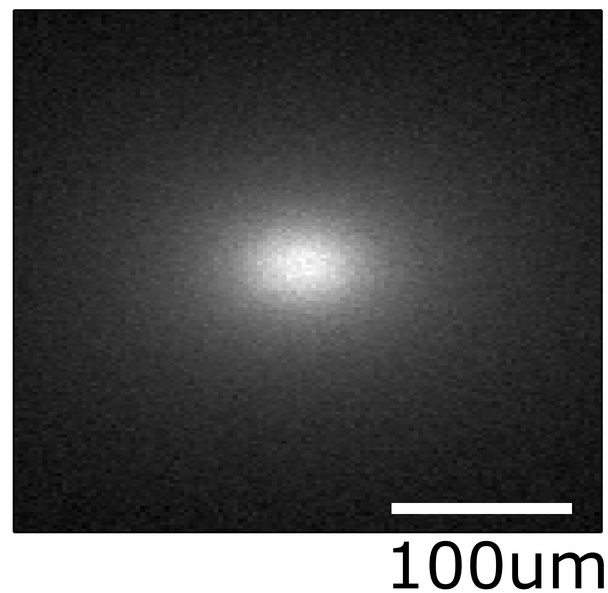
Laser on: hot



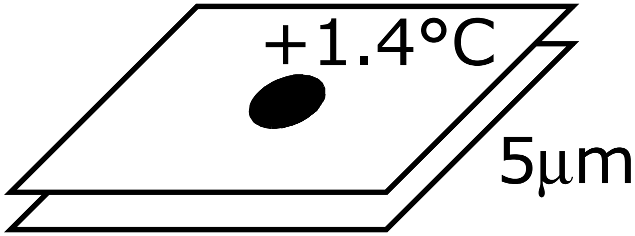
z-Profile



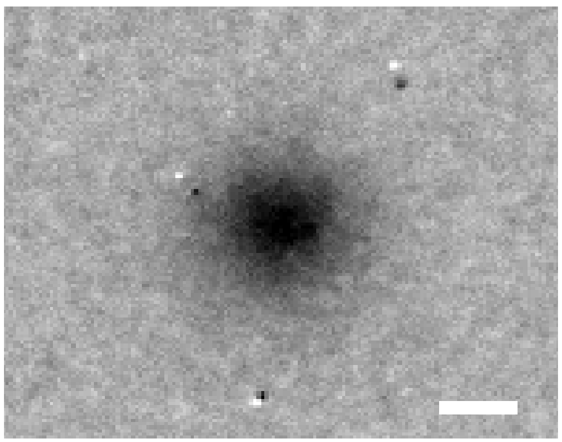

Temperature Image (z-average)



