# Principles of Electronic Nanobiosensors

Unit 2: Settling Time

Lecture 2.9: First Passage and Narrow Escape Time II

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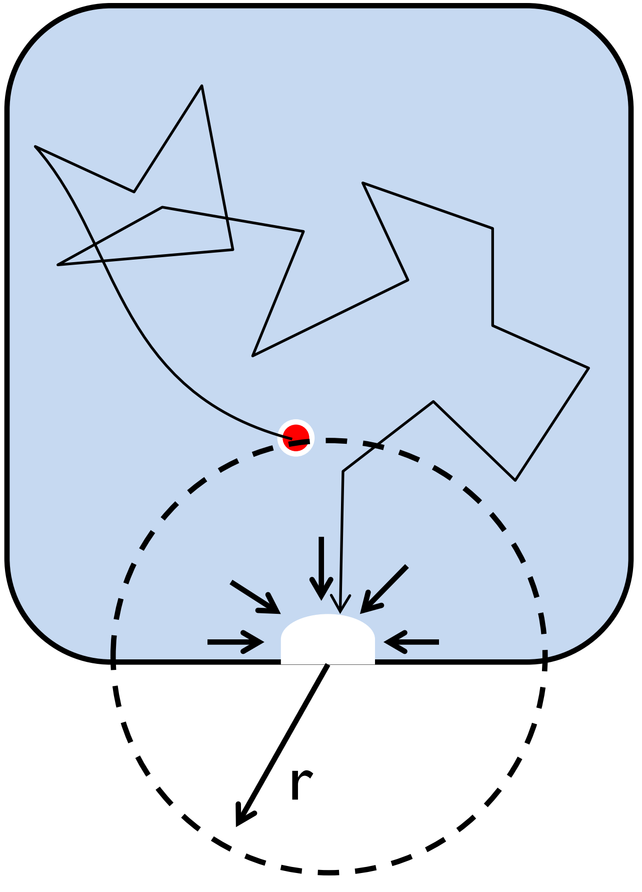
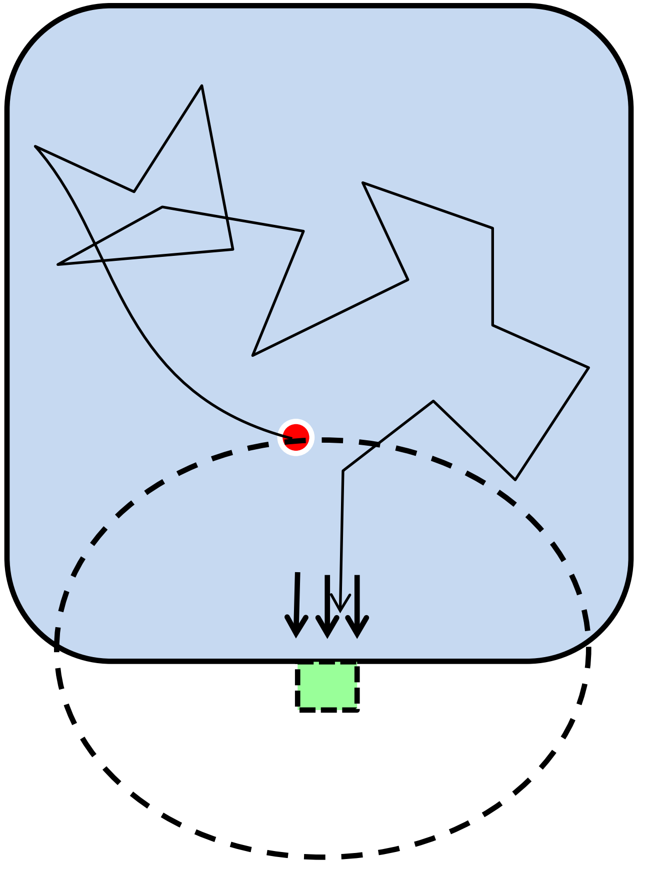
# Outline

- 'Blind' molecule escaping from a cell
- First passage time (FPT)
- First passage time (FPT): examples
- Narrow escape time (NET)
- Conclusion

