Lecture 14

Steady State approximation for solving Diffusion equation (part II)

-Spherical coordinate, Biological example: drug delivery to tissue

-Diffusion limited reactions: examples in cell biology

In the previous lecture:
Steady State approximation for solving Diffusion equation (part II)

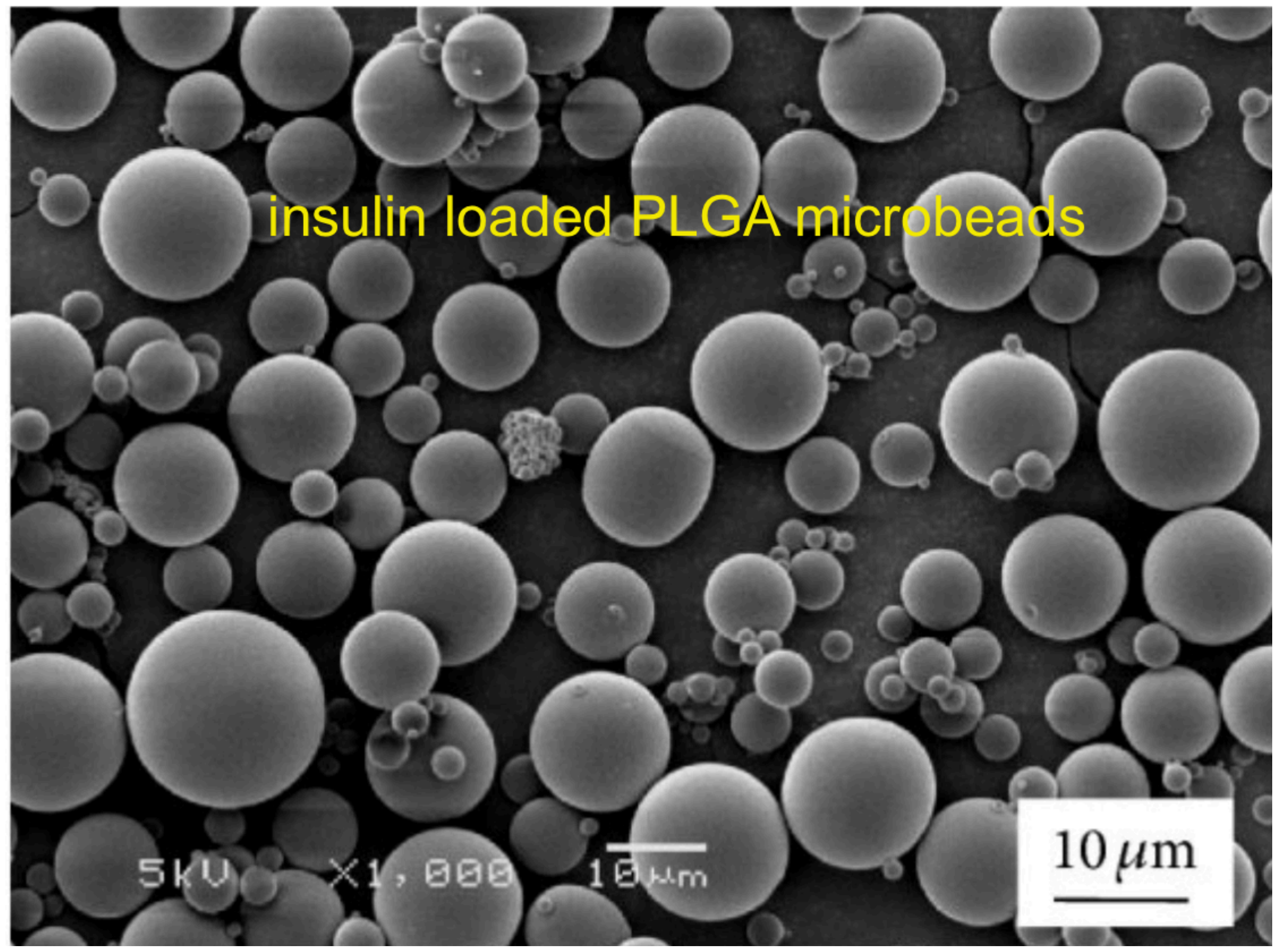
$$\frac{\partial C(x,t)}{\partial t} = 0 \text{ or } C(\vec{x})$$

$$\cancel{\frac{\partial C(\vec{x},t)}{\partial t}} = D\,\nabla^2 C(x,t) \Rightarrow D\,\nabla^2 C(\vec{x}) = 0$$