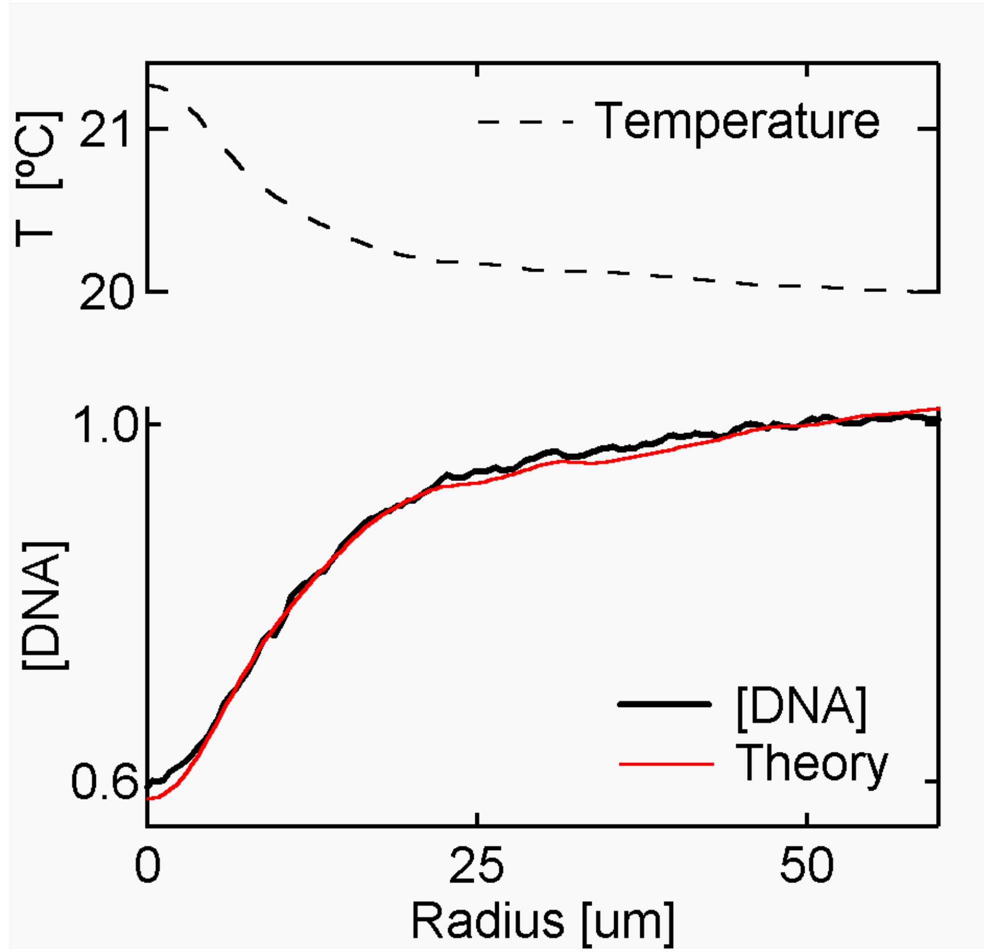
# Thermophoresis




5000bp DNA



50µm




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

$D_T/D=0.38K^{-1}$

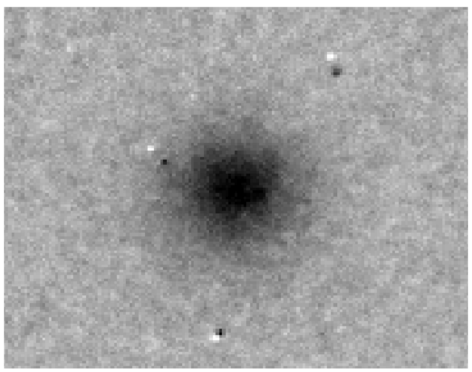
Backdiffusion $\longrightarrow$

$D=1.0x10^{-8}cm^2/s$

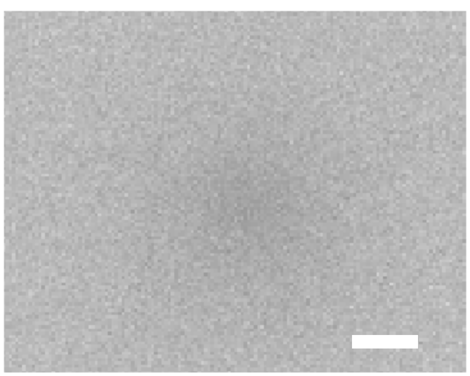
$D_T=0.4x10^{-8}\ cm^2/(sK)$

# Exponential Dependence on Length and Temperature ?

5000bp DNA

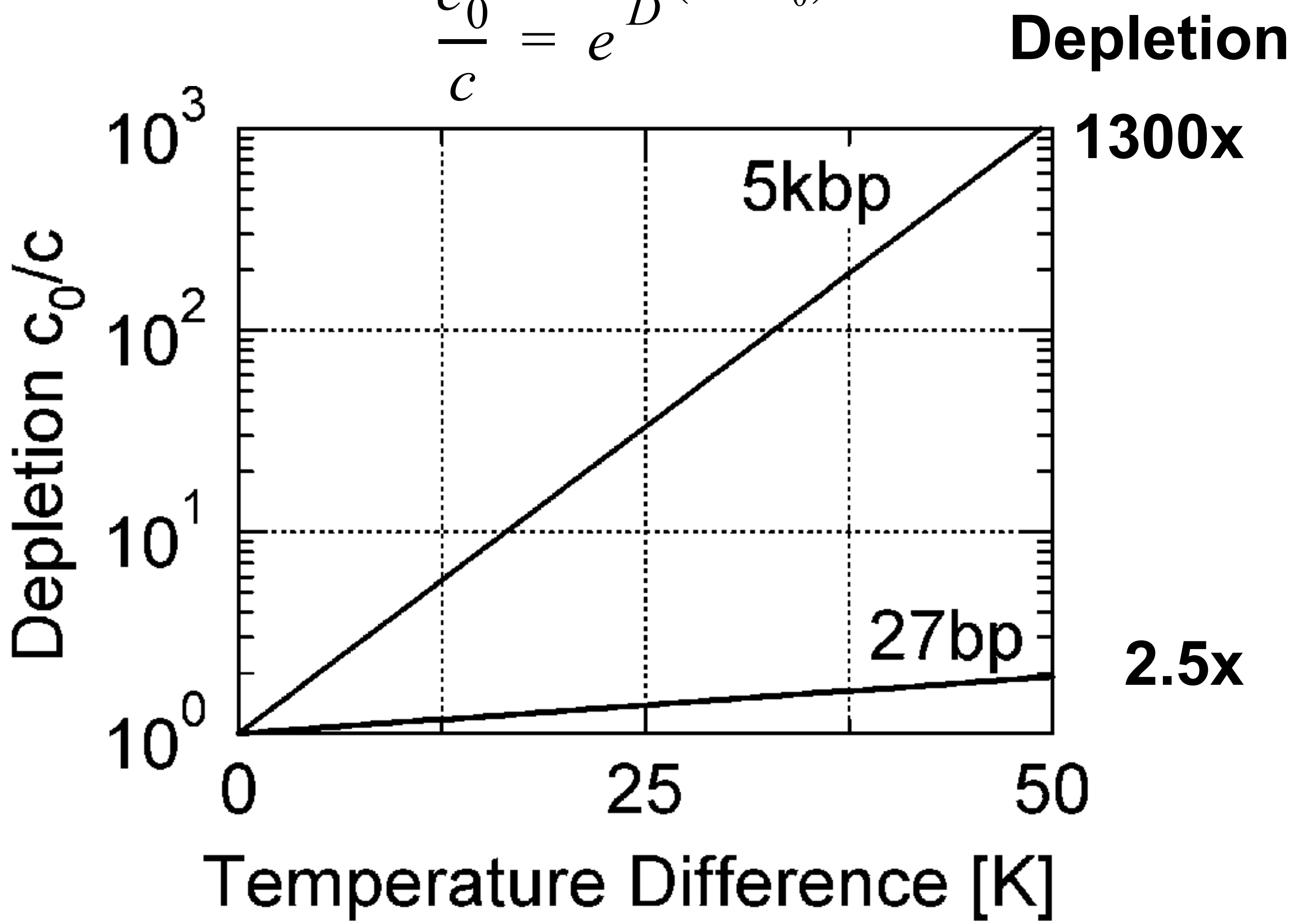


27bp DNA



50μm

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



# Origin of Thermophoresis?

## Phenomenological approach

$$j = -D\nabla c - D_T c(1-c)\nabla T \overset{!}{=} 0 \xrightarrow[D_T = \text{const.}]{} \frac{c}{c_0} = e^{-\frac{D_T}{D}(T-T_0)}$$

## Interfacial Free Energy argument for ionic thermophoresis (Piazza 2002, Ruckenstein 1981)

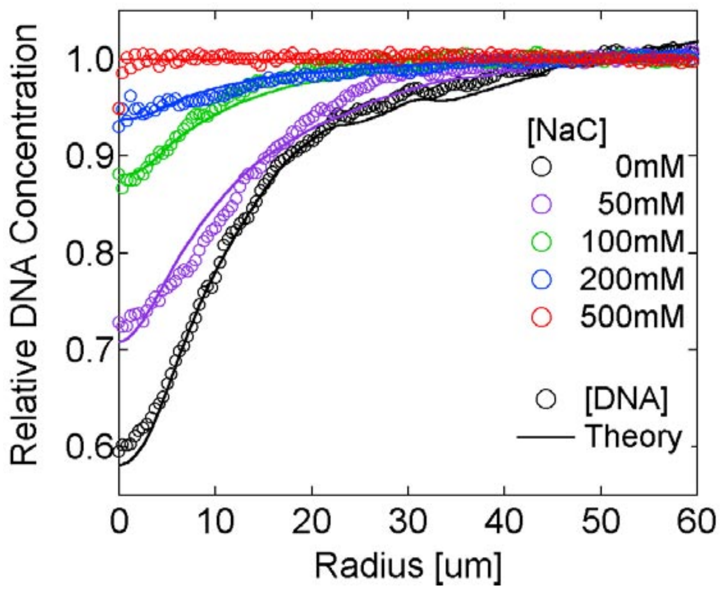
Debye Hückel Length $\lambda_{DH} = \sqrt{(\varepsilon k_B T)/[2c_S e^2]}$

Interfacial Free Energy $\gamma = -\varepsilon\psi_S^2/8\pi\lambda_{DH}$

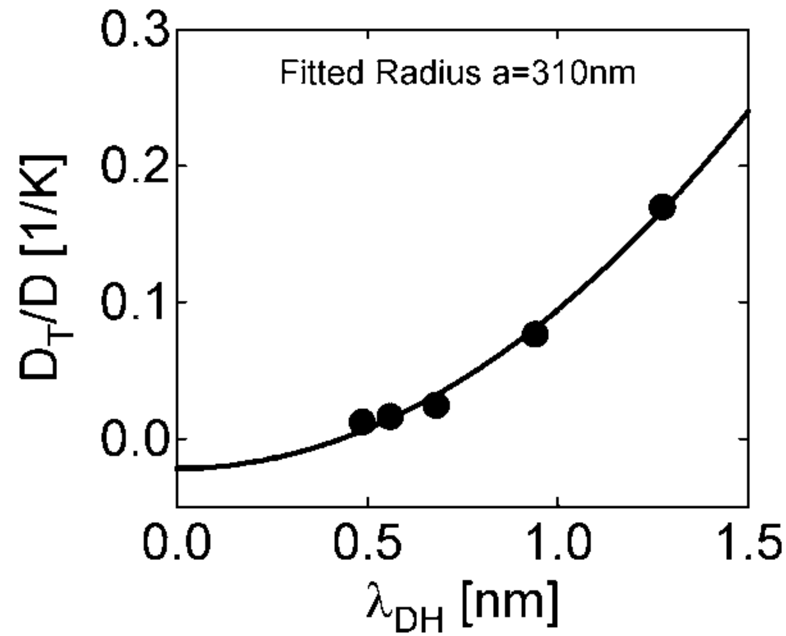
Drift velocity (Ruckenstein) $v = -l\nabla\gamma/\eta = -\frac{\varepsilon\psi_S^2}{32\pi\eta T}\nabla T$

$$\begin{aligned} \psi_S^2 &= Z_{eff} e\lambda_{DH}/\varepsilon a^2 \\ l_B &= e^2/4\pi\varepsilon k_B T \\ f_0 &= 6\pi\eta a \\ D_0 &= k_B T/f_0 \end{aligned} \longrightarrow \left.\frac{D_T}{D_0}\right|_{ionic} = \frac{3\pi l_B Z_{eff}^2}{4Ta^3}\lambda_{DH}^2 \sim \lambda_{DH}^2$$

# Scaling with Salt Concentration

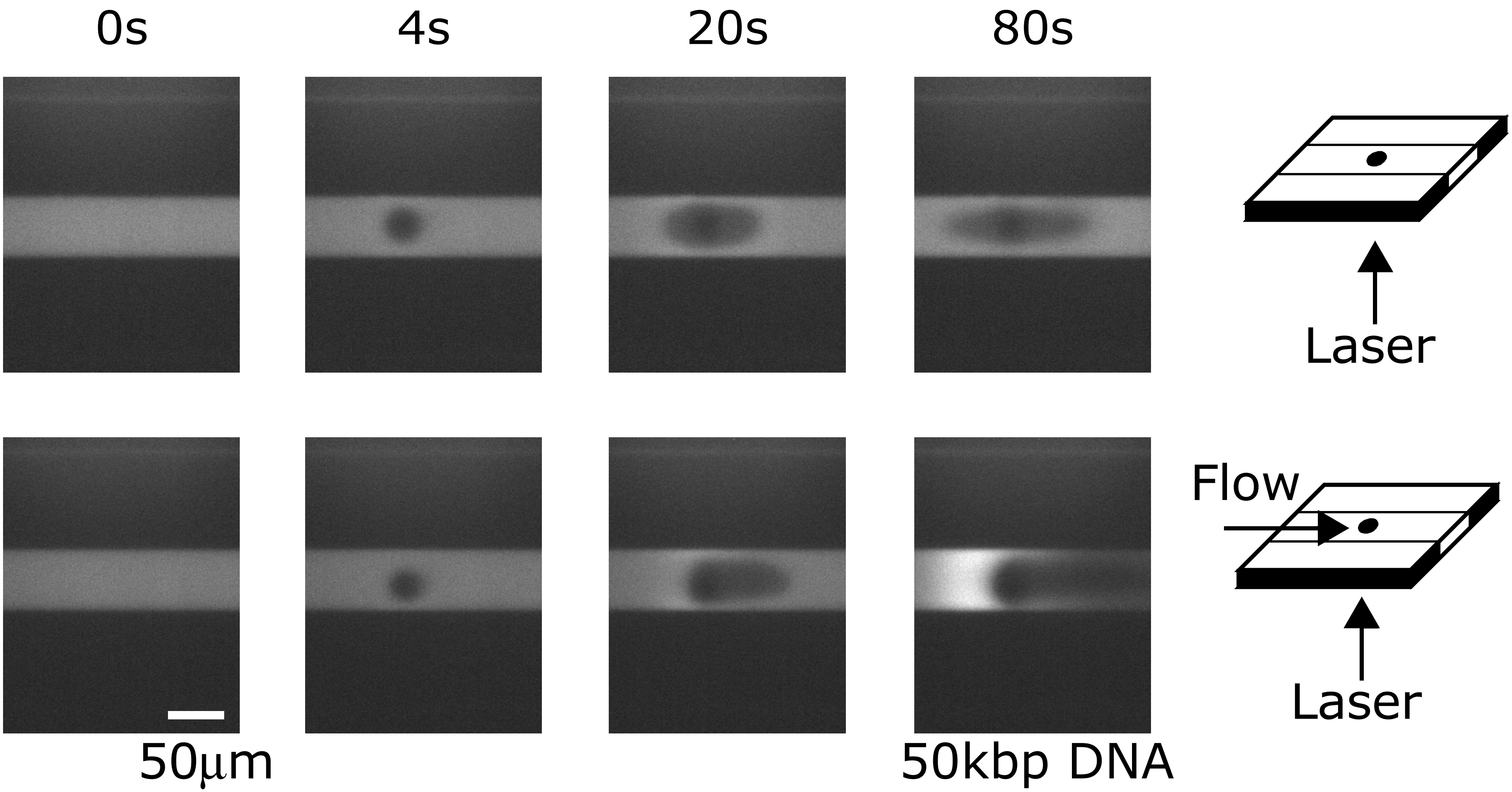



[Similar for 40nm Beads]