# MFPT and NET

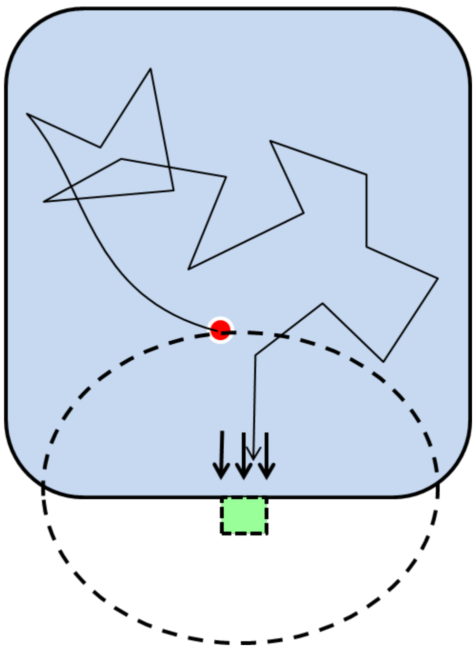



Concentric spheres

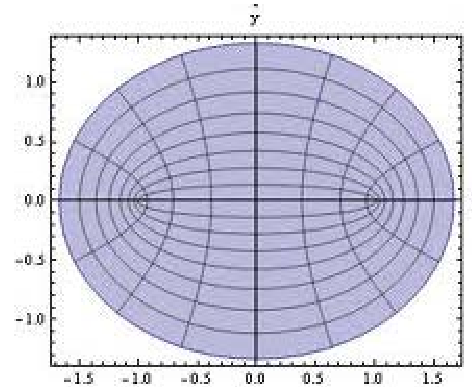


One disk and one sphere

# Example: NET in 2D



$$\frac{x^2}{c^2\cosh^2(\mu)} + \frac{y^2}{c^2\sinh^2(\mu)} = 1$$




$$a = c \times \cosh(\mu) \quad b = c \times \sinh(\mu)$$

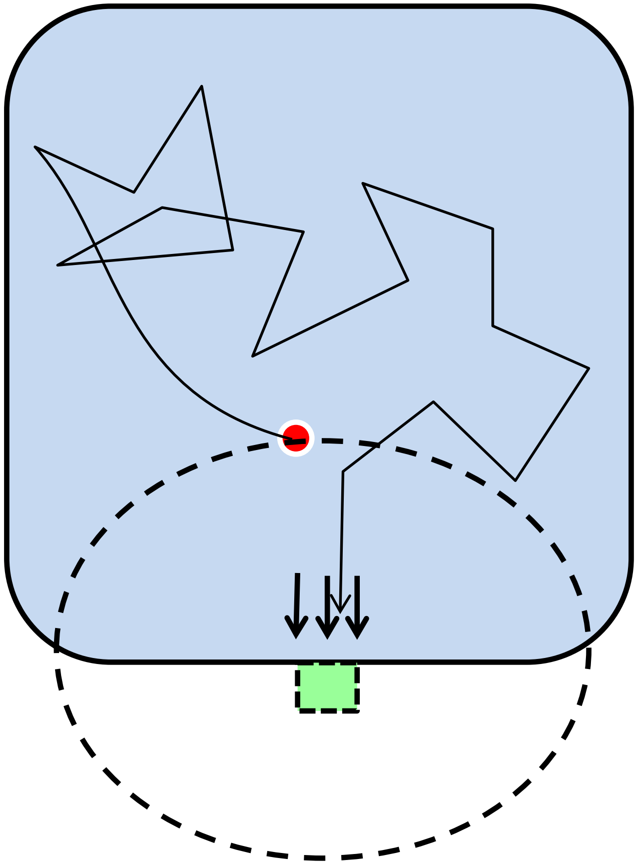
$$\left(\frac{\tau_{NET}}{V}\right)^{-1} \sim C_{D,ss} = \frac{\mu D}{\pi} \sim \frac{\pi D}{\ln(r/a)}$$

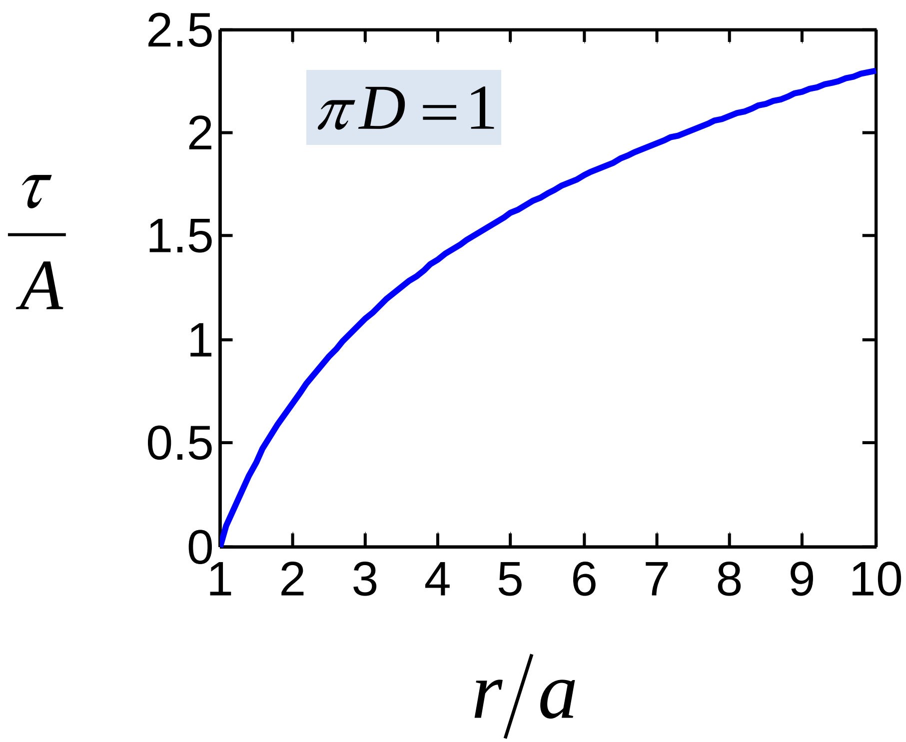
$$C_{D.ss}^{con-cyl} = \frac{2\pi D}{\ln(r/a)}$$

