POD 20: Designing a Biodetector

- For large systems diffusion is sufficiently slow that we don't ever get to a point where the SL asymptote is reached.

- For small (Microfluidic) systems this isn't true! This is important in things like biodetectors: ident. small conc. of molecules

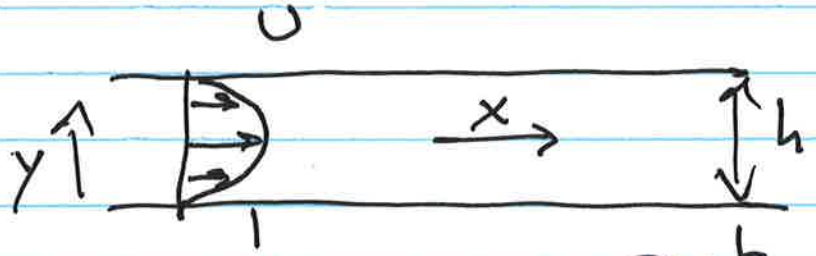
Suppose we have a microchannel 100μm deep by 200μm wide

We have a flow rate of 0.2 μl/min

If our detector is 200μm wide by 500 μm long, what is the max diffusivity that 50% of entering solute molecules would reach detector?

The easy way of doing this is determining how much remains at the end.

That way we are dominated by the lead eigenfunction!



$$6\bar{U}\frac{y}{h}\left(1-\frac{y}{h}\right)\frac{\partial c}{\partial x} = D\frac{\partial^2 c}{\partial y^2}$$

$$c\Big|_{x=0} = c_0 \qquad c\Big|_{y=0} = 0 \qquad \frac{\partial c}{\partial y}\Big|_{y=h} = 0$$

so: $y^* = y/h$, $c^* = c/c_0$, $x^* = \frac{x}{x_c}$

$$\therefore\ 6y^*(1-y^*)\frac{\partial c}{\partial x^*}\frac{\bar{U}c_0}{x_c} = D\frac{c_0}{h^2}\frac{\partial^2 c^*}{\partial y^{*2}}$$

Divide out:

$$6y^*(1-y^*)\frac{\partial c^*}{\partial x^*} = \left[\frac{D x_c}{\bar{U}h^2}\right]\frac{\partial^2 c^*}{\partial y^{*2}}$$

$$x_c = \frac{\bar{U}h^2}{D}$$

Define $L^* \equiv \frac{L}{x_c} = \frac{LD}{\bar{U}h^2}$

We seek L^* s.t. the flow avg of c^* at $L^* = \frac{1}{2}$

So:

$$6y^*(1-y^*)\frac{\partial c^*}{\partial x^*} = \frac{\partial^2 c^*}{\partial y^{*2}}$$

$$c^*\big|_{x^*=0} = 1, \quad c^*\big|_{y^*=0} = 0, \quad \frac{\partial c^*}{\partial y^*}\Big|_{y^*=1} = 0$$

We have already gotten homogeneous BC's!

$$\therefore c^* = G(x^*)F(y^*)$$

$$\frac{G'}{G} = \frac{F''}{6y^*(1-y^*)F} = -\sigma^2$$

$$\therefore G = e^{-\sigma^2 x^*}, \quad F'' + \sigma^2 6y^*(1-y^*)F = 0$$

$$F(0) = 0, \quad F'(1) = 0$$

To get an analytic estimate, we replace parabolic velocity profile w/ average!

$$\int_0^1 6y^*(1-y^*)\,dy^* = 1$$

So our approximate problem is:

$$F'' + \sigma^2 F = 0 \qquad F(0) = 0 \quad F'(1) = 0$$

$$\therefore \quad F = A\sin\sigma y^*, \qquad \sigma = \left(n - \tfrac{1}{2}\right)\pi$$

$$A_n = \frac{\int_0^1 \sin\sigma y^*\,dy^*}{\int_0^1 \sin^2\sigma y^*\,dy^*} = \frac{-2}{\sigma_n}\cos\sigma y^*\Big|_0^1$$

$$= \frac{+2}{\left(n-\frac{1}{2}\right)\pi}$$

$$\therefore \quad C^*_{app} = \sum_{n=1}^{\infty} \frac{2}{\left(n-\frac{1}{2}\right)\pi}\, e^{-\left(\left(n-\frac{1}{2}\right)\pi\right)^2 x^*} \sin\left(\left(n-\tfrac{1}{2}\right)\pi y^*\right)$$

Now we want $\dfrac{\int_0^h C\big|_{x=L}\, u\,dy}{\int_0^h u\,dy} = \dfrac{C_0}{2}$