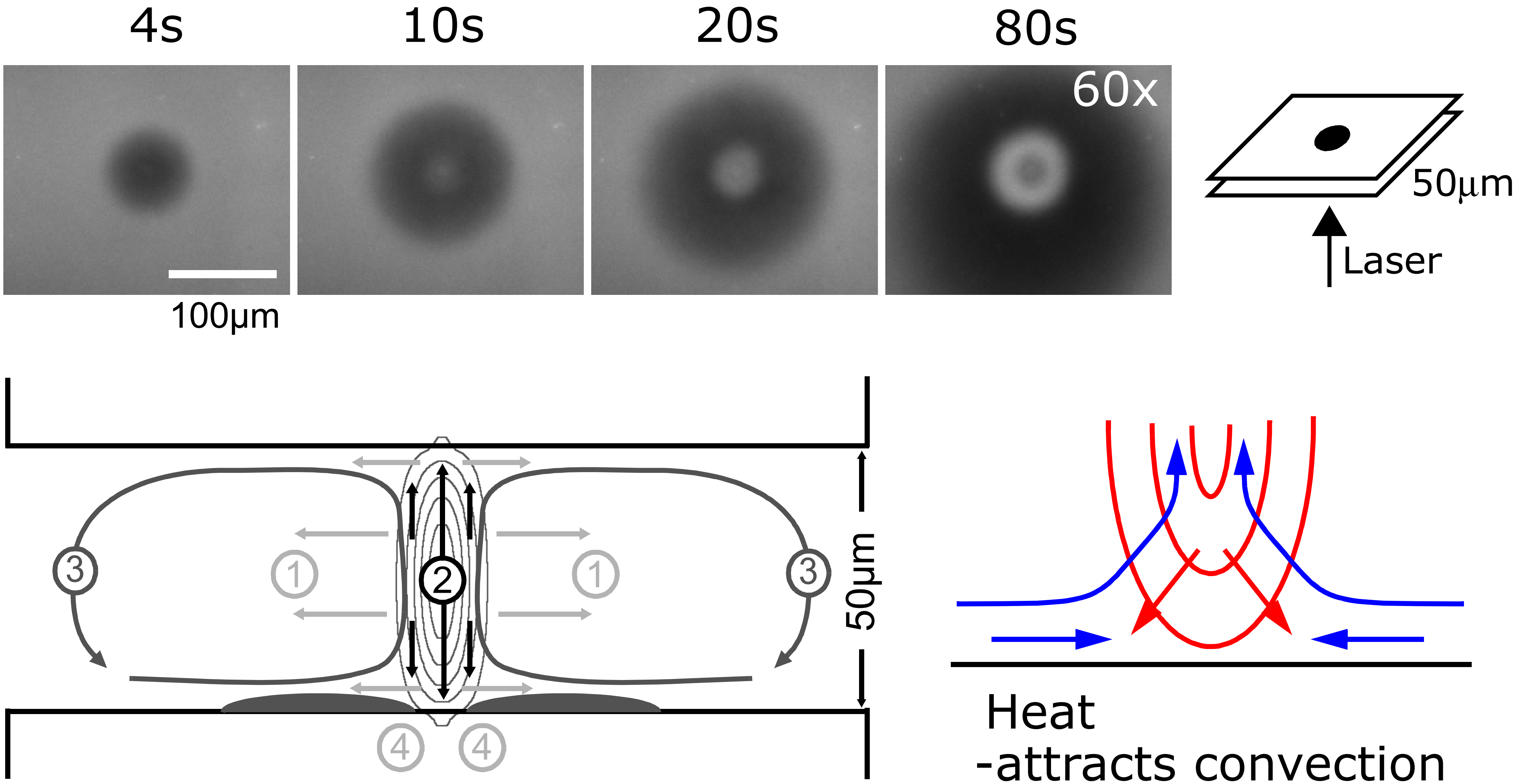



$$\left.\frac{D_T}{D_0}\right|_{ionic} = \frac{3\pi l_B Z_{eff}^2}{4Ta^3}\lambda_{DH}^2 \sim \lambda_{DH}^2$$

