Principles of Electronic Nanobiosensors

Unit 2: Settling Time

Lecture 2.5: Beating the Limits – Barcode Sensors

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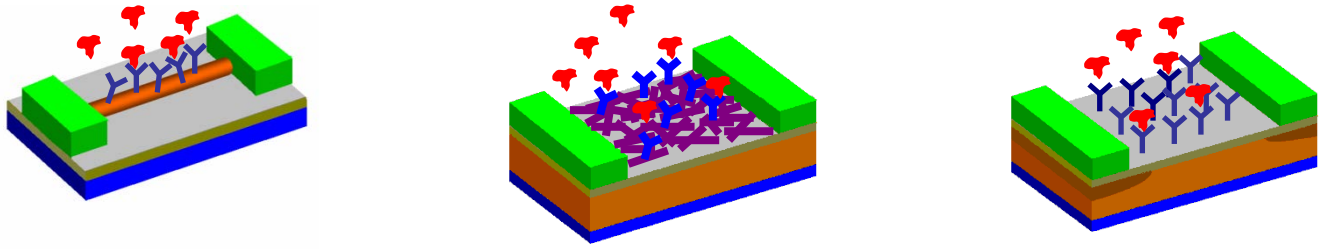
A ‘fundamental’ relationship of biosensor



D=1 1<D<2 D=2

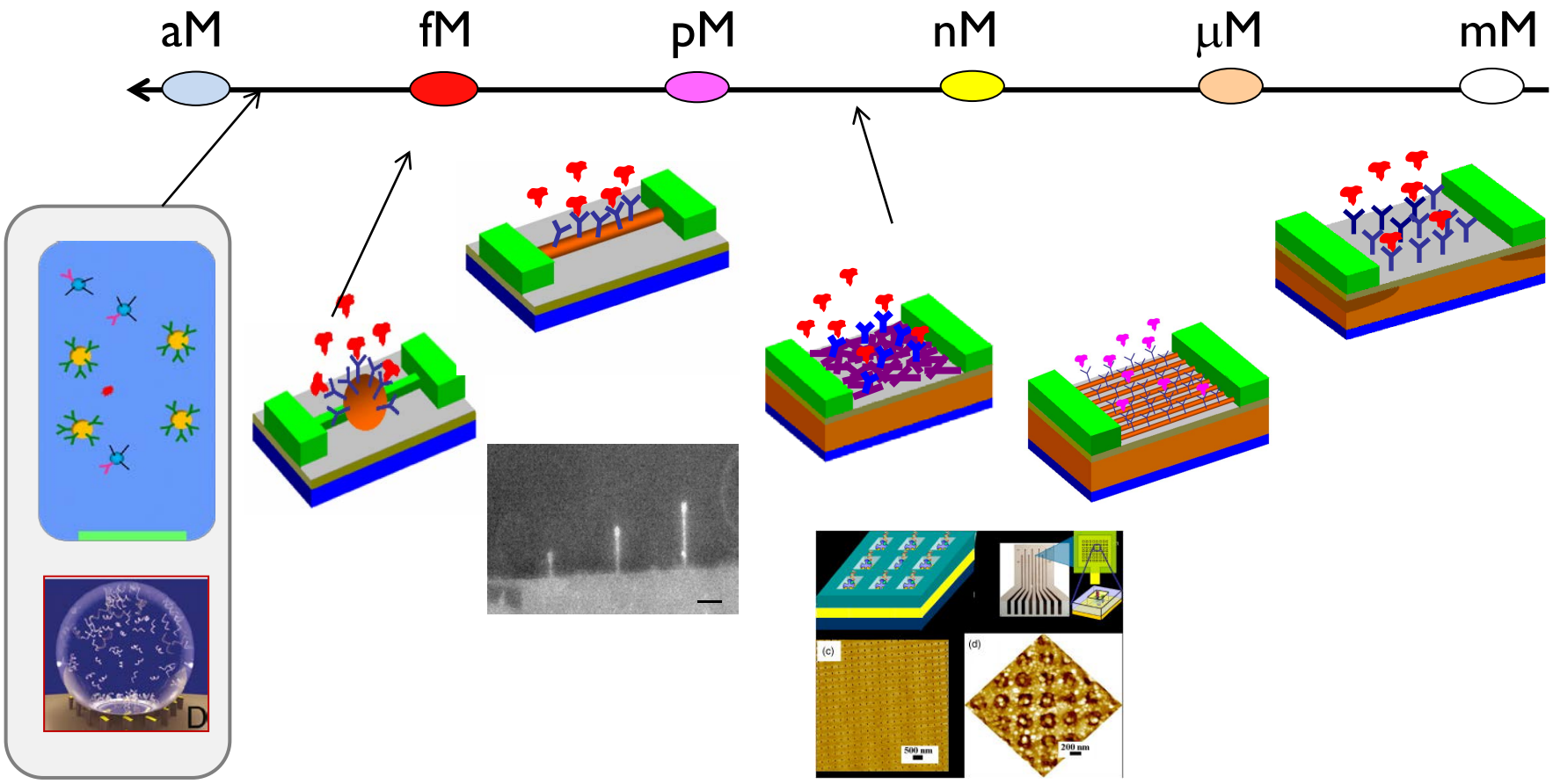
$$\rho_0 = N_s \times t_s^{-\left(\frac{3-D_F}{2}\right)}$$