So: $\int_0^1 C^*\,dy^* = \sum_{n=1}^{\infty} \dfrac{2}{\sigma_n^2}\, e^{-\sigma_n^2 x^*}$

We are dominated by the lead eigenvalue by the time $C^* \to \frac{1}{2}$

So: $$\frac{2}{\left(\frac{\pi^2}{4}\right)} e^{-\frac{\pi^2}{4} L^*} = \frac{1}{2} \quad \text{(target)}$$

$$\therefore e^{-\frac{\pi^2}{4} L^*} = \frac{\pi^2}{16}$$

$$\text{or } L^* = \frac{4}{\pi^2} \ln\left(\frac{16}{\pi^2}\right) = 0.196 \simeq \underline{0.2}$$

So:

$$0.2 = \frac{L D}{\bar{U} h^2}$$

and $$\bar{U} = \frac{Q}{Wh}$$

$$\therefore D_{min} = 0.2 \frac{\bar{U} h^2}{L} = 0.2 \frac{Qh}{WL}$$

Now $Q = 0.2 \times 10^{-3}$ cm^3/min $= 3.3 \times 10^{-6}$ cm^3/s

$h = 0.01$ cm, $W = 0.02$ cm

$$\therefore \bar{U} = 0.0165 \text{ cm/s}$$

(for a 1 cm channel, this takes ~1 min to clear - a bit long)

So we get

$$D_{min} = (0.2)\frac{(3.3\times10^{-6}\,cm^3/s)(10^{-2}\,cm)}{(2\times10^{-2}\,cm)(5\times10^{-2}\,cm)}$$

$$= 6.66\times10^{-6}\,cm^2/s$$

This means it would only work (for these conditions) for a fairly small molecule.

How does D depend on the size of a molecule?

$$\text{Stokes-Einstein } D.f \equiv \frac{kT}{6\pi\mu a}$$

Now $V = \frac{4}{3}\pi a^3 = \frac{MW}{\rho}\frac{1}{N_{AV}}$ ($N_{AV} \to 6.02\times10^{23}$)

$$\therefore MW = \frac{4}{3}\pi\left(\frac{1}{6\pi}\right)^3 \rho \left(\frac{kT}{\mu D}\right)^3 \times 6.02\times10^{23}$$

$$= \frac{1}{\pi^2}\frac{1}{27\times6}(1)\left(\frac{1.38\times10^{-16}\times300}{(0.01)(6.7\times10^{-6})}\right)^3\times6.02\times10^{23}$$

$$= 89\ g/mol$$ (say, fairly small molecule - although the formula is off for this.)

What if we need to catch a larger molecule? We have the scaling!

$$MW_{max} \sim D_{min}^{-3}$$

$$D_{min} \sim \frac{Qh}{WL}$$

$$\therefore MW_{max} \sim \left(\frac{WL}{Qh}\right)^3 !$$

If we increase L from 500μm to 5mm we would increase MW_{max} by 10^3!

This, for other parameters the same, yields $MW_{max} \sim 90$ kDa

this is comparable to, say, BSA.