# Thermophoresis in Microfluidics: Flow turns depletion into accumulation

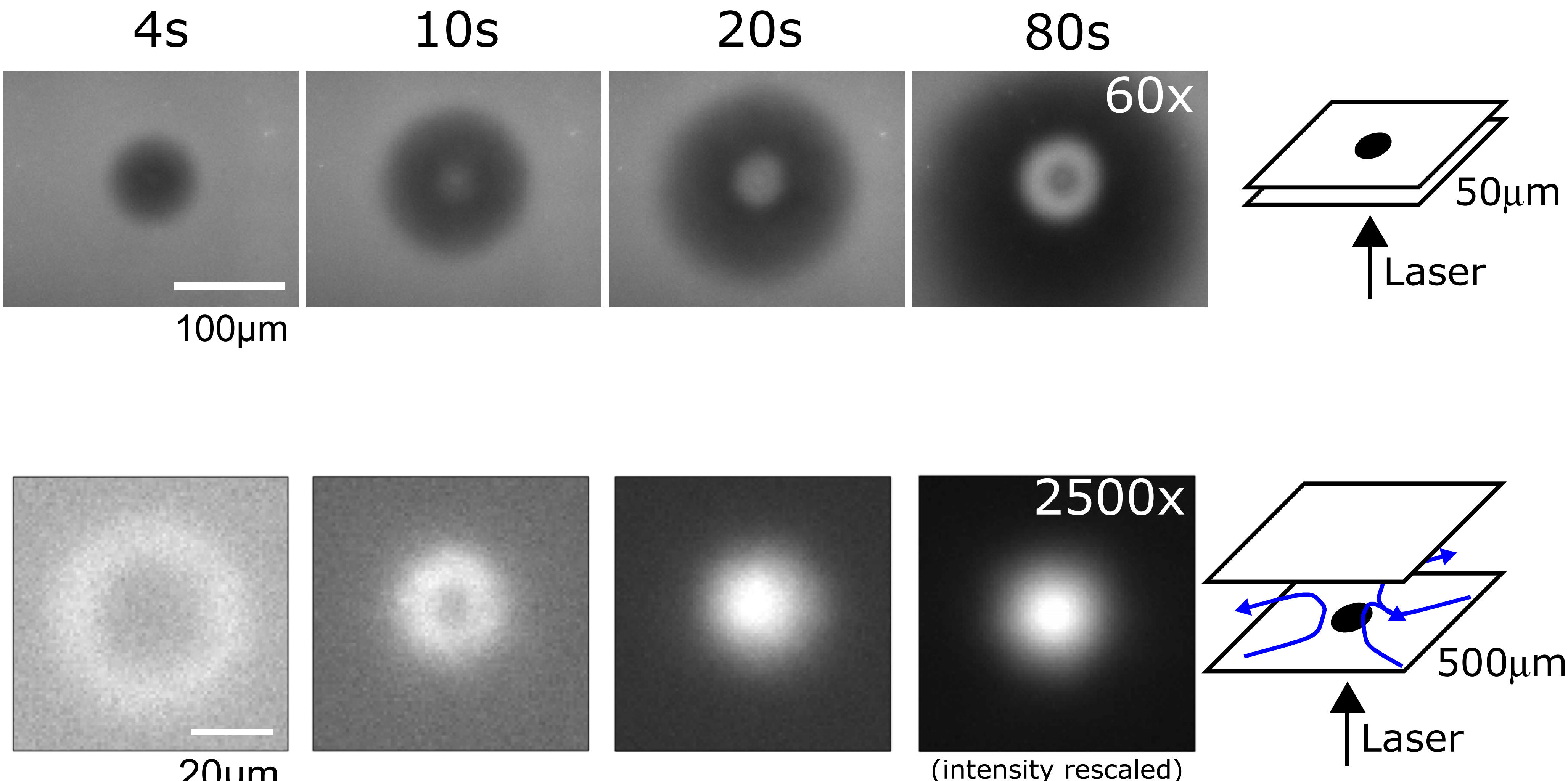


# Thermophoretic Trapping by Convection



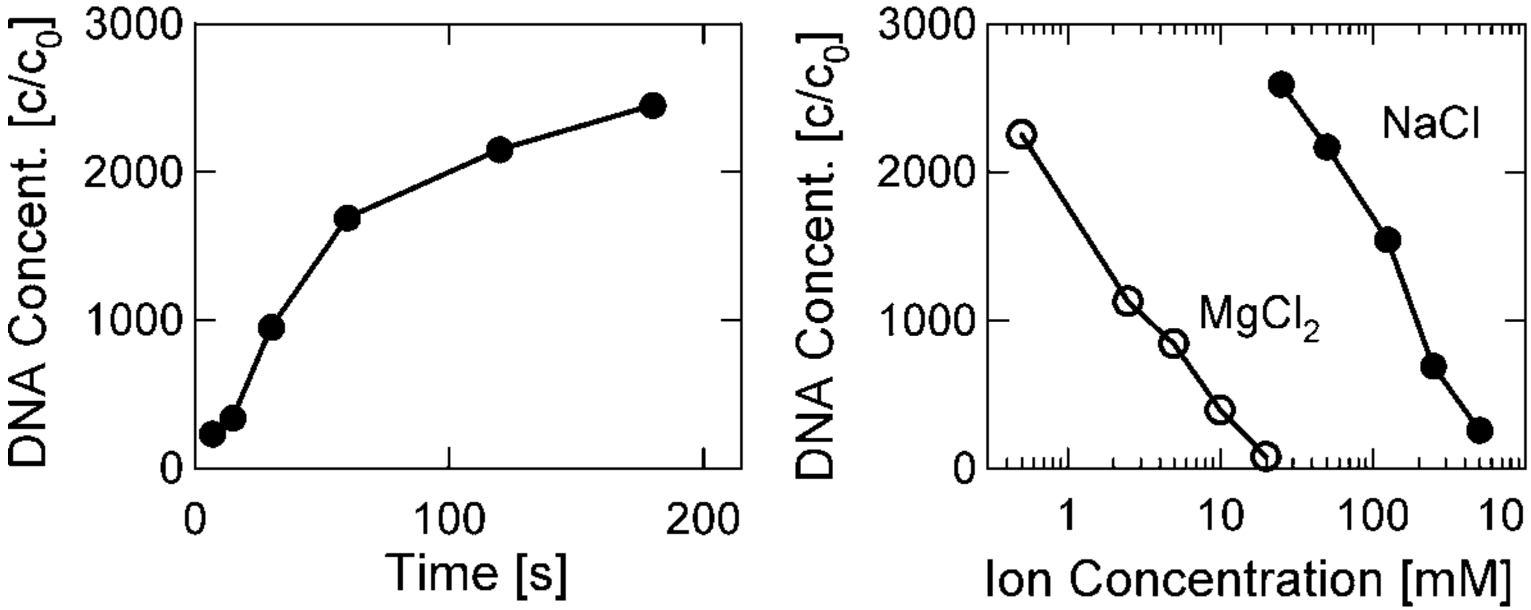

Heat
-attracts convection
-repels DNA

# Thermophoretic Trapping by Convection

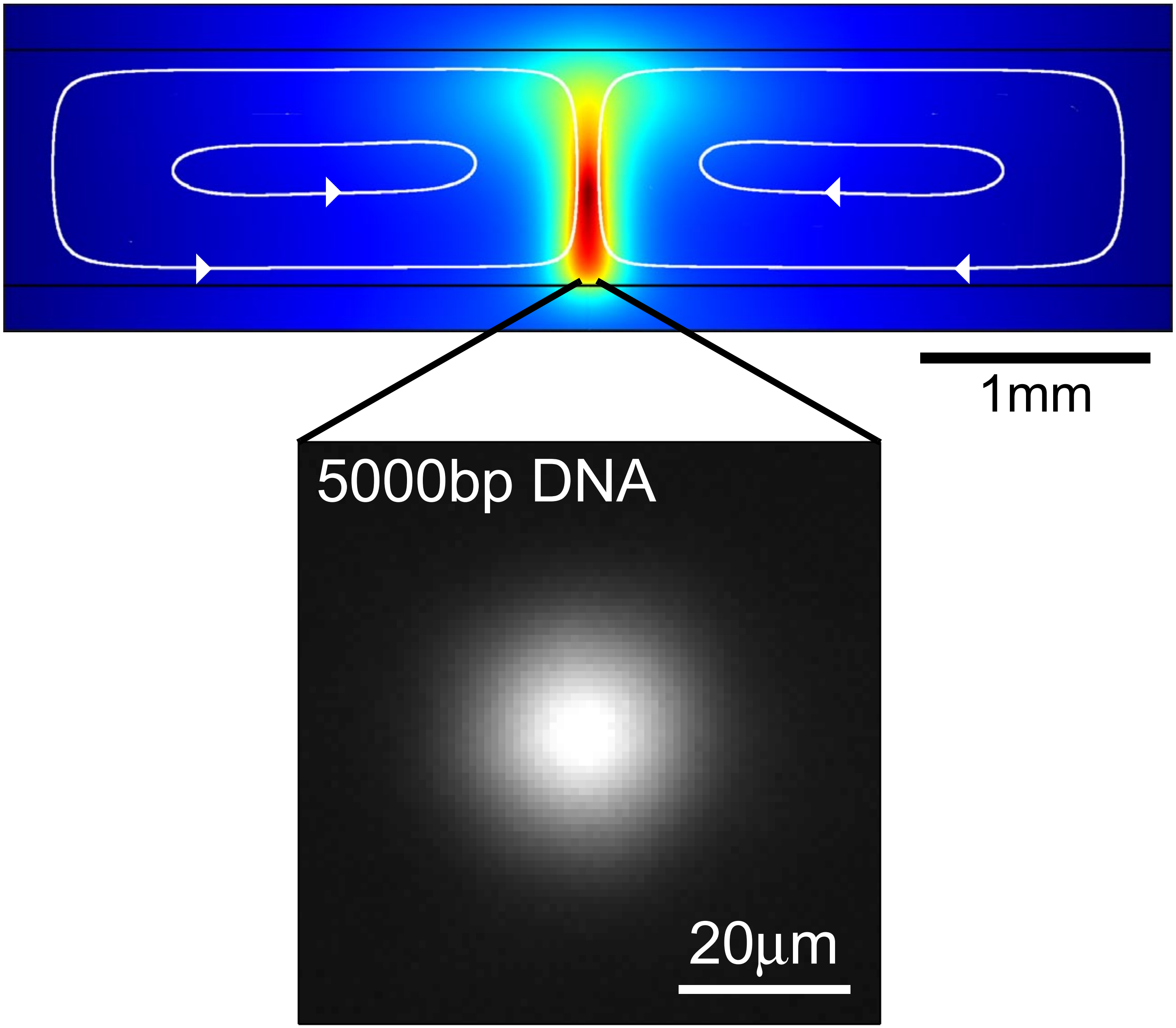



PRL 89:188103 (2002)