… not as fundamental as the uncertainty principle!

Outline

- Three approaches to beat the diffusion limit
- Technique of distributed sensors: Biobarcode
- Physics of biobarcode operation
- Enhancement of detection limits by biobarcode and closely related approaches
- Conclusion

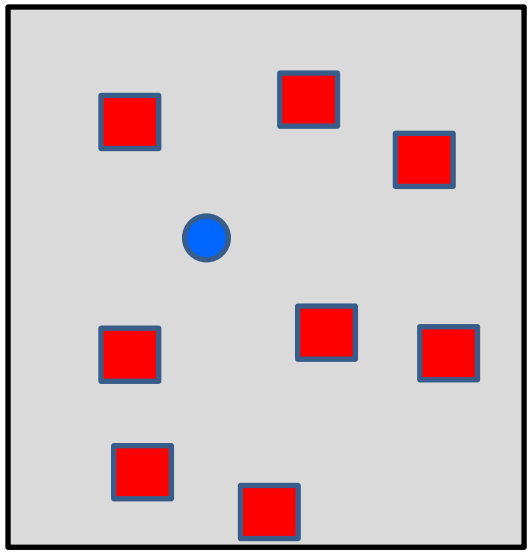
A ‘Mendeleev table’ for biosensors



Strategies to beat the diffusion limit

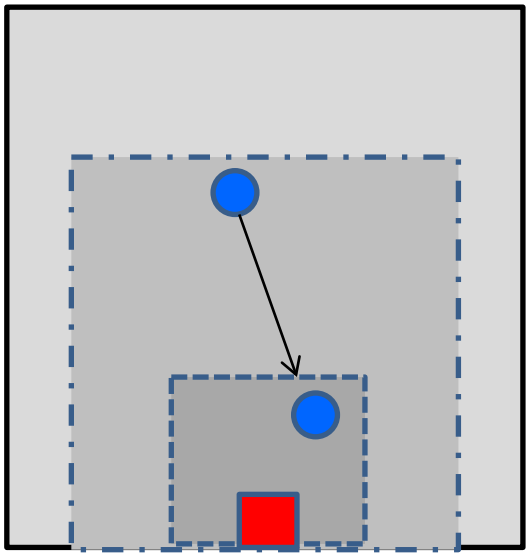
$$\tau \sim L^2/D$$

Fragment the space



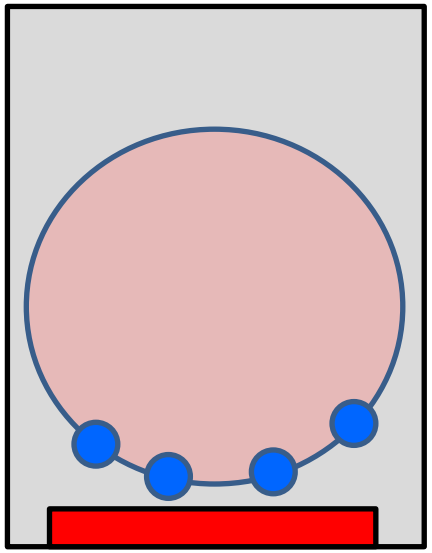
Magnetic biobarcode

Reduce the space