	Cartesian Coordinates	Cylindrical Coordinates	Spherical Coordinates
Laplacian $\nabla^2\phi$	$\frac{\partial^2\phi}{\partial x^2}+\frac{\partial^2\phi}{\partial y^2}+\frac{\partial^2\phi}{\partial z^2}$	$\frac{1}{\rho}\frac{\partial}{\partial\rho}\left(\rho\frac{\partial\phi}{\partial\rho}\right)+\frac{1}{\rho^2}\frac{\partial^2\phi}{\partial\varphi^2}+\frac{\partial^2\phi}{\partial z^2}$	$\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial\phi}{\partial r}\right)+\frac{1}{r^2\sin\theta}\frac{\partial}{\partial\theta}\left(\sin\theta\frac{\partial\phi}{\partial\theta}\right)+\frac{1}{r^2\sin^2\theta}\frac{\partial^2\phi}{\partial\varphi^2}$

Example 1: Microbeads, also known as microspheres, are widely used in drug delivery systems to encapsulate drugs and release them in a controlled manner. These tiny particles, typically made of biodegradable materials, are engineered to deliver a variety of therapeutic agents.

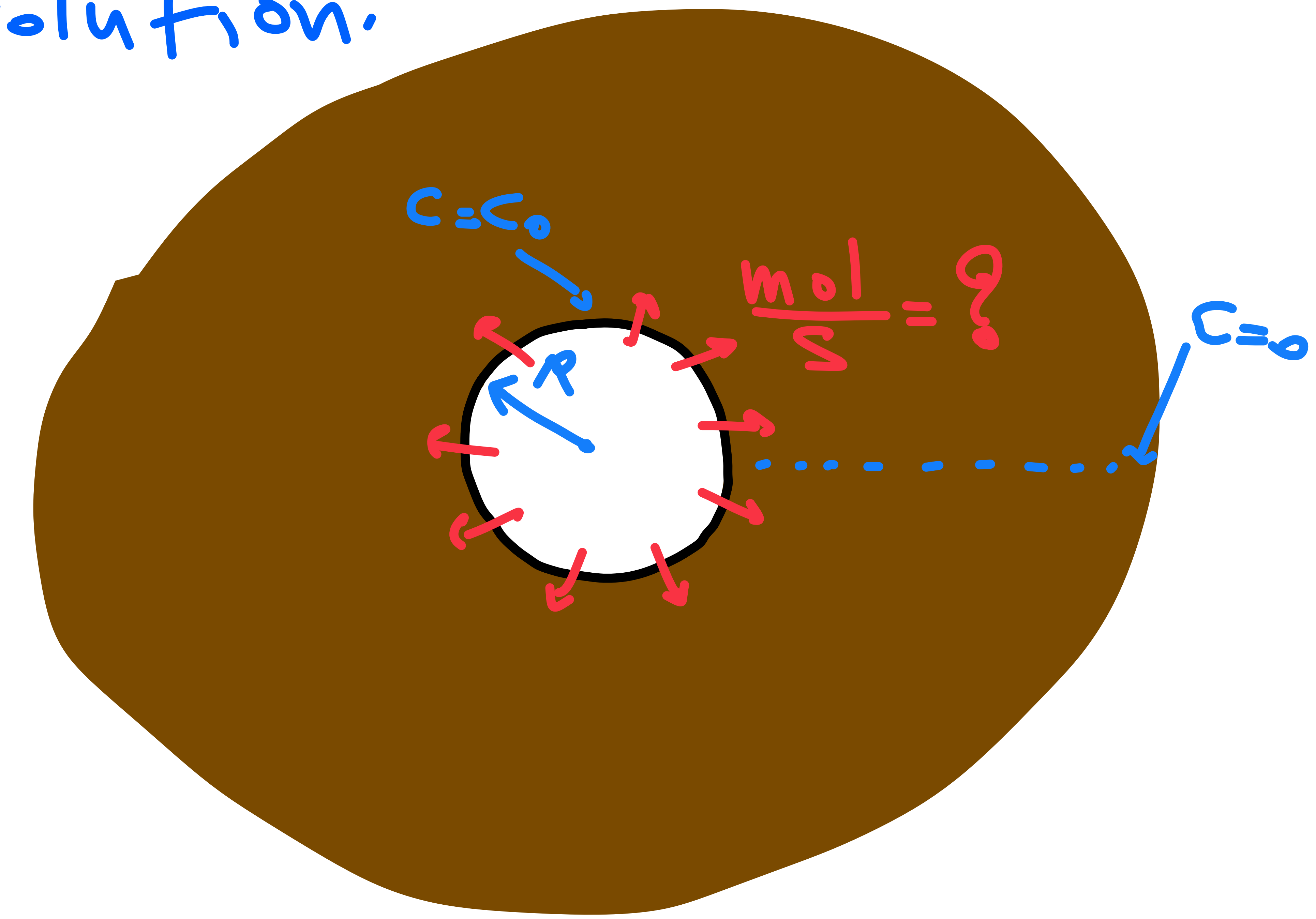
A biotech company has developed microbeads to encapsulate insulin for controlled and prolonged release in diabetic patients. These microbeads can be administered subcutaneously, providing a steady release of insulin and helping maintain more stable blood glucose levels compared to conventional insulin injections.