Physics Today Feb. 2003

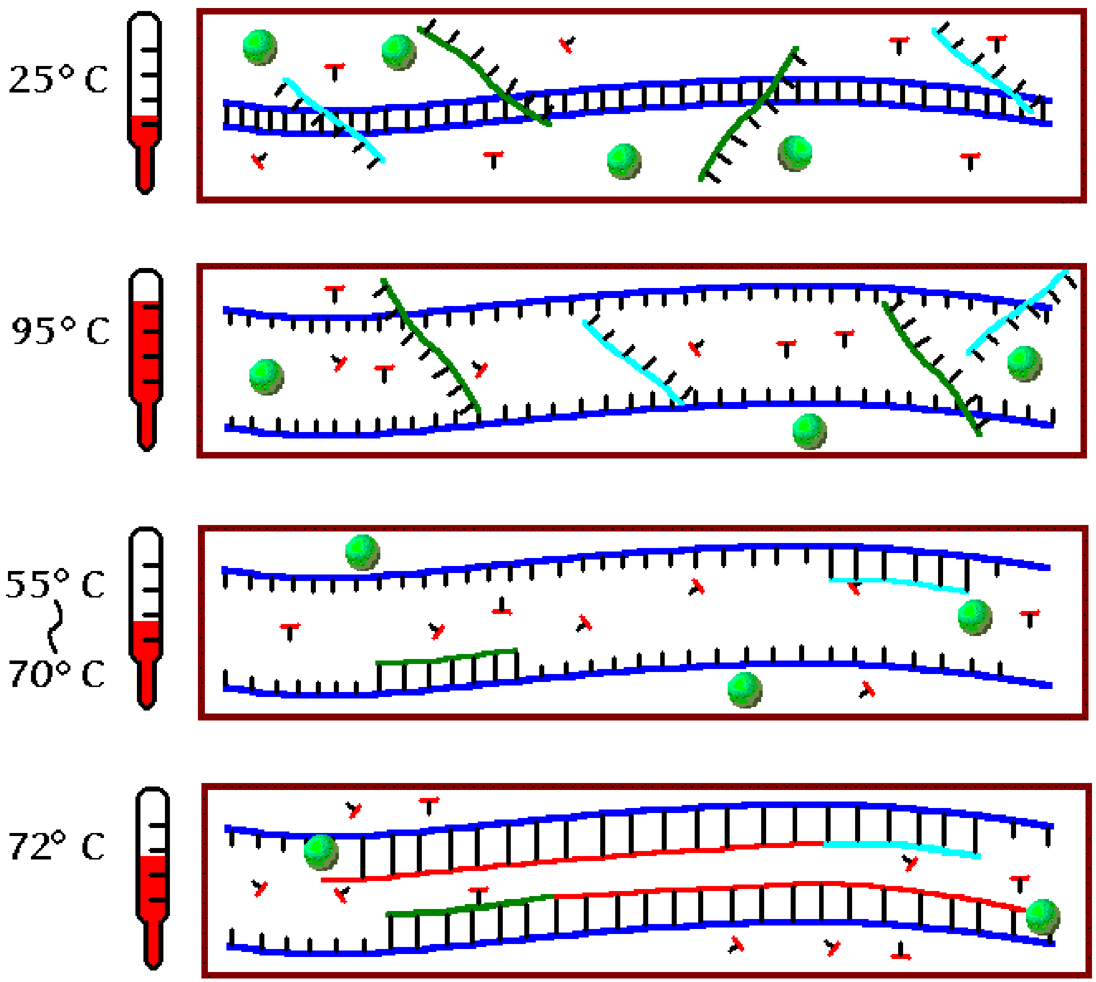
# Strong accumulation



# Thermophoretic Trapping by Convection



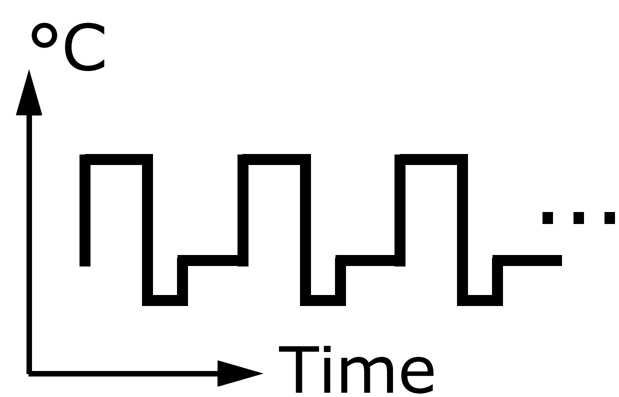
# Polymerase Chain Reaction (PCR)



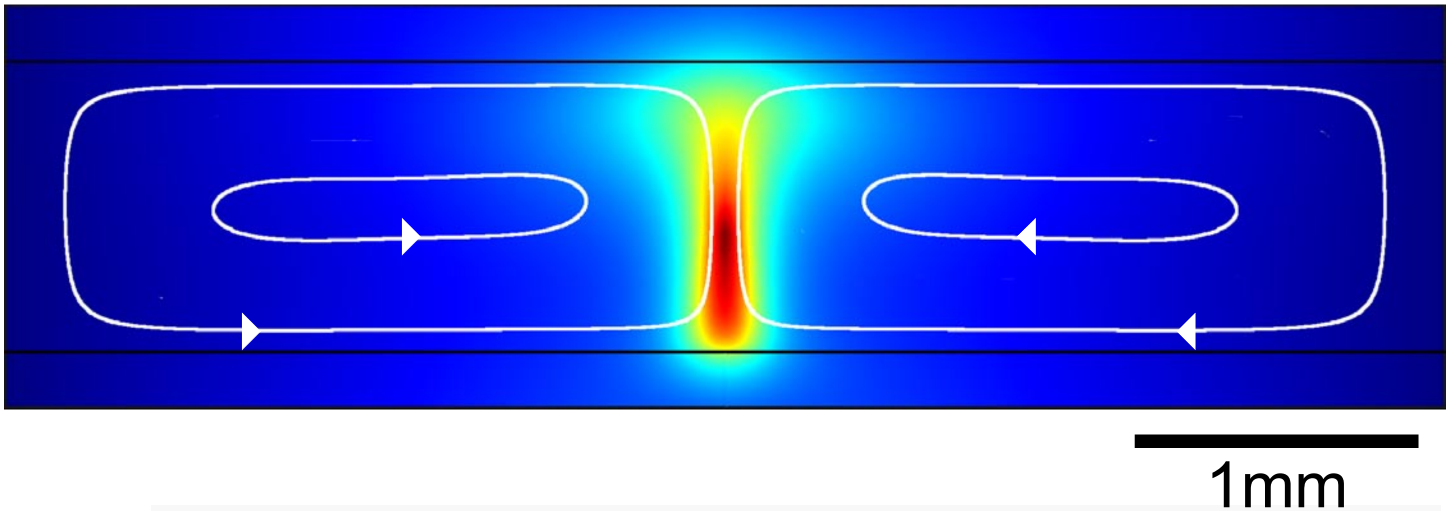

DNA Detection down to single Molecules

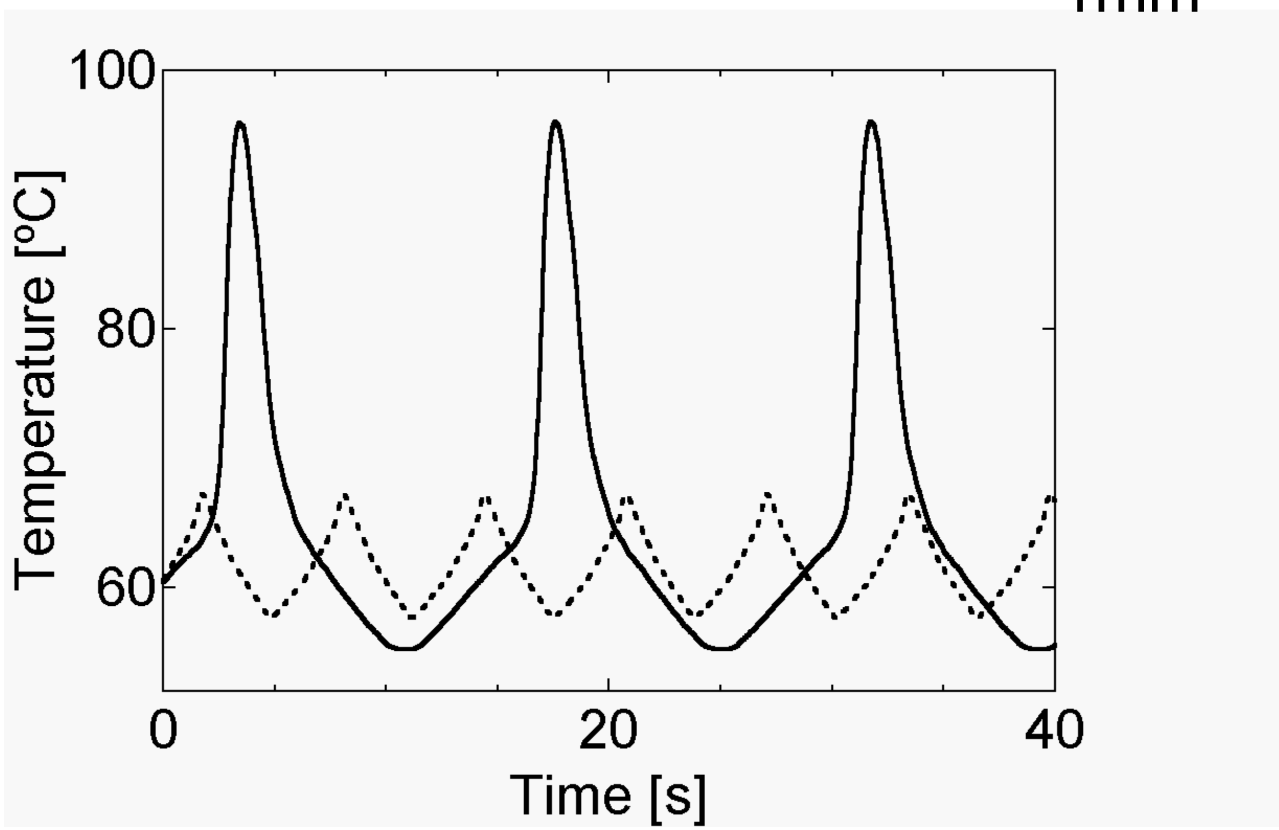
AIDS-Test

Future of DNA Chips ?!