Droplet evaporation

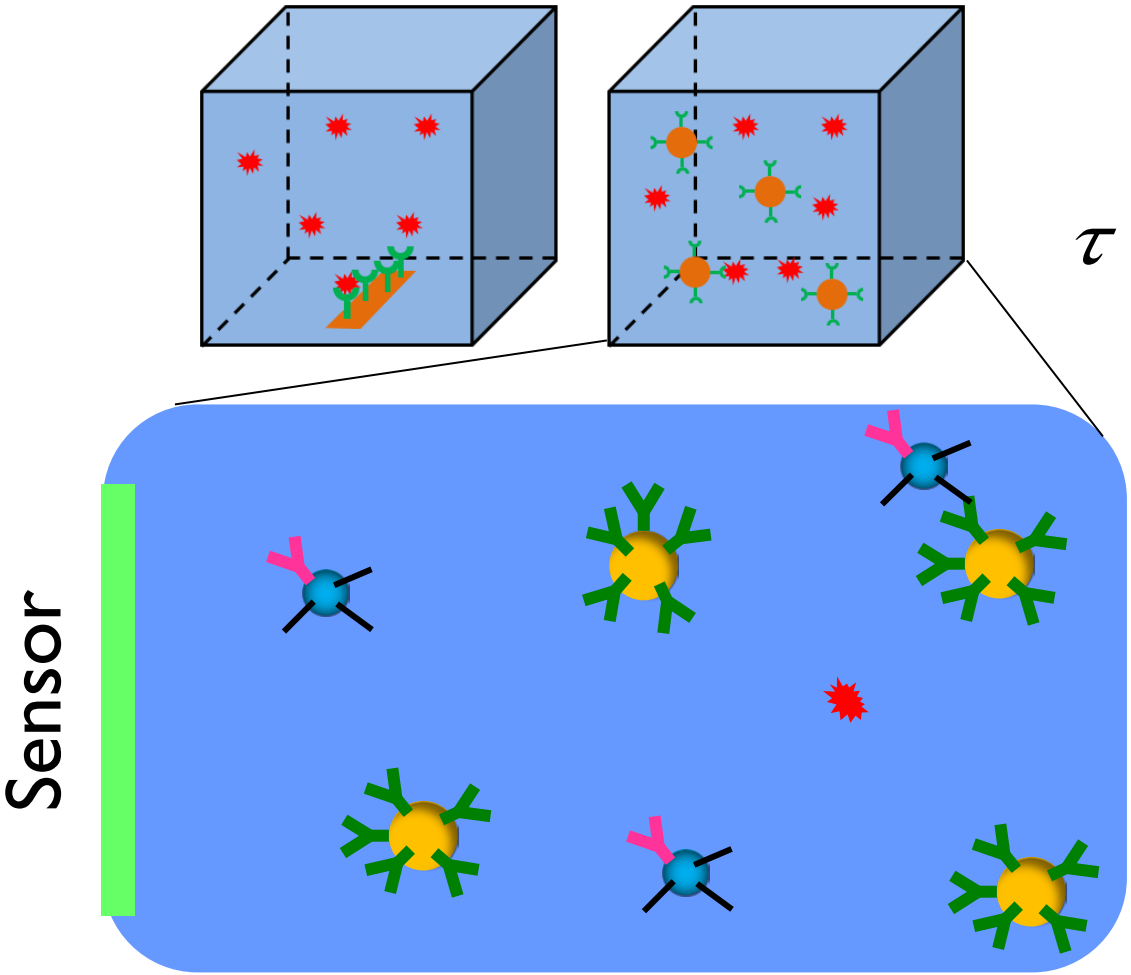
Generate locally



Ion torrent approach

All can achieve sub-fM detection in reasonable time

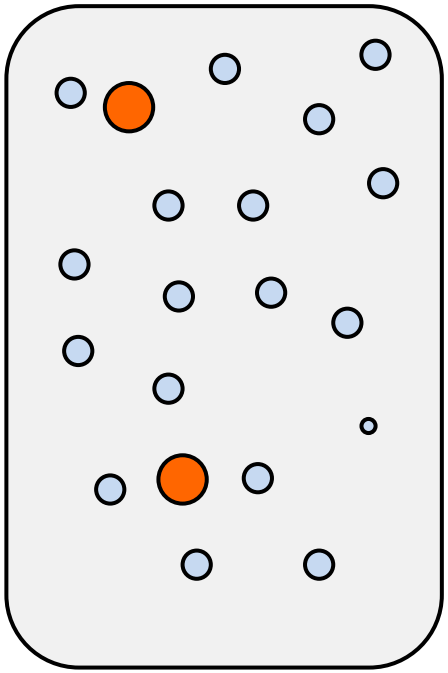
Magnetic nanoparticle barcode sensor

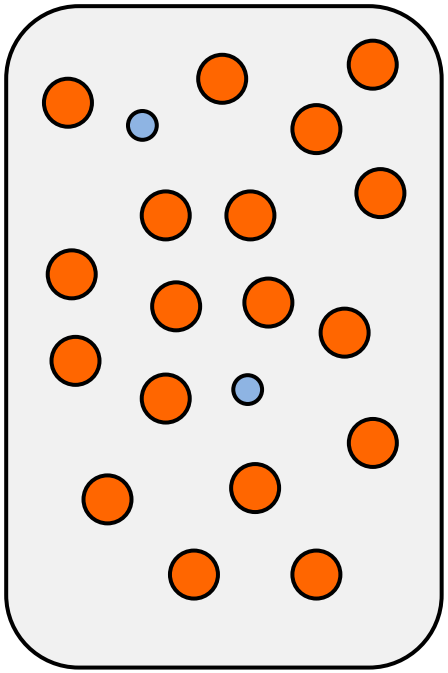


$$\tau \sim L^2/D$$

In sum, a police-thief story!

Analytical solution: two limits





$$t_S = \frac{N_S}{4\pi D a_0 \rho_T} \quad \text{(Ia)}$$

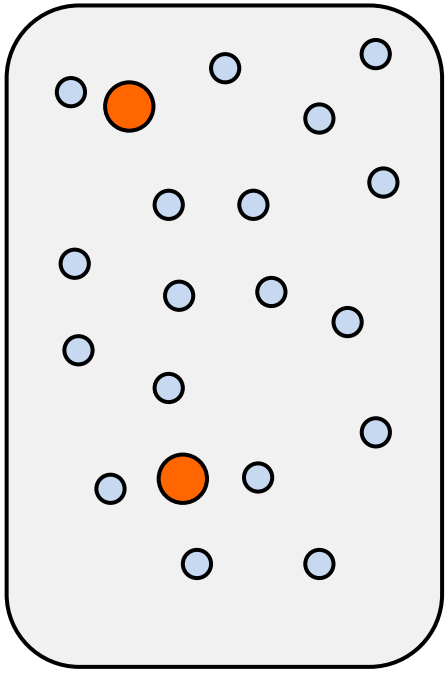
$$\left(\rho_{MP} \le \rho_T, N_S \ge 1\right)$$

$$t_S = \frac{N_S}{4\pi D a_0 \rho_{MP}} \quad \text{(Ib)}$$