Q1: Model insulin concentration profile in space if at the surface of the Microbeads (r = R), the insulin concentration in the tissue is C0. Far from the surface, the insulin concentration drops to zero. Develop an expression for the steady state release rate (moles/s) of the insulin from the Microbeads.

Nanda, Himansu Sekhar, et al. "Collagen scaffolds with controlled insulin release and controlled pore structure for cartilage tissue engineering." *BioMed research international* 2014.1 (2014): 623805.

solution.



Question is asking for

we know

$$\frac{\text{total mass transferred}}{\text{time}} = J \times A$$

at the surface of pellet

$\Rightarrow$ we should find C, then we can find J.

a) S.S ✓ b) coordinate system: it is a sphere and we are not looking at a thin wall, therefore spherical.

c)
$$\overset{S.S}{\cancel{\frac{\partial C}{\partial t}}} = D\left(\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C}{\partial r}\right) + \overset{0}{\cancel{\frac{1}{r^2\sin\theta}\frac{\partial}{\partial\theta}\left(\sin\theta\frac{\partial C}{\partial\theta}\right)}} + \overset{0}{\cancel{\frac{1}{r^2\sin^2\theta}\frac{\partial^2 C}{\partial\phi^2}}}\right)$$

symmetry

d) $D\left(\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C}{\partial r}\right)\right) = 0 \Rightarrow \frac{\partial}{\partial r}\left(r^2\frac{\partial C}{\partial r}\right) = 0$

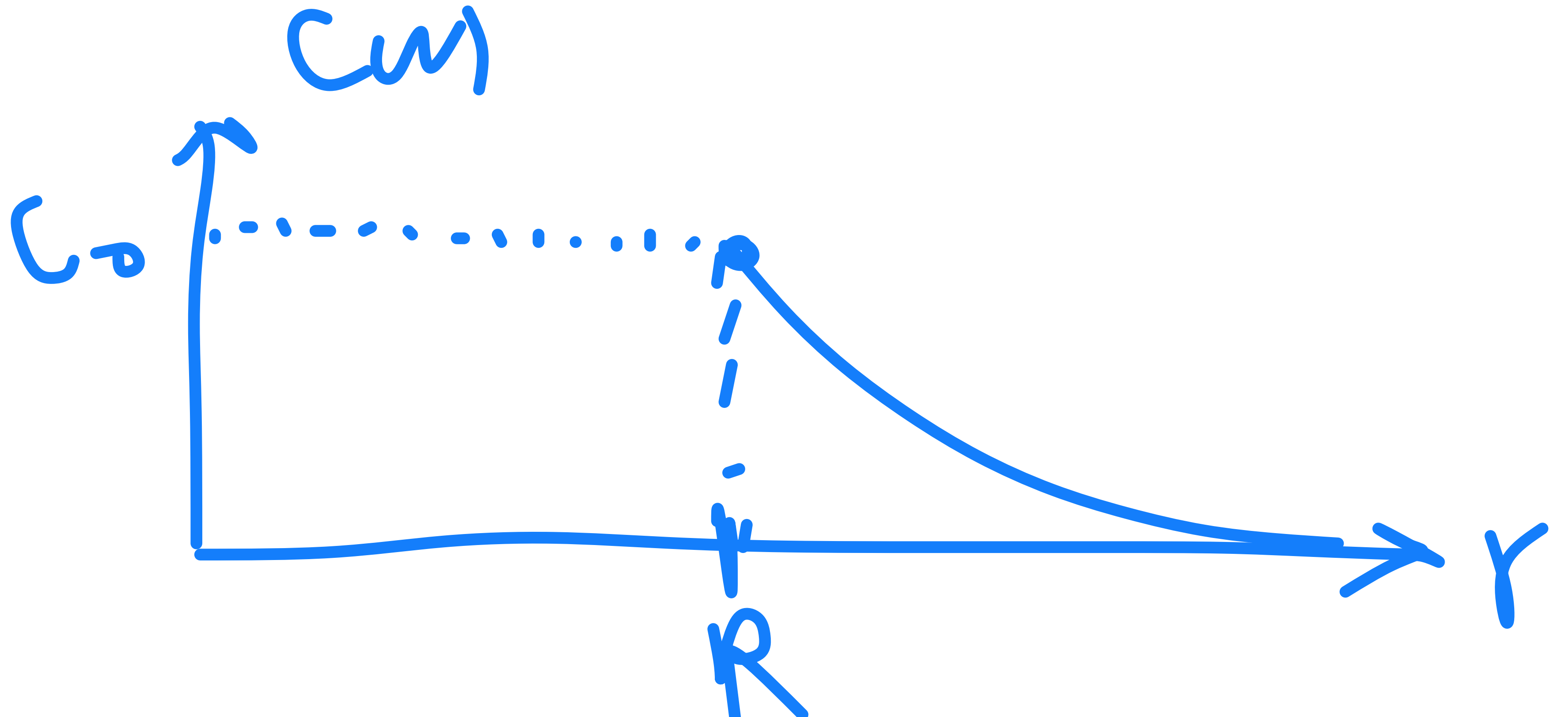
e) it is an ODE $\xrightarrow{\int}$ $r^2\frac{dC}{dr} = C_1 \Rightarrow C(r) = C_2 - \frac{C_1}{r}$