NET is twice as long as MFPT

# Example: NET in 2D

$$\frac{\tau_{NET}}{A} = \frac{\ln(r/a)}{\pi D} = \frac{2\tau_{MFPT}}{A}$$



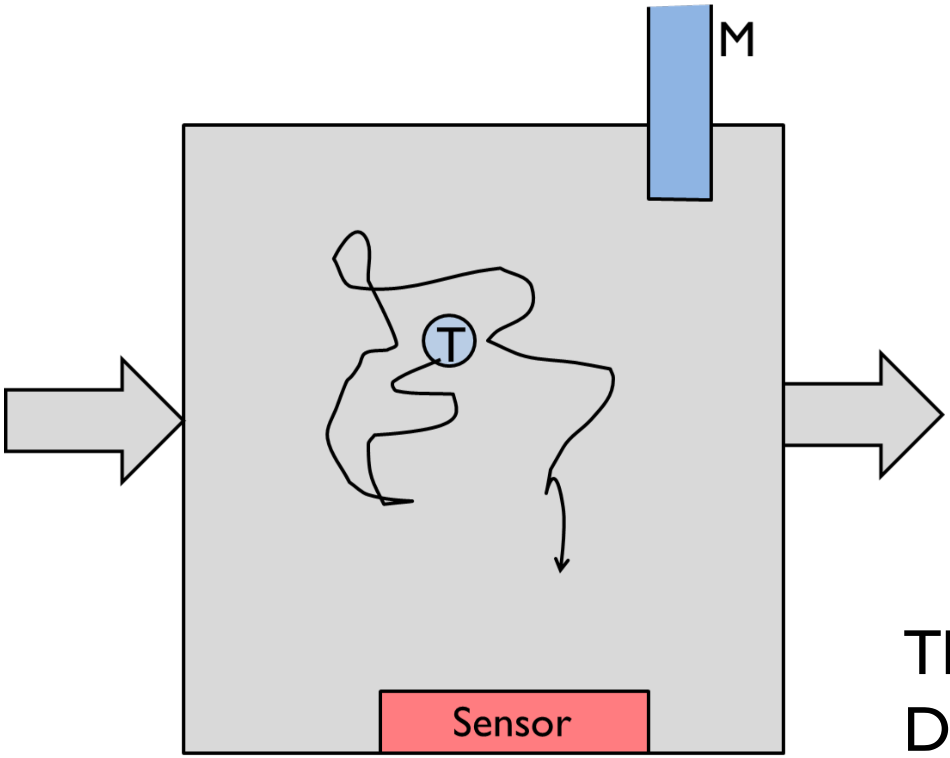


# Conclusions

- Diffusion capacitance allows us to calculate two fundamental quantities in cell physics: mean-first passage time and narrow escape time.
- Narrow escape time is slightly larger than mean-first passage time, because narrow escape requires flux normal to the cell surface.
- All there times – settling time, first passage time, and narrow escape times – are statistical average. The distribution of these times are very important as well.

# SUMMARY OF LECTURES 2.2-2.9

# Settling time defines the fundamental limits of detection (Lectures 2.2-2.9)




Heisenberg principle

$$\Delta E \times \Delta t \sim \hbar$$

Settling time principle

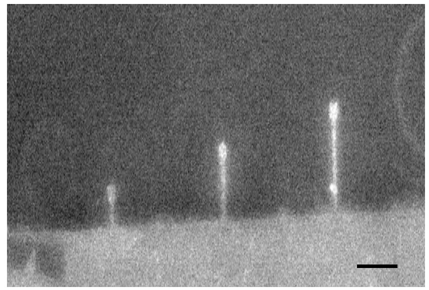
$$\rho_0 \times t_s^{(3-D_F)/2} \sim c$$

The result is technology agnostic

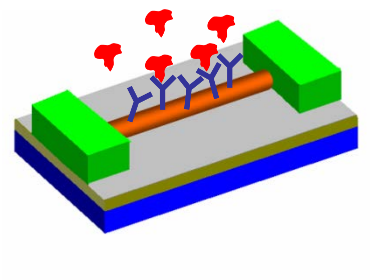
Defined by the geometry of diffusion

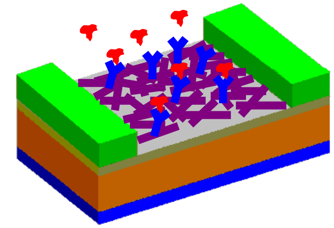
# Broad range of nanobiosensors

Nano Cantilever (~pM)



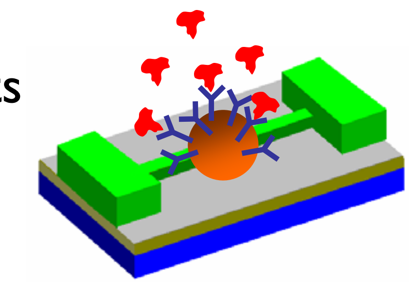
Si-NW/CNT (nM-aM)

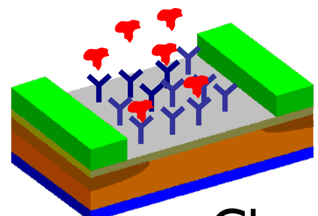




Nano-Net (nM-pM)

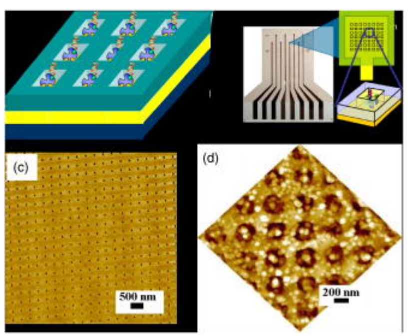
Nanodots

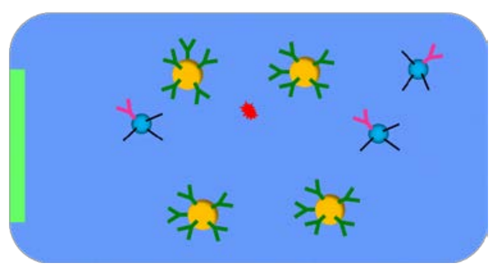




ChemFET/IsFET (~mM)