$$\left(\rho_{MP} \ge \rho_T, N_S = 1\right)$$

Analytical solution ($\rho_T < \rho_{MP}$)

Capture probes are widely separated



$$\frac{\partial \rho}{\partial t} = D\nabla^2 \rho$$

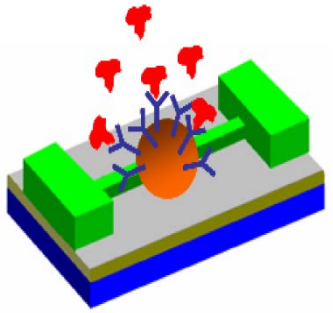
$$\rho_s = 0$$

$$N(t) = C_{D(t)} \rho t$$

$$C_{D(t)} = \frac{D}{a_0^{-1} - \left(\sqrt{Dt}\right)^{-1}}$$

$$N(t) = 4\pi D a_0 \rho t$$

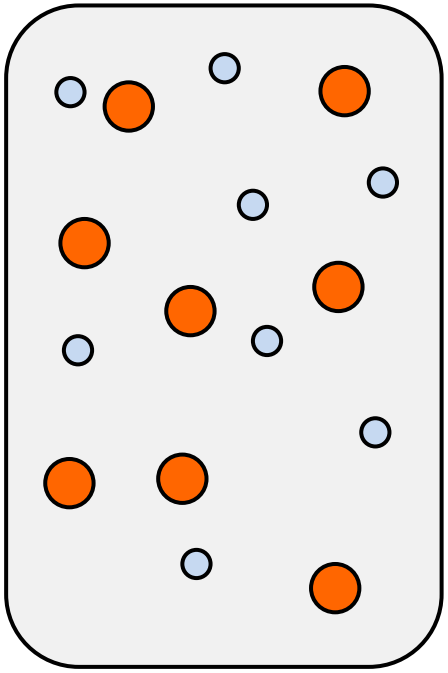
$$t_s = N_s / 4\pi D a_0 \rho$$



No different than a spherical sensor

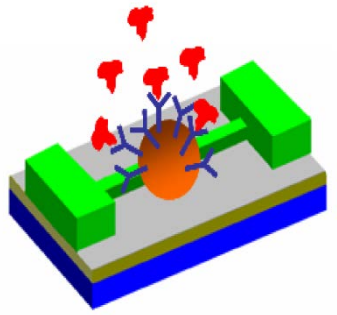
Analytical solution ($\rho_T = \rho_{MP}$)