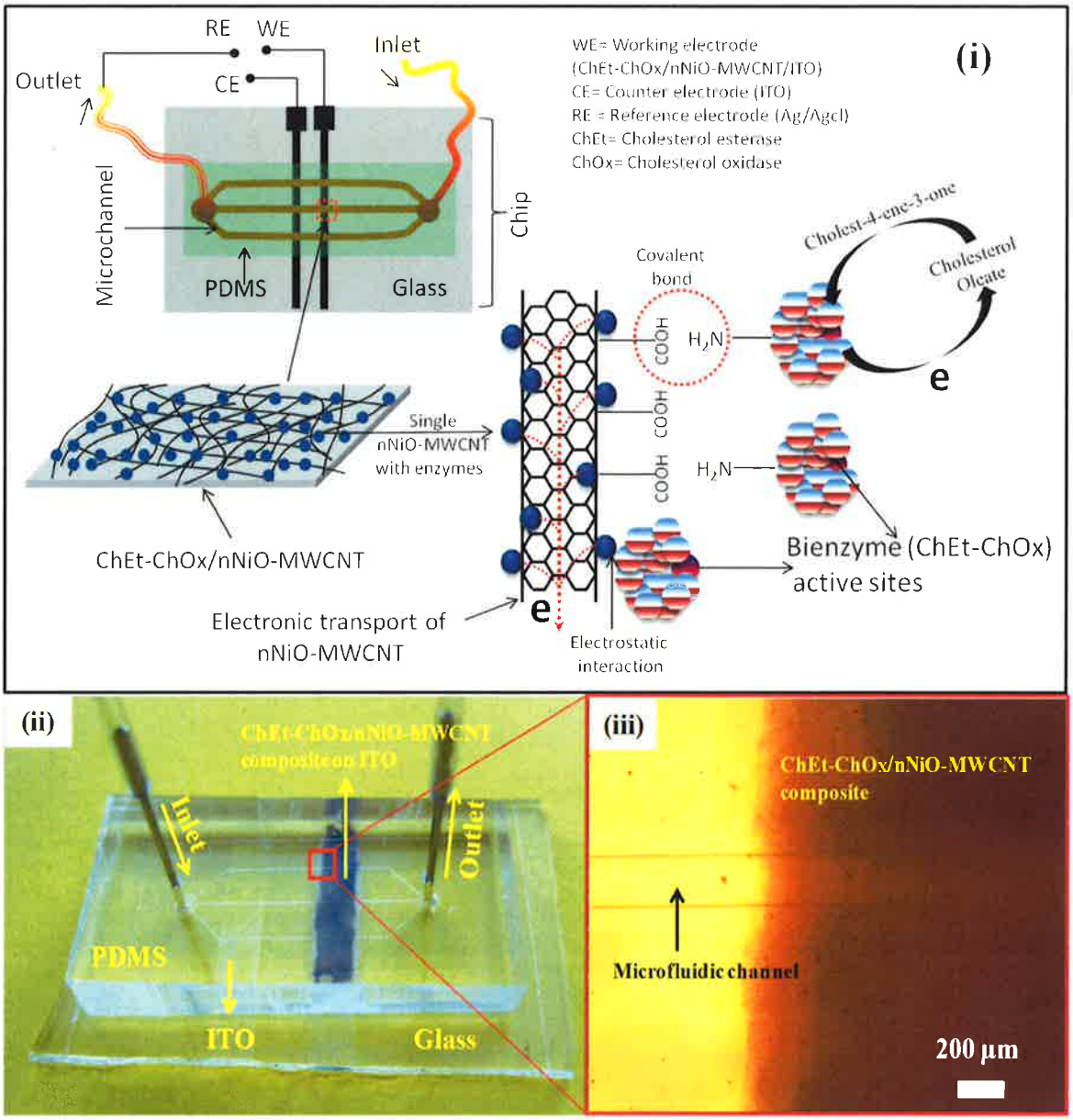


Figure 1 | (i) The schematic of the microfluidic biochip used for total cholesterol detection (the ordered arrangement of this microsystem is assumed). (ii) The photograph of real microfluidic biochip for cholesterol detection and (iii) the enlarged view of optical microscopic image of the microfluidic biochip.

open to reactions[14]. The MWCNTs are known to produce changes in energy bands close to the Fermi level[15,16]. The exciting electronic properties and high electrochemical reactivity of MWCNTs suggest that fast electron transfer reaction occurs when they are used as the electrode in an electrochemical biochip[15,16]. Lin et al. have developed a microfluidics electrochemical sensor for on-site, non-invasive monitoring of lead and chlorophenols[17]. Wisitsoraat et al. have developed an electrochemical biochip for cholesterol detection that has a sensitivity of 0.0512 nA/mg/dl, which is attributed to the direct growth of CNT on glass[18]. However, MWCNTs are known to agglomerate via *Van der Waals* interactions, resulting in poor film-forming ability. To overcome this problem, nanostructured metal oxides (NMOx) may be used to control the agglomeration of MWCNTs[19]. The covalent binding (or sidewall functionalization) of biomolecules (e.g., proteins, enzymes, and nucleic acids) to carboxyl-functionalized MWCNTs via diimide-activated amidation may provide improved stability and reproducibility[20–24]. In such a case, the large surface area of the MWCNTs and the presence of abundant functional groups may offer a suitable platform for biofunctionalization[20–25]. Additionally, MWCNTs may facilitate continuous conducting pathways to transport the charge carriers, allowing for a higher sensitivity[25]. Shim et al. have used functionalized CNT for biomolecular recognition in a streptavidin/biotin approach to investigate the adsorption of proteins on the sidewalls of carbon nanotubes[20].

A biosensor based on nanostructured nickel oxide (nNiO) has recently been explored to detect biomolecules such as DNA, antibody-antigen interactions, glucose, and cholesterol[26,27]. However, nNiO-based biosensors have limited applications due to the inherently poor electrical conductivity of nNiO[26]. The non-covalent immobilization of enzymes onto nNiO-based biochip has recently been found to result in poor stability of the desired biomolecules[26–28]. To improve the characteristics of a biosensing device, nNiO can be integrated with MWCNTs[29,30]. Zhang et al. have used CNT-NMOx to develop solar cells and gas sensors[21]. The sp^2 hybridization and