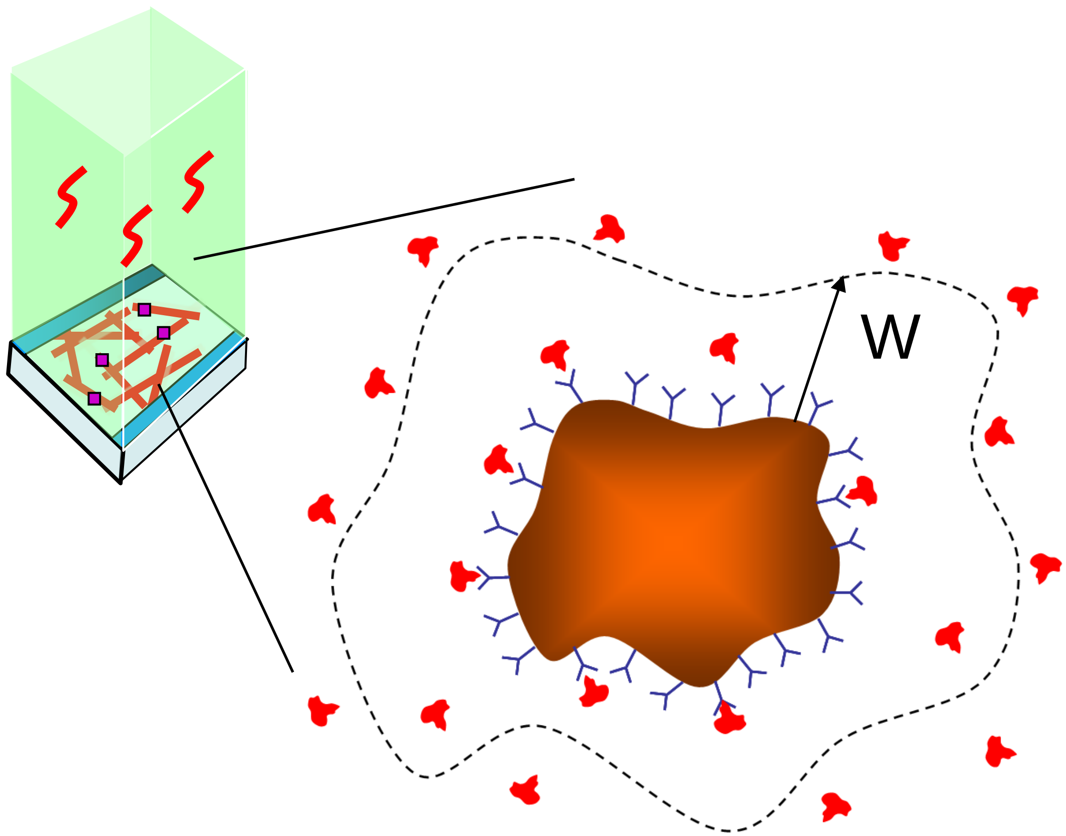
Array sensors (~pM)



Biobarcode (~aM)

# Settling time: Problem definition




$$\frac{d\rho}{dt} = D\nabla^2\rho$$

$$\frac{dN}{dt} = k_F(N_0 - N)\rho_s$$

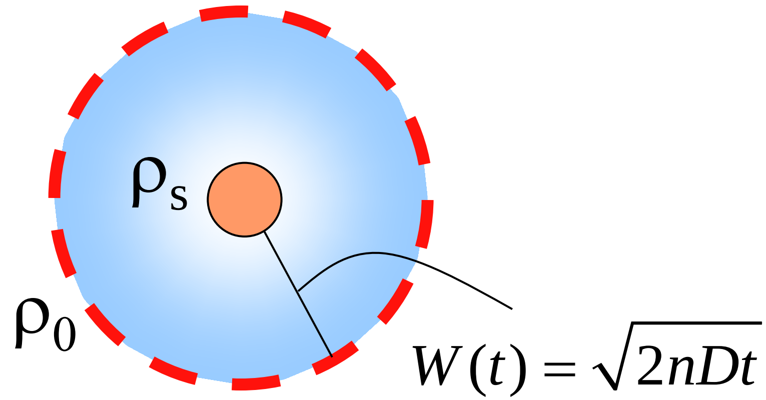
The diffusion-capture problem is very challenging, especially for complex capture surfaces

# Strategy: Solution of the Diffusion-capture problem by Transient diffusion capacitance

1. $N(t) = C_0 \rho_0 t / A$
2. Look up electrostatic $C_0$

   $\varepsilon \rightarrow D \quad W \rightarrow \sqrt{2nDt}$
3. Calculate time to reach

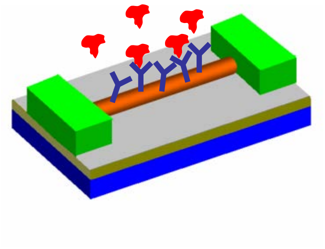
   $N(t_s) = N_s$
4. Plot $\log t_s$ vs. $\log \rho_0$