Each MP captures on average one target particles, $N_S = 1$



$$\frac{\partial \rho}{\partial t} = D\nabla^2 \rho$$

$$\rho = 0$$



$$N(t) = C_{D(t)} \rho t$$

$$C_{D(t)} = \frac{D}{a_0^{-1} - \left(\sqrt{Dt}\right)^{-1}}$$

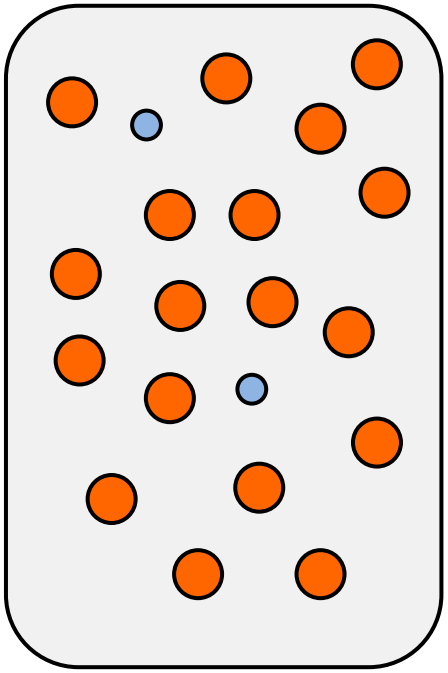
$$t_S = N_S / 4\pi D a_0 \rho$$

1

$$N(t) = 4\pi D a_0 \rho t$$

Analytical solution ($\rho_T > \rho_{MP}$)

Each probe captures at most 1 target particle



$$\frac{\partial \rho}{\partial t} = D\nabla^2 \rho - \frac{\rho}{\tau} \leftarrow$$

Captured by spherical probes

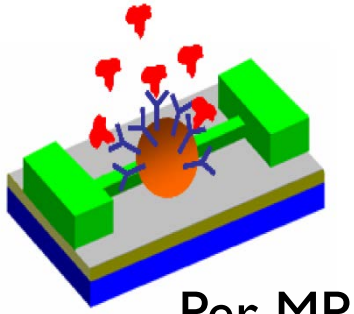
$$\rho_s = 0$$

$$N(t) = 4\pi D a_0 \rho t$$

$$R_1 = N(t)/t = 4\pi D a_0 \rho$$

$$R = 4\pi D a_0 \rho \rho_{MP} \equiv \rho/\tau$$

$$\tau = \frac{1}{4\pi D a_0} \frac{1}{\rho_{MP}}$$



Per MP

Analytical solution: transient solution

$$\frac{\partial \rho}{\partial t} = D\nabla^2 \rho - \frac{\rho}{\tau} \qquad \tau \equiv \frac{1}{4\pi D a_0} \frac{1}{\rho_{MP}}$$

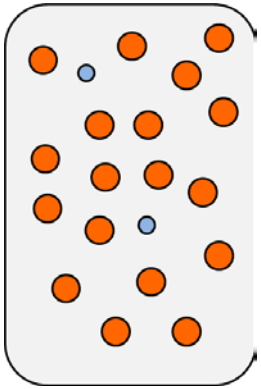
$$\rho(r,t) = At^{-3/2} e^{-t/\tau} e^{-\left(\frac{r^2}{4Dt}\right)}$$

