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

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

… not as fundamental as the uncertainty principle!

Alam, Principles of Nanobiosensors, 2013
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

\[ \begin{array}{cccccc}
\text{aM} & \text{fM} & \text{pM} & \text{nM} & \text{µM} & \text{mM} \\
\end{array} \]

Alam, Principles of Nanobiosensors, 2013
Strategies to beat the diffusion limit

\[ \tau \sim \frac{L^2}{D} \]

- Fragment the space
- Reduce the space
- Generate locally

Magnetic biobarcode

Droplet evaporation

Ion torrent approach

All can achieve sub-fM detection in reasonable time
In sum, a police-thief story!
Analytical solution: two limits

\[ t_S = \frac{N_S}{4\pi Da_0 \rho_T} \]  \hspace{1cm} (1a)

\[ (\rho_{MP} \leq \rho_T, N_S \geq 1) \]

\[ t_S = \frac{N_S}{4\pi Da_0 \rho_{MP}} \]  \hspace{1cm} (1b)

\[ (\rho_{MP} \geq \rho_T, N_S = 1) \]
Analytical solution \((\rho_T < \rho_{MP})\)

Capture probes are widely separated

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

\[\rho_s = 0\]

\[N(t) = C_D(t) \rho t\]

\[C_D(t) = \frac{D}{a_0^{-1} - (\sqrt{Dt})^{-1}}\]

\[N(t) = 4\pi Da_0 \rho t\]

\[t_s = N_s / 4\pi Da_0 \rho\]

No different than a spherical sensor

Alam, Principles of Nanobiosensors, 2013
Analytical solution \((\rho_T = \rho_{MP})\)

Each MP captures on average one target particles, \(N_S = 1\)

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

\(\rho = 0\)

\[
N(t) = C_{D(t)}\rho t
\]

\[
C_{D(t)} = \frac{D}{a_0^{-1} - (\sqrt{Dt})^{-1}}
\]

\[
N(t) = 4\pi Da_0 \rho t
\]

\(t_S = N_S / 4\pi Da_0 \rho\)
Analytical solution \( (\rho_T > \rho_{MP}) \)

Each probe captures at most 1 target particle

\[
\frac{\partial \rho}{\partial t} = D \nabla^2 \rho - \frac{\rho}{\tau}
\]

Captured by spherical probes

\( \rho_s = 0 \)

\[
N(t) = 4\pi Da_0 \rho t
\]

\[
R_1 = N(t)/t = 4\pi Da_0 \rho
\]

\[
R = 4\pi Da_0 \rho \rho_{MP} \equiv \rho/\tau
\]

\[
\tau = \frac{1}{4\pi Da_0} \frac{1}{\rho_{MP}}
\]
Analytical solution: transient solution

\[ \frac{\partial \rho}{\partial t} = D \nabla^2 \rho - \frac{\rho}{\tau} \]

\[ \tau \equiv \frac{1}{4\pi Da_0} \frac{1}{\rho_{MP}} \]

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

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

Alam, Principles of Nanobiosensors, 2013
Analytical solution for barcode sensor

Eq. 1b

\[ t_s \propto \rho_{MP}^{-1} \]

Eq. 1a

\[ t_s \propto \rho_T^{-1} \]

Alam, Principles of Nanobiosensors, 2013
A ‘Mendeleev table’ for biosensors

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

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Sensor array: fragmenting sensor volume

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

**Disadvantage**
- “Dead Space” competition (i.e., adsorption between sensors)
- cost of multiplexing (potentially $100k ‘s)
- loss of signal-to-noise
- complexity, power use, etc.

Alam, Principles of Nanobiosensors, 2013
Local generation/fast diffusion

\[ \tau \sim \frac{L^2}{D} \]
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.