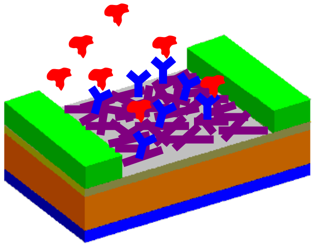


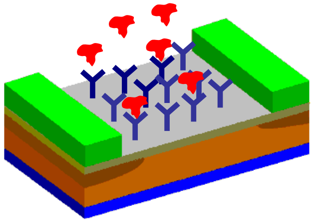

$$C_{0,0} = \frac{4\pi D}{a_0^{-1} - (W + a_0)^{-1}}$$

$$C_{D(t)} = \frac{4\pi D}{a_0^{-1} - \left(\sqrt{6Dt} + a_0\right)^{-1}}$$

# A fundamental relationship of biosensor




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

Limits of detection → $\rho_0$

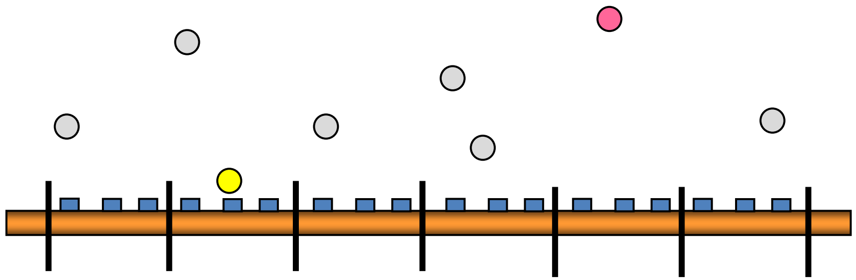
Fractal dimension → $D_F$

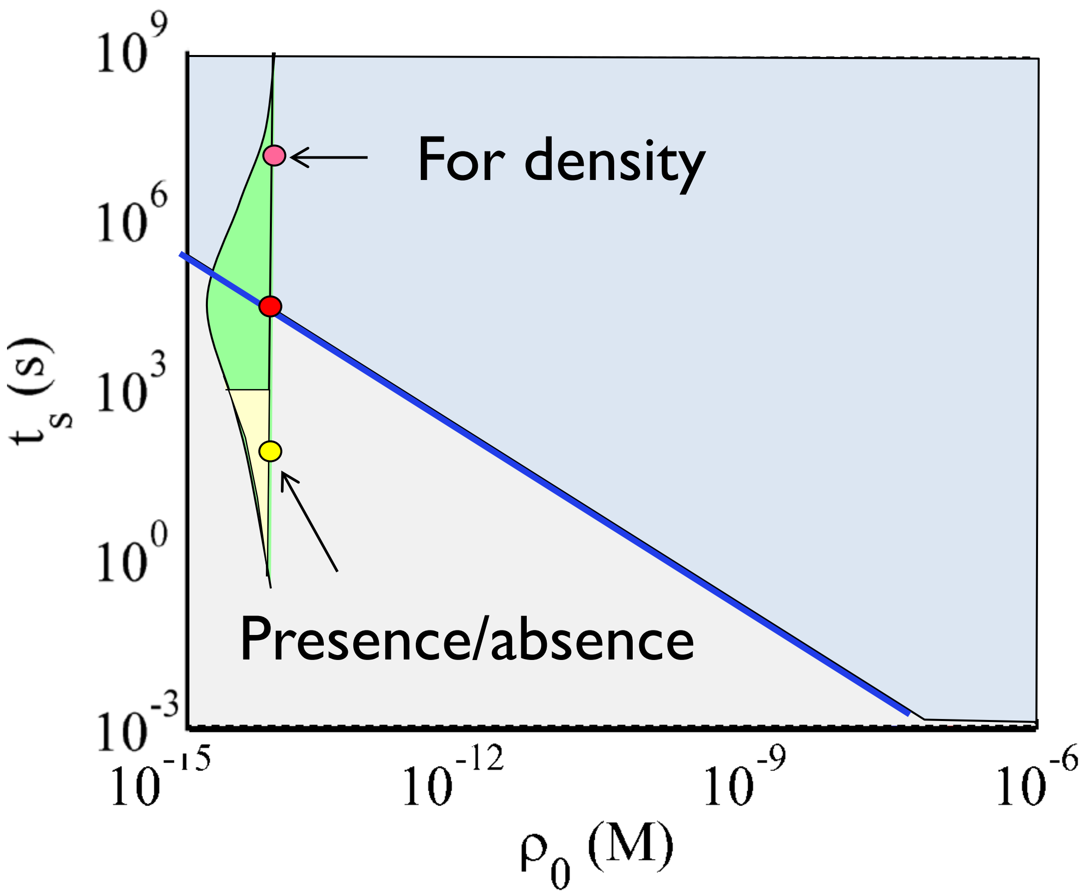
Settling (response) time → $t_s$

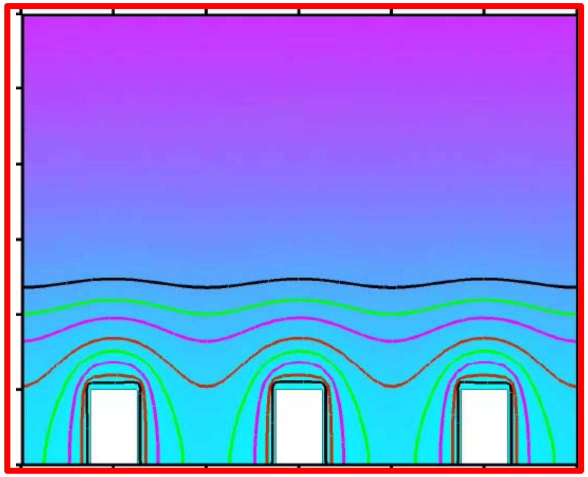
Minimum number of analyte (depends on transduction) → $N_s$