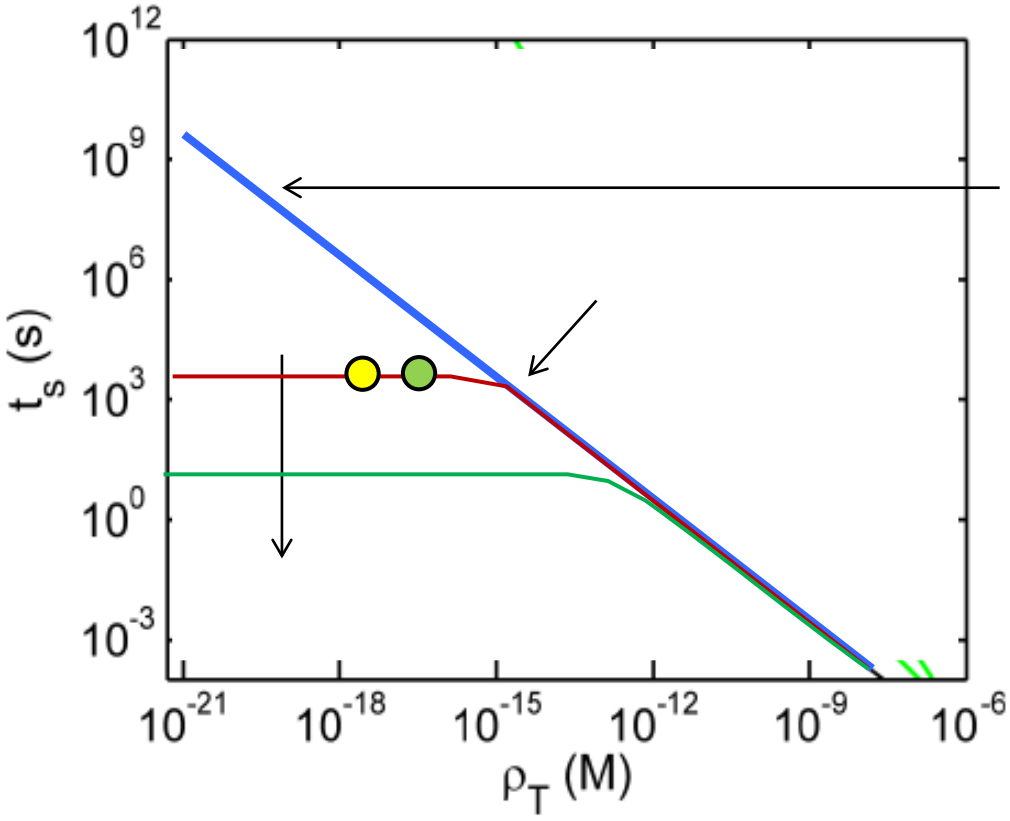
$$S(t) = \frac{\int_0^\infty \rho(r,t) 4\pi r^2 dr}{\int_0^\infty \rho(r,t=0) 4\pi r^2 dr} = \frac{e^{-t/\tau}}{\tau}$$