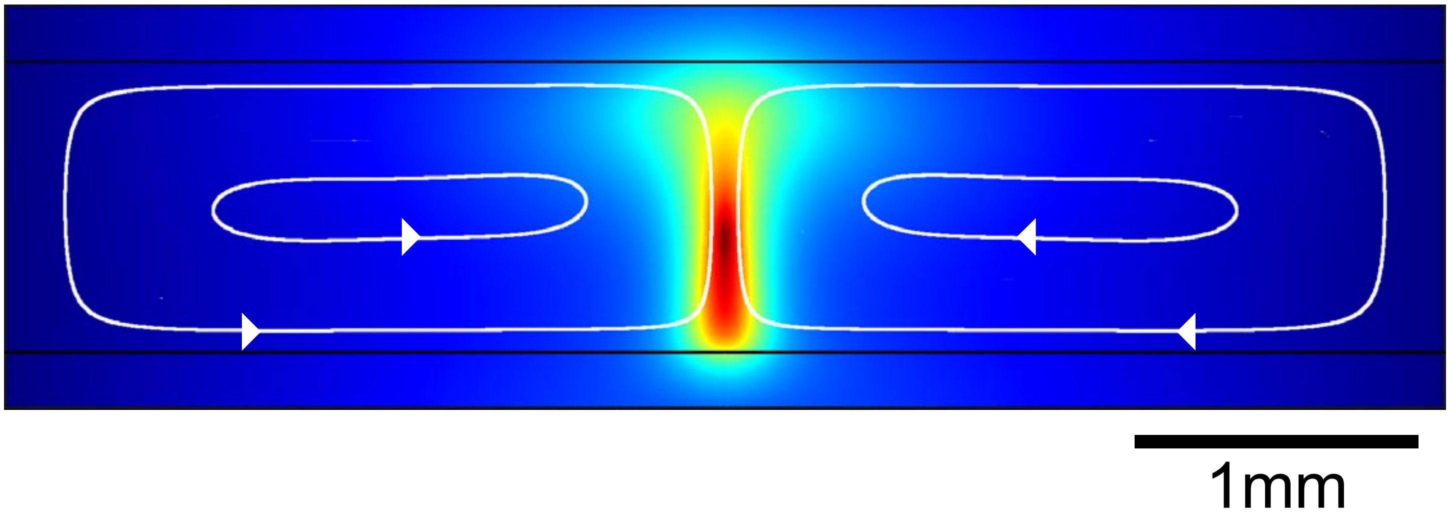


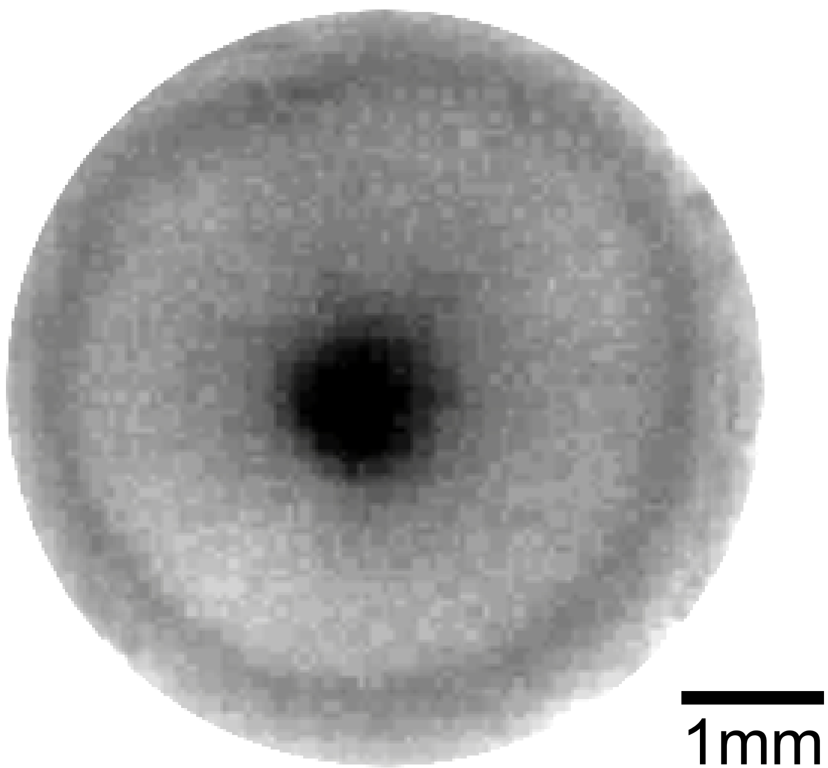
# PCR by Convection



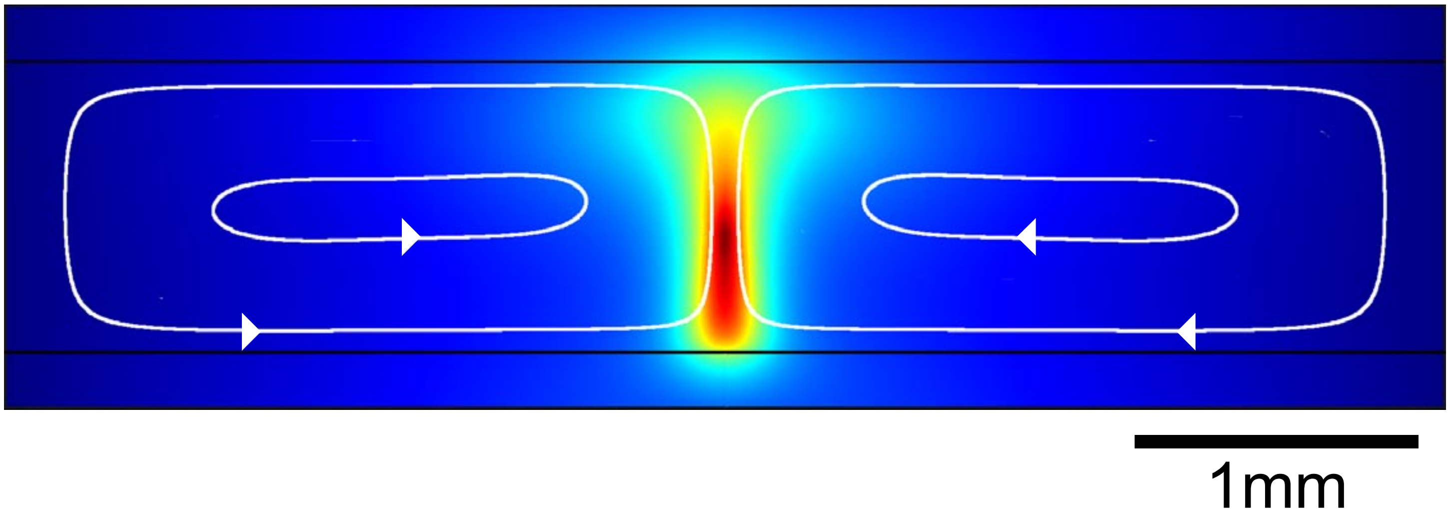



# PCR by Convection

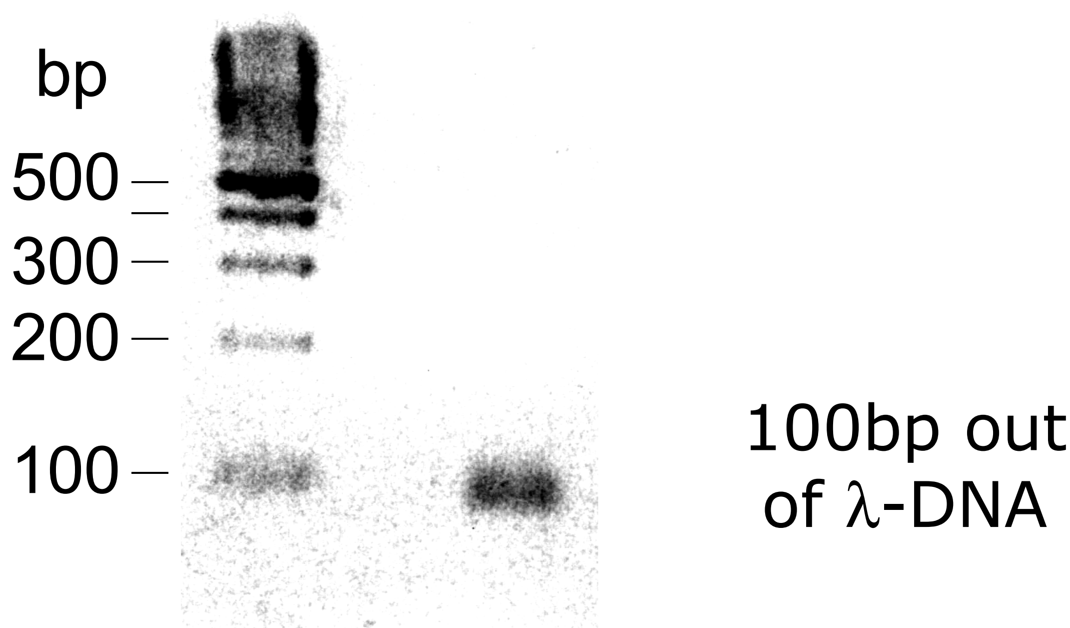


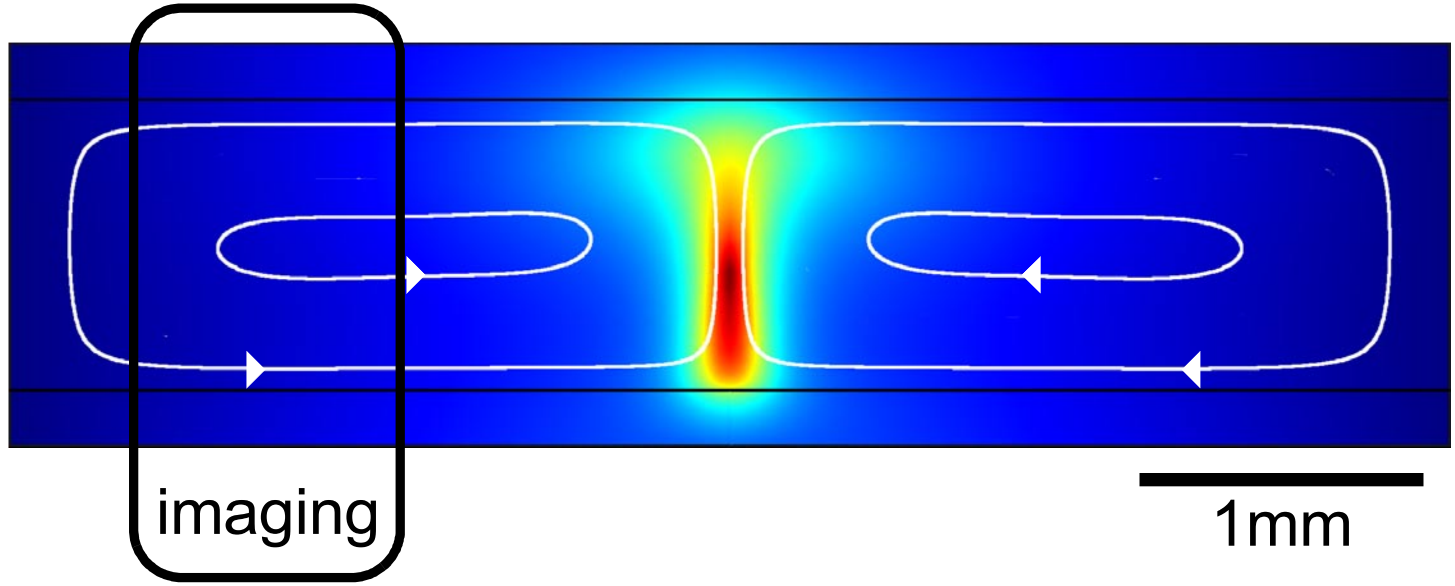