… and the relationship applies even for complex sensors

# Density: Average vs. first arrival time

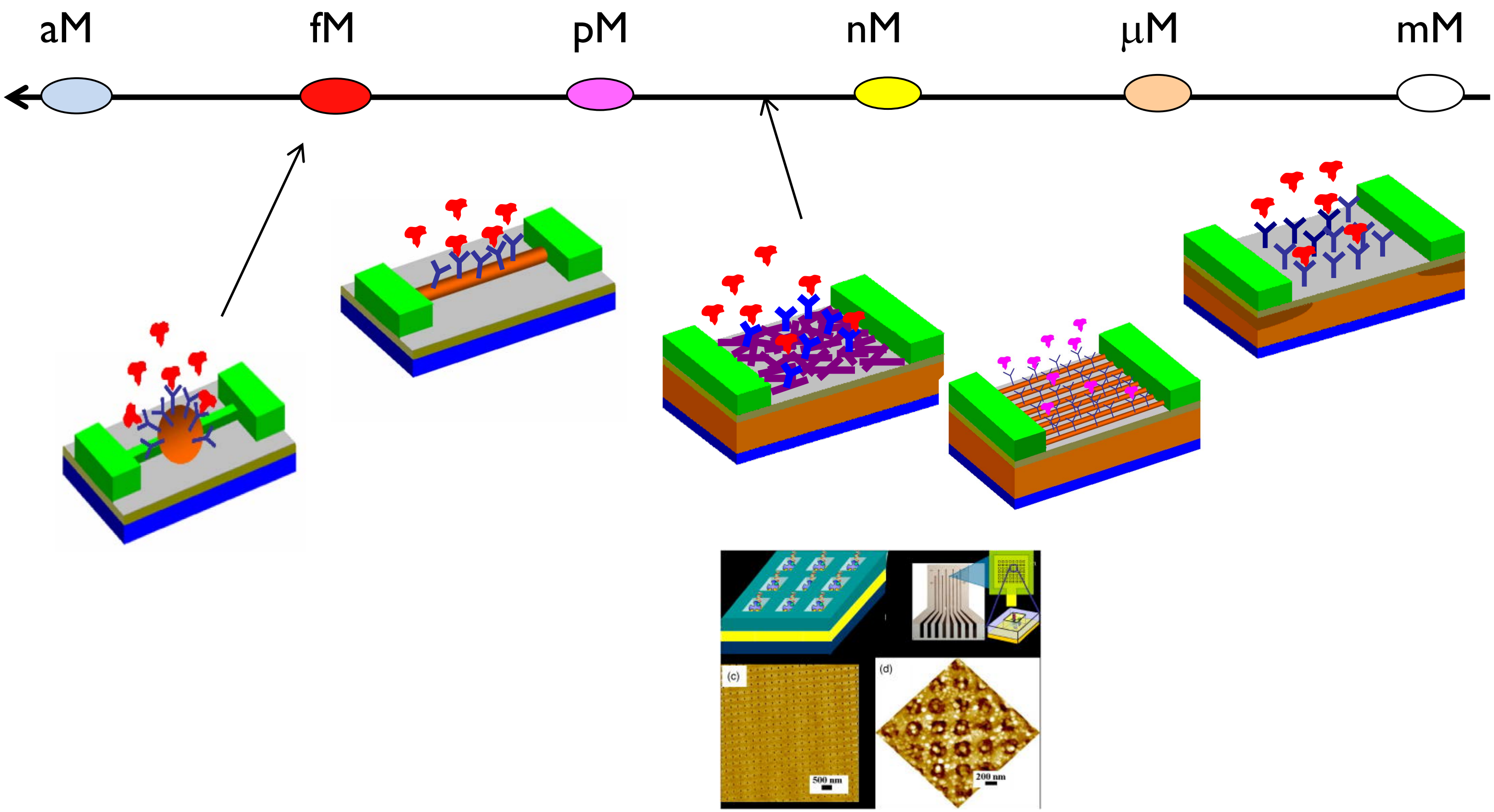




Ensemble composite

# A ‘Mendeleev table’ for biosensors

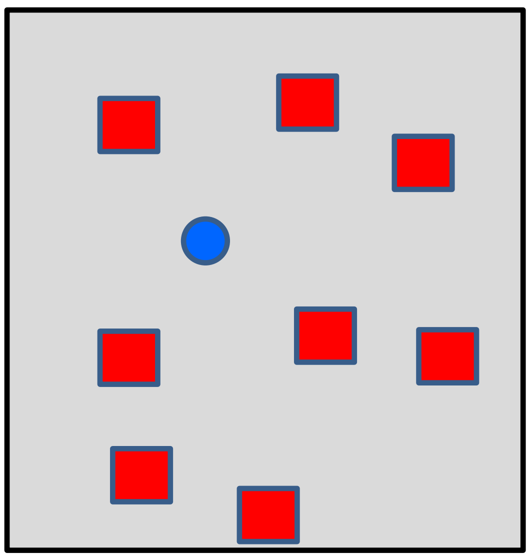



Provides the organization principles for sensors

# Biomimetic Strategies to beat diffusion (1)

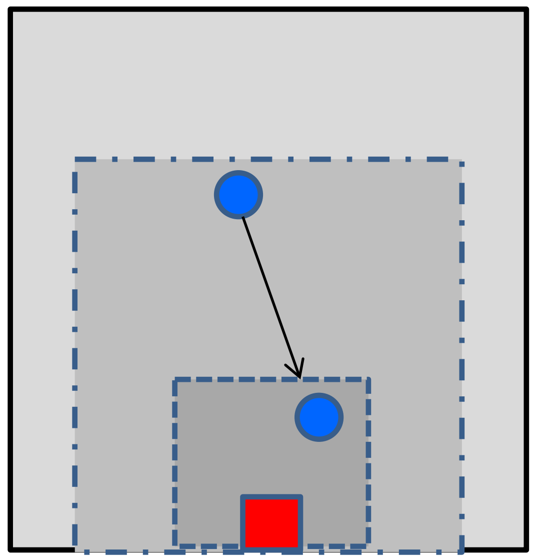