Analytical solution for barcode sensor

Eq. 1b

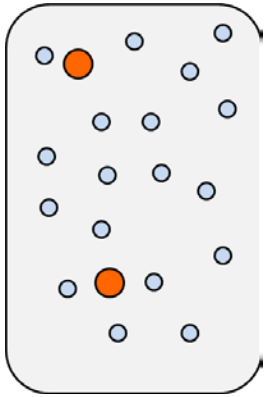
$$t_s \propto \rho_{MP}^{-1}$$



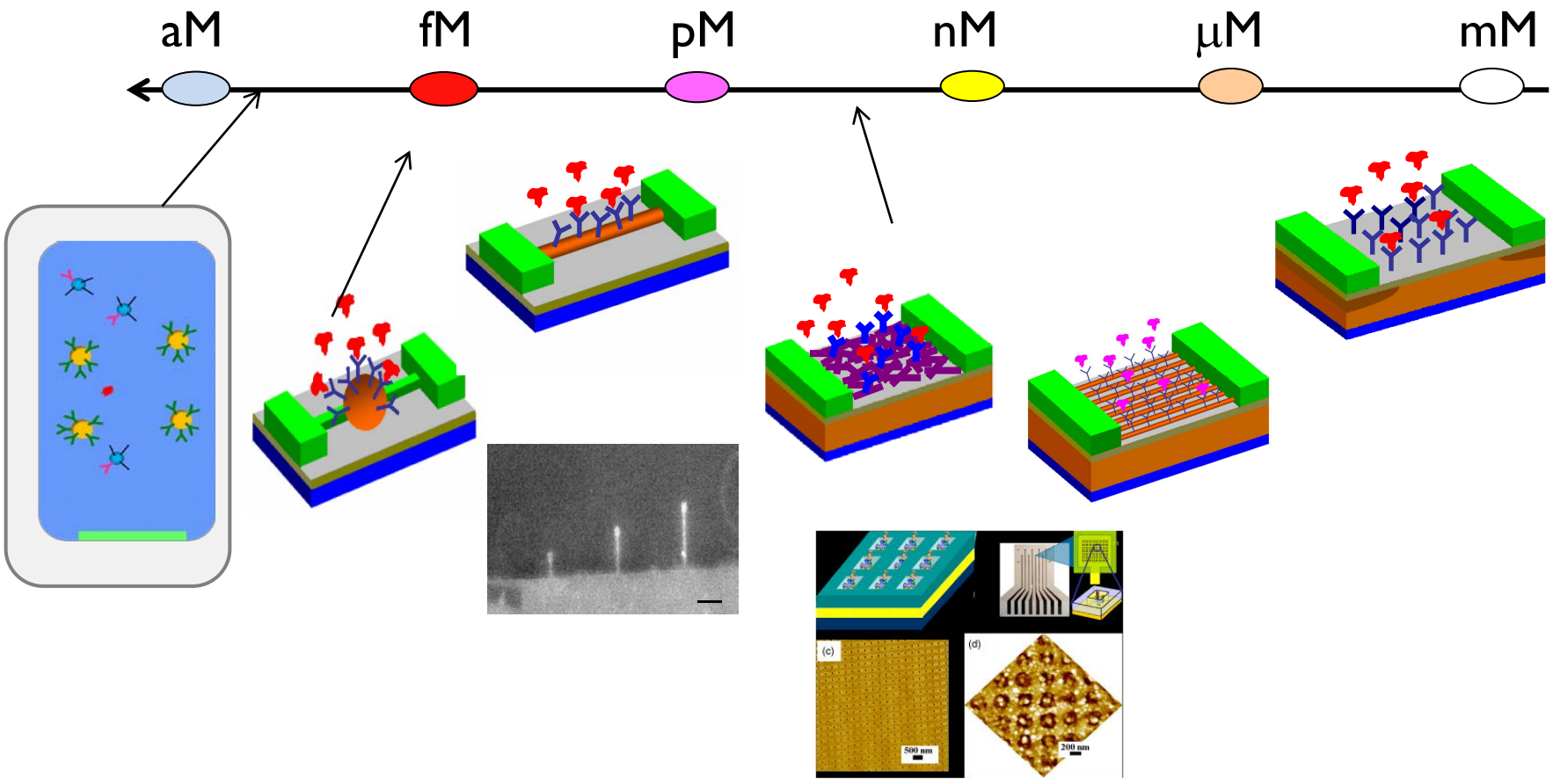


Eq. 1a

$$t_s \propto \rho_T^{-1}$$

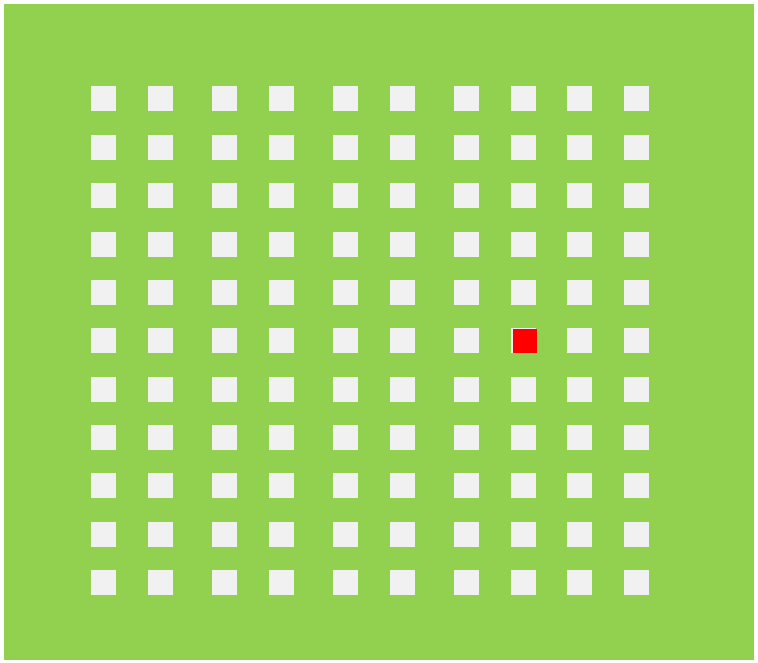


A ‘Mendeleev table’ for biosensors



Biobarcode sensors ‘beat’ the diffusion limit by fragmenting the space

Sensor array: fragmenting sensor volume



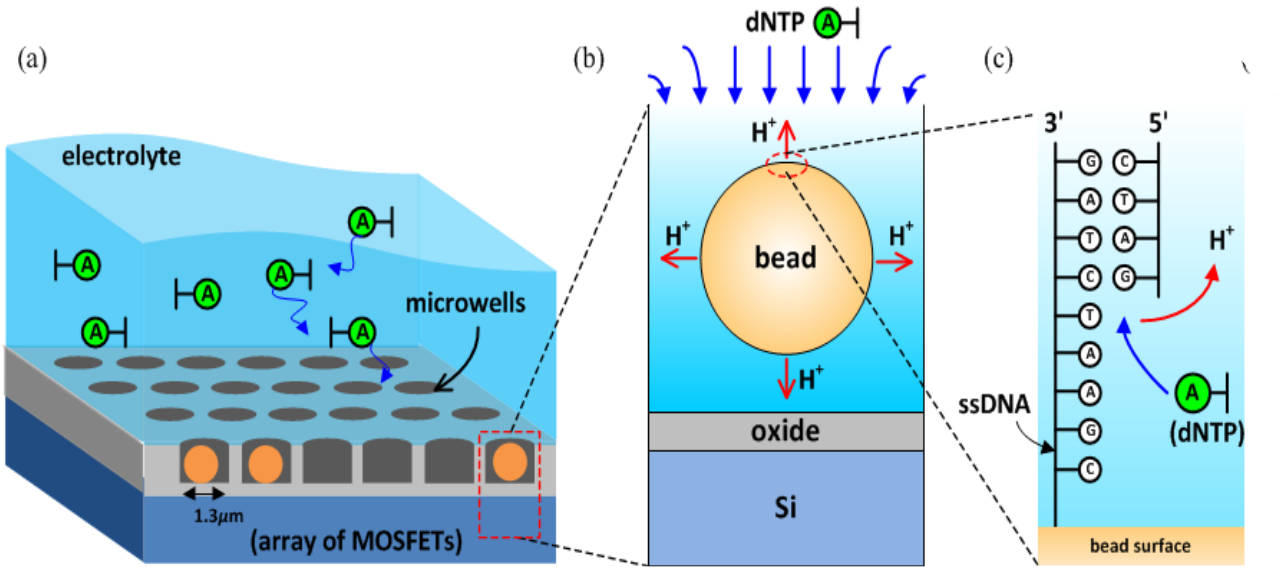
Advantage

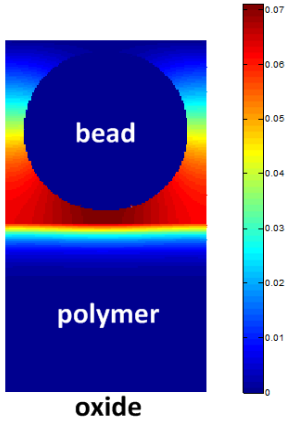
- much greater area
- redundancy
- multiple analytes
- *etc.*

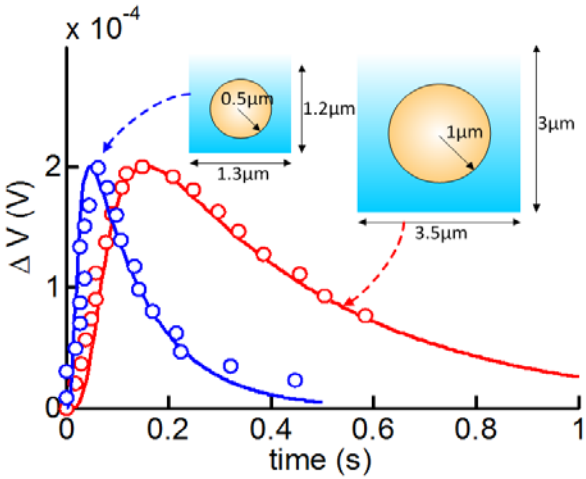
Disadvantage

- "Dead Space" competition (i.e., adsorption bet^{n} sensors)
- cost of multiplexing (potentially $100k 's)
- loss of signal-to-noise
- complexity, power use, etc.

Local generation/fast diffusion







$$\tau \sim L^2/D$$

Conclusions

- Biobarcode approach is still defined by diffusion limits – it just reduces diffusion time by using many probes.
- Biobarcode does not sense anything. It just catches the molecules. Sensing is done in a later step using amperometric or potentiometric methods.
- Using multiple sensors to detect the single analyte is equivalent to distributing probes in solution. Therefore, one anticipates similar gain in settling time.
- Both approaches increase cost and processing time, but could be necessary for detection at ultra-low concentration.