# PCR by Convection

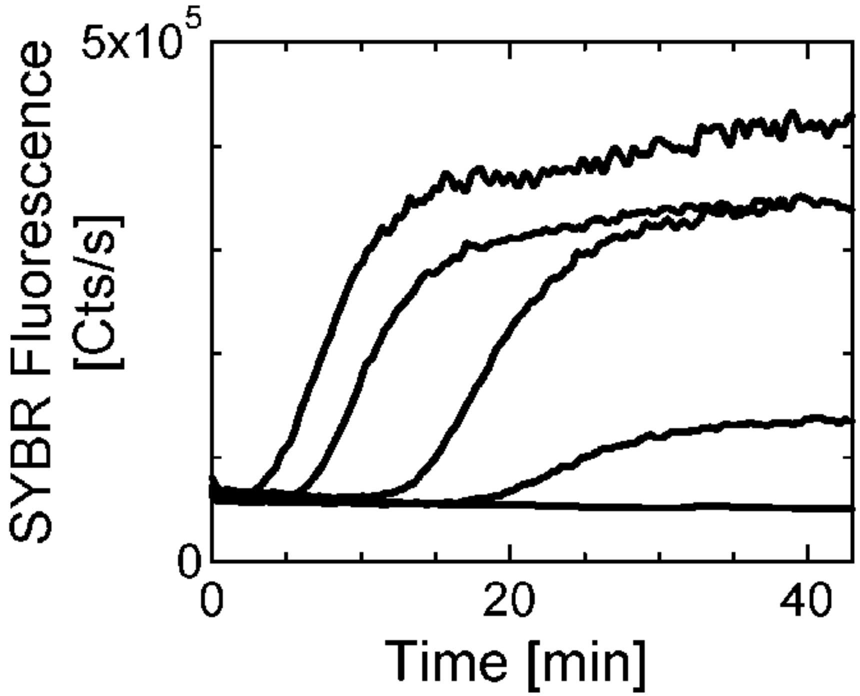


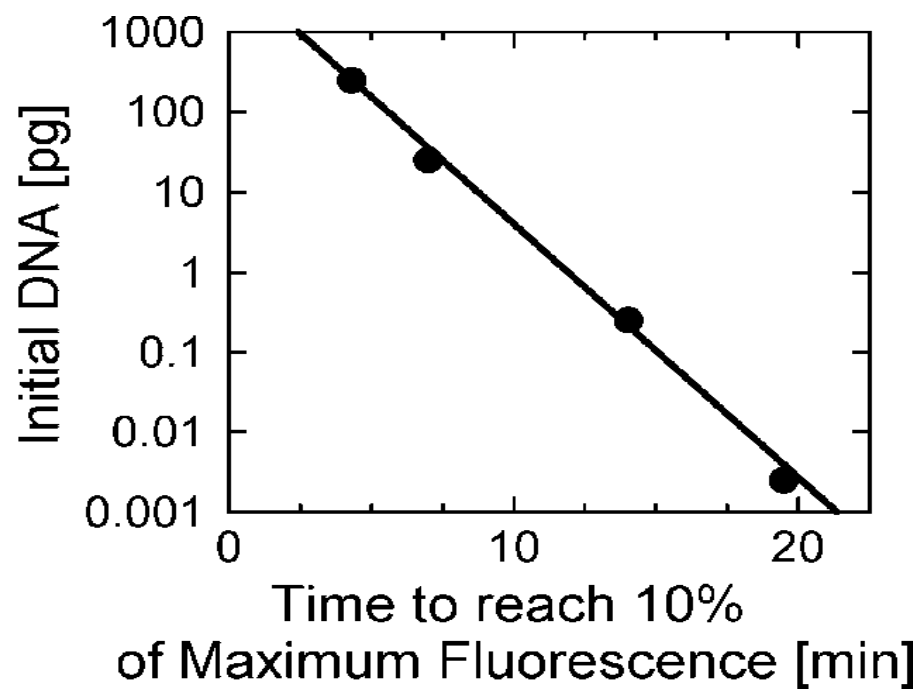

Amplification 100.000x
in 25 Minutes



# Quantitative PCR by Convection

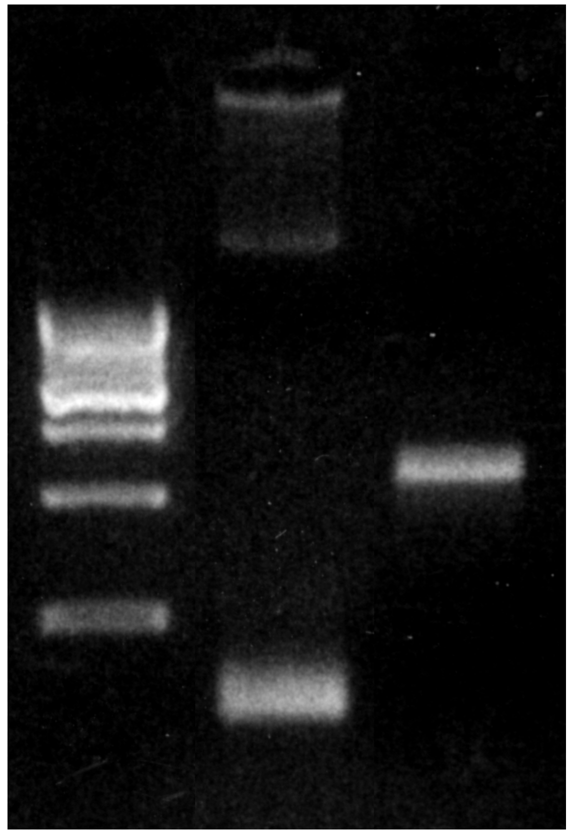


# Standard PCR by Convection

Chamber size **10x0.5mm** (before: 5x1mm)