$$\tau \sim L^2 / D$$

Fragment the space



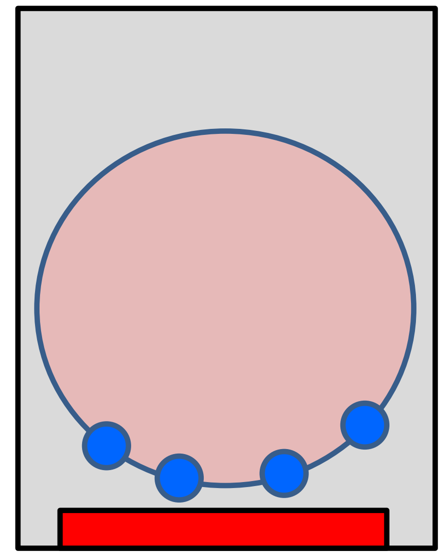
Magnetic biobarcode

Reduce the space



Droplet evaporation

Generate locally

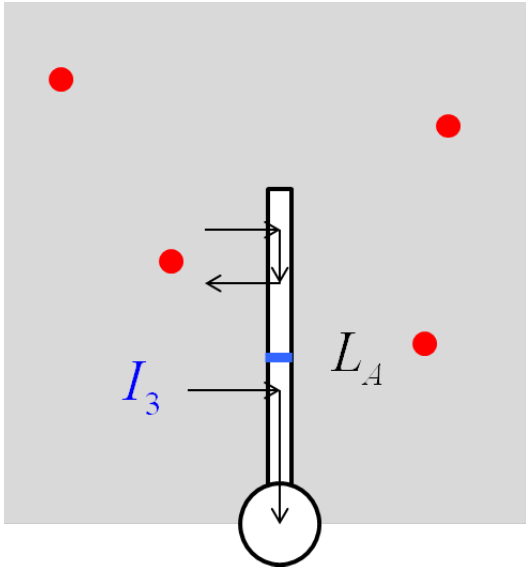


Ion torrent approach

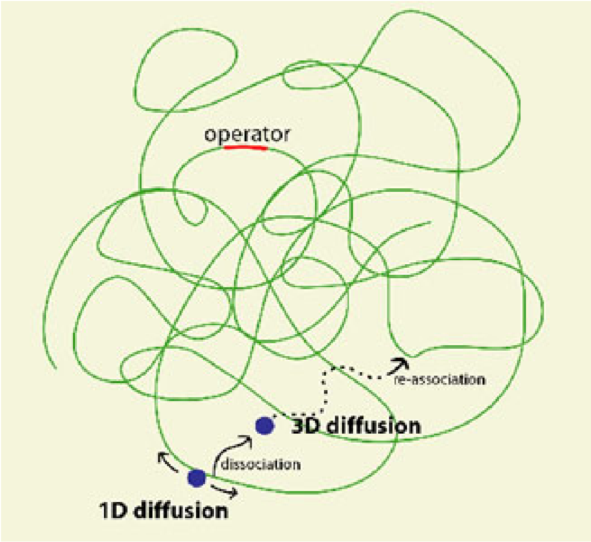
All can achieve sub-fM detection in reasonable time