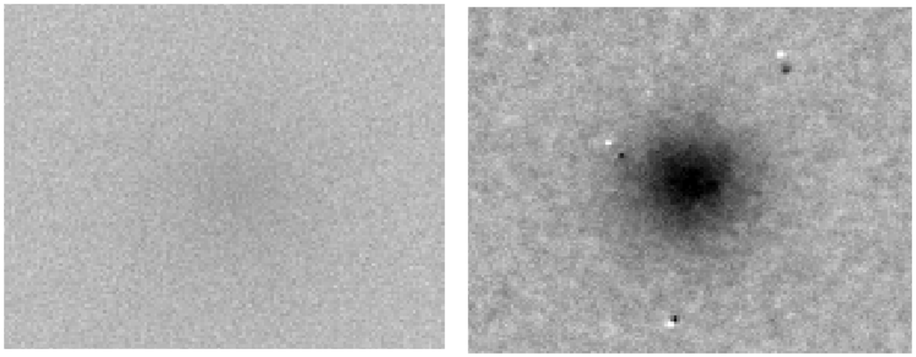


350bp of β-Actin out of human DNA

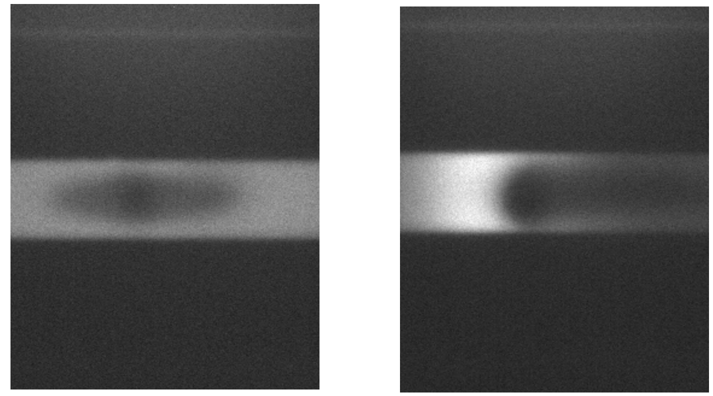
1100bp out of λ-DNA

# Localized Heating

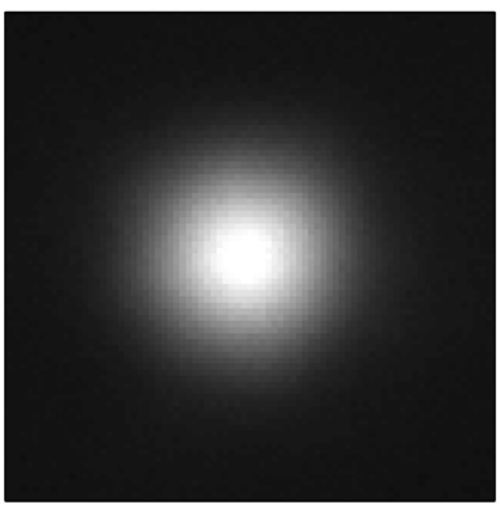
## Depletion is highly length dependent



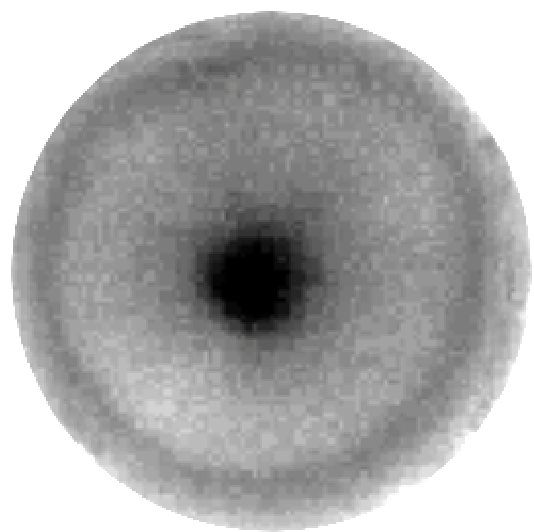
## IR heating compatible with microfluidics



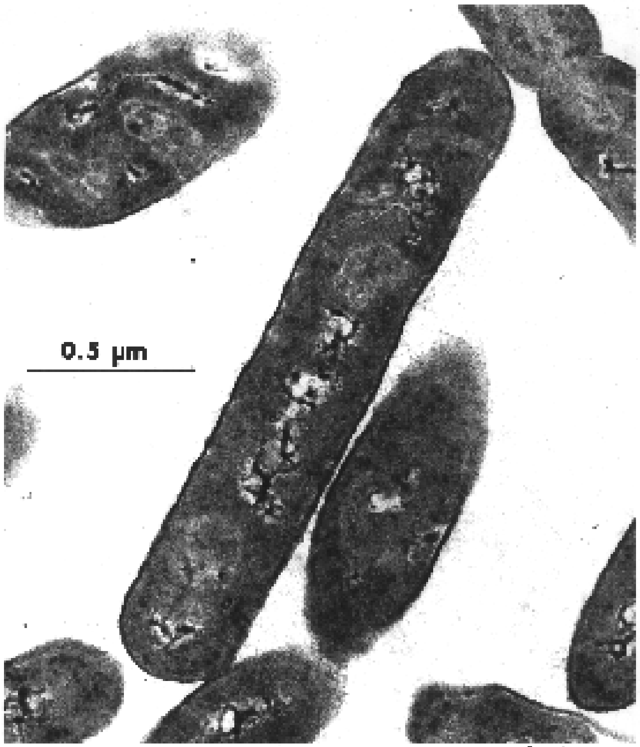
## With Convection leads to strong accumulation



## Laminar Convection can drive PCR fast



## Archaea



Stetter, Regensburg

## “The unseen majority”

(Whitman, PNAS, 95:6578, 1998)

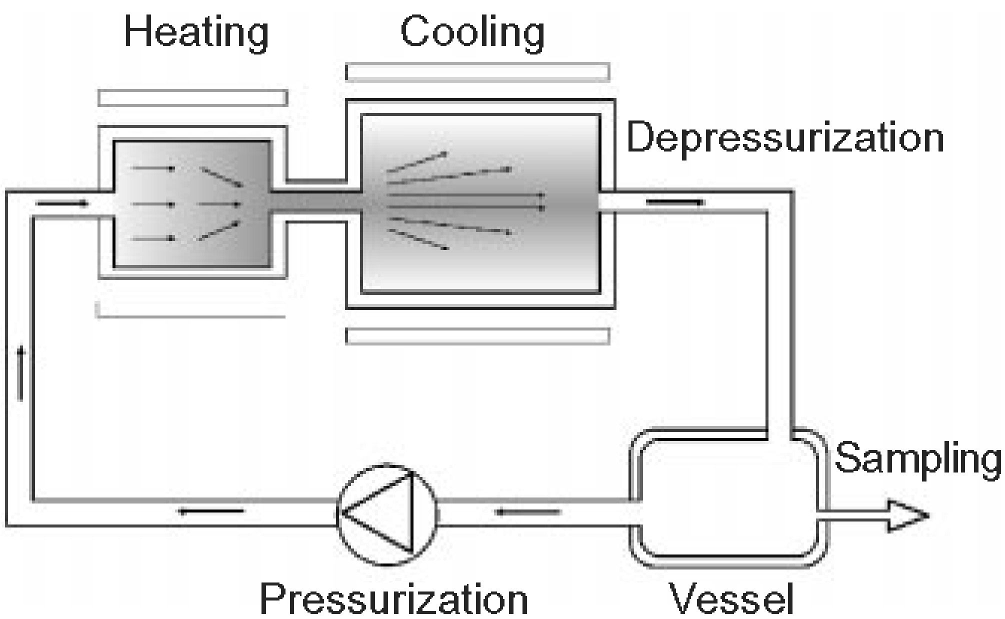
Table 5. Number of prokaryotes in the world

| Environment | No. of prokaryotic cells, $\times 10^{28}$ |
|---|---|
| Aquatic habitats | 12 |
| Oceanic subsurface | 355 |
| Soil | 26 |
| Terrestrial subsurface | 25–250 |
| Total | 415–640 |

## “There is plenty of room at the bottom”

# Peptide Synthesis from quenched Heating

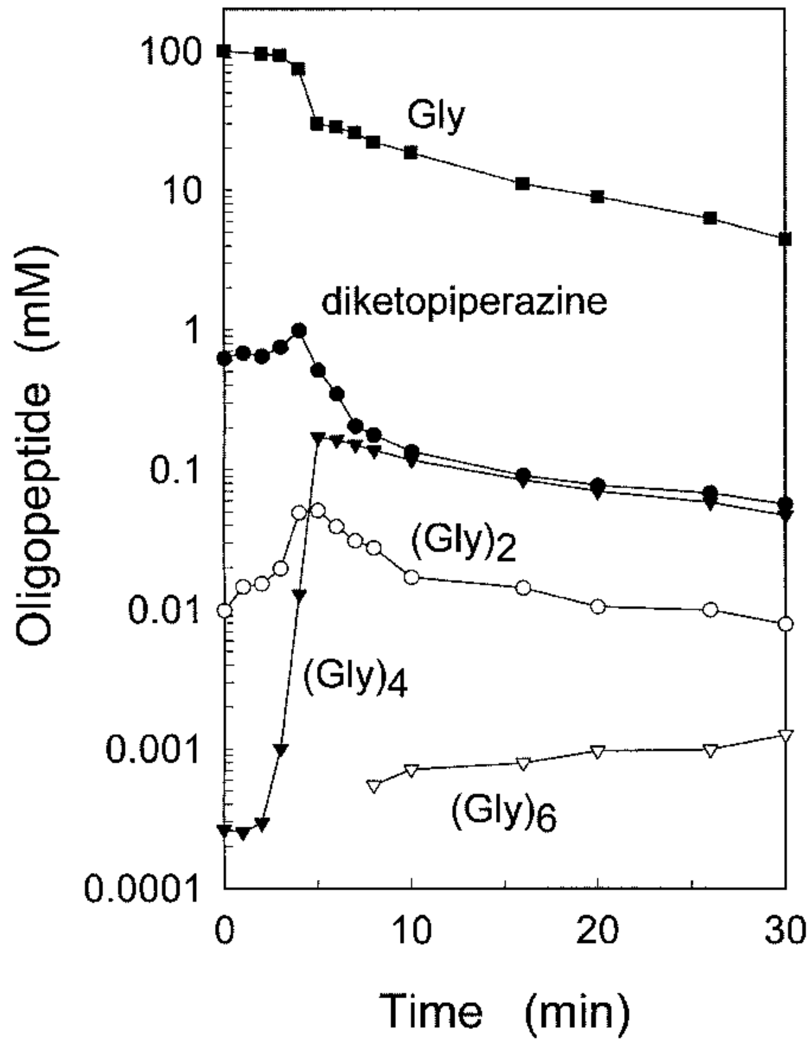
Koichiro Matsuno et.al. Science 283:831 (1999)




250bar, 220°C

10ms

4°C



# Temperature Gradients

Accumulate DNA
Induce DNA Replication
Synthesize Peptides (?)

=> A convective Protocell ?

# Origin of Life in pores near Hydrothermal Vents?