# Biomimetic Strategies to beat diffusion (2)

Enhanced diffusion limited capture

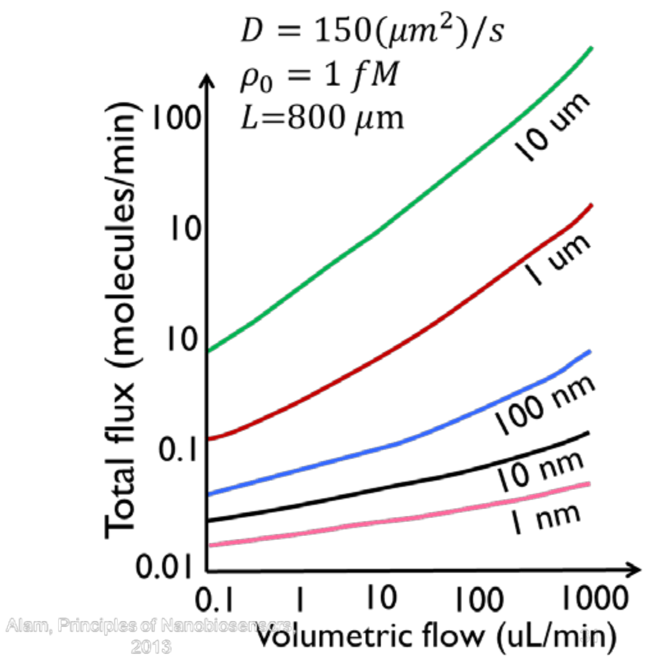


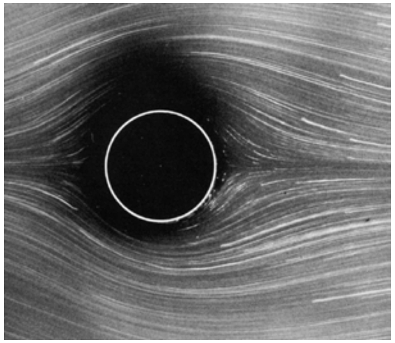

Looking for a target on a DNA

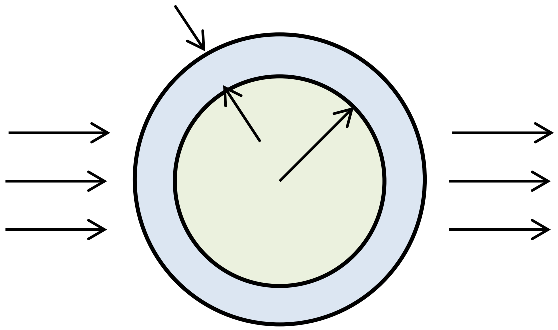



Looking for a lost child in a city

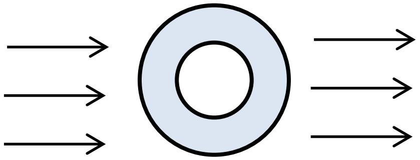
# Strategies to beat diffusion (3)



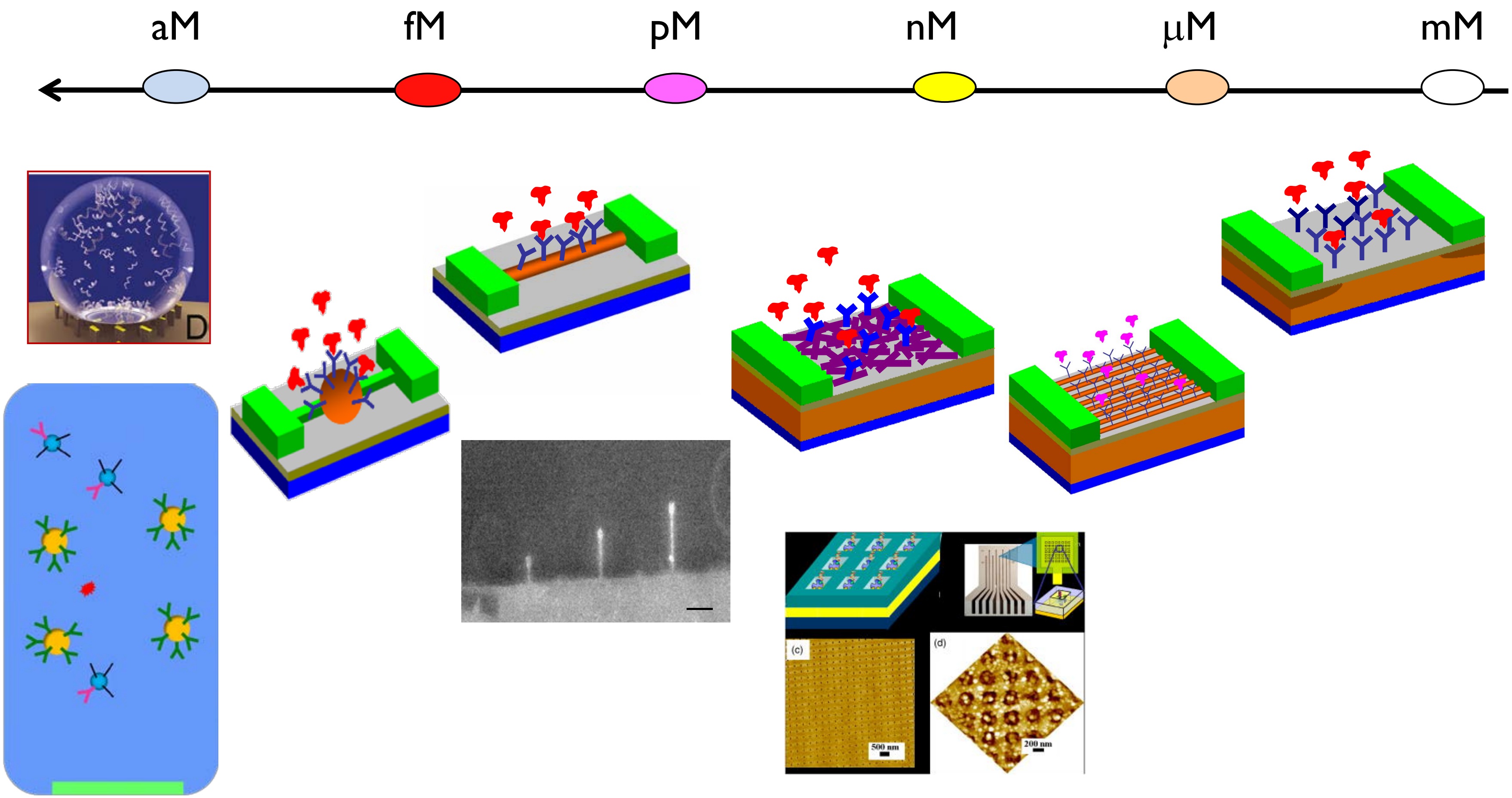


$$\frac{I_S}{I_S^{\max}} = \left(1 + \frac{a}{\delta}\right)$$



Nanobiosensors do not benefit as much compared to larger sensors

# Response time for various geometries




Zoo of sensors are now cleanly categorized.

# Summary: Lectures 2.2-2.9

- Understanding the diffusion limit of a nanobiosensors is the first step in understanding its operation.
- There are a number of biomimetic approaches to beat the diffusion limit. These include biobarcode approach, droplet evaporation, local generation, multi-dimensional diffusion; but increasing flow does not give significant advantage.
- The understanding gained from the generic features of the sensor response can be used to solve important problems of biophysics.