* note that we are looking at: $r \geq R$

f) B.C $\rightarrow$ $C(r=R) = C_0 \Rightarrow C_1 = -RC_0$

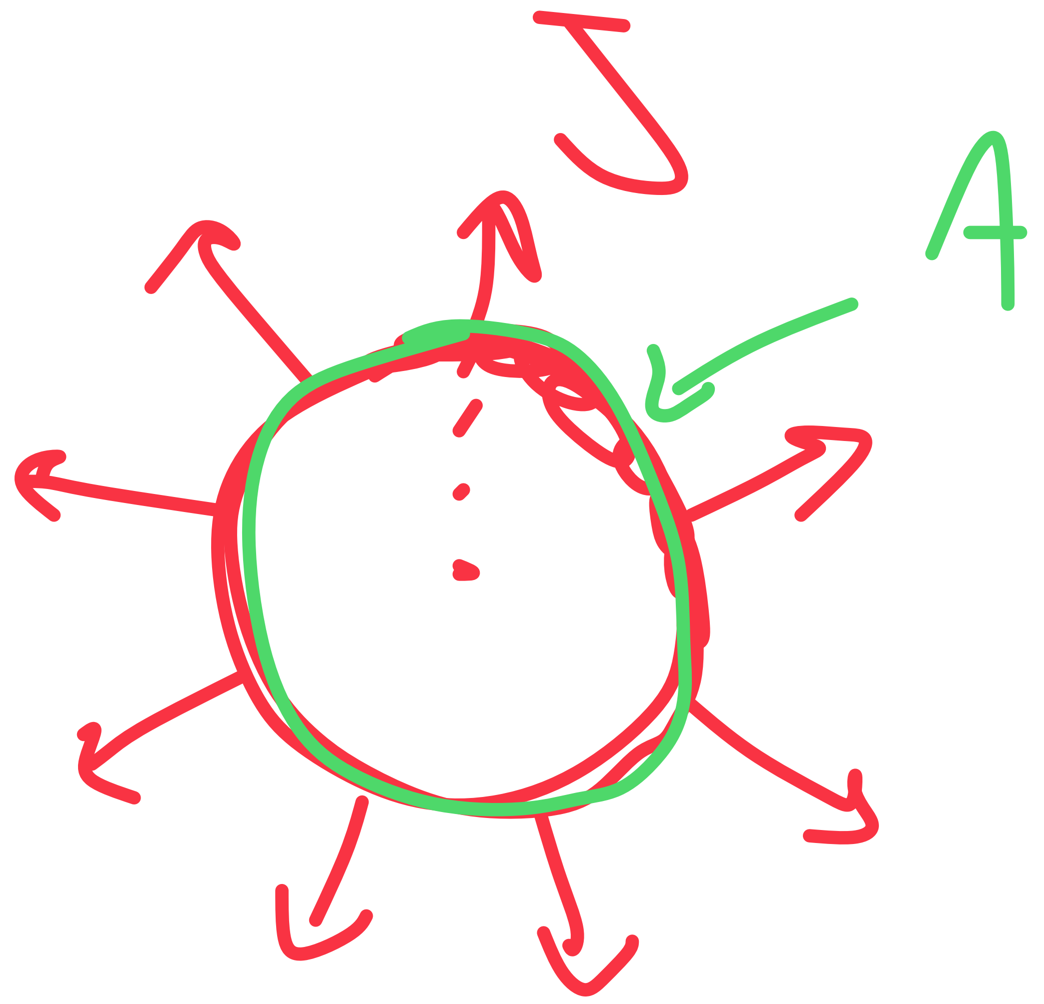
$C(r=\infty) = 0 \Rightarrow C_2 = 0$

g) $C(r) = C_0\frac{R}{r}$



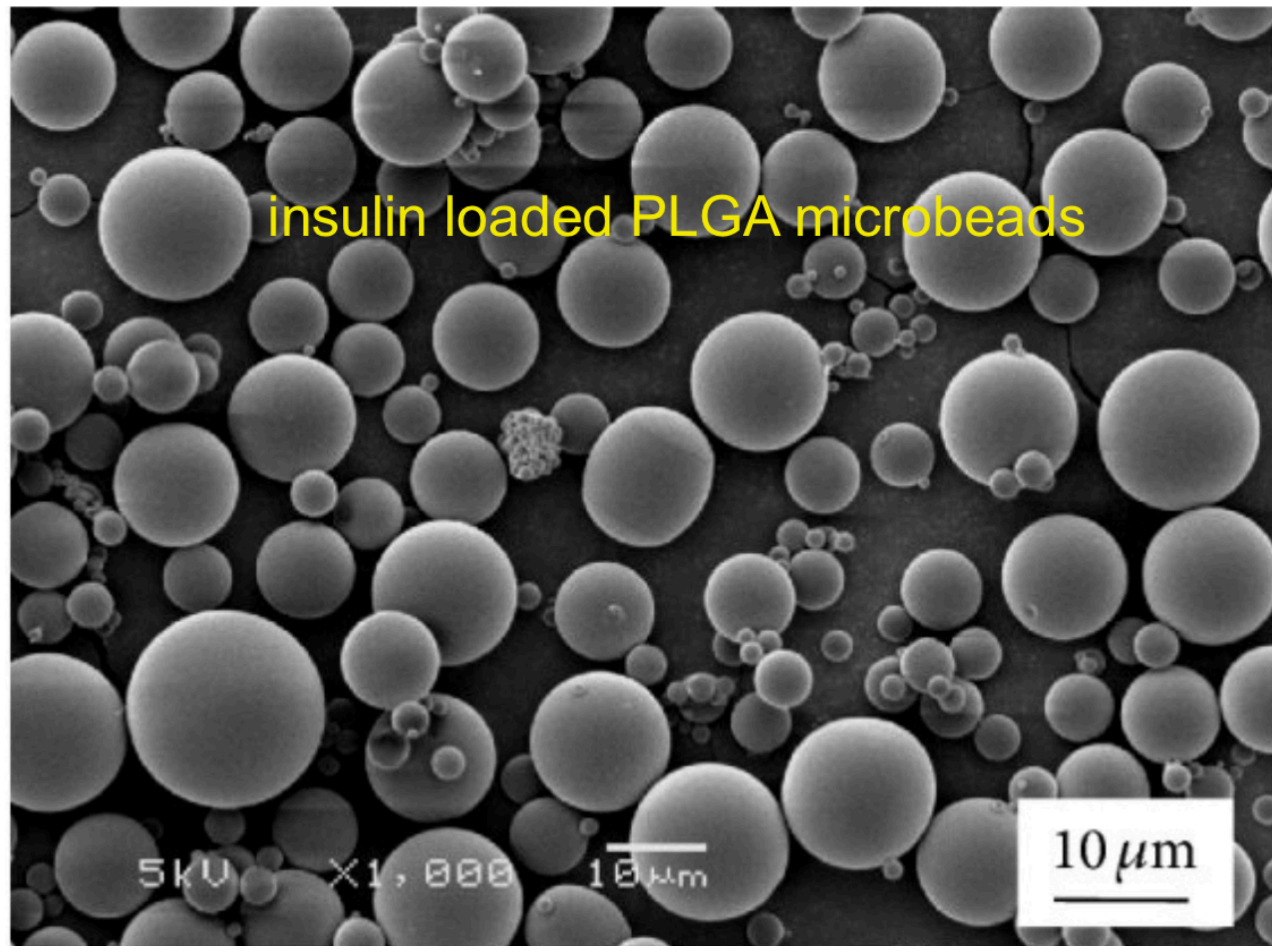
now flux : $\vec{J} = -D\,\vec{\nabla} C \xrightarrow{C(r)}$

$$\vec{J} = -D\,\frac{\partial C}{\partial r}\,\hat{r} = D\,\frac{C_0 R}{r^2}\,\hat{r}$$



for the surface: $\dfrac{T.m.t}{time} = J \times A\Big|_{r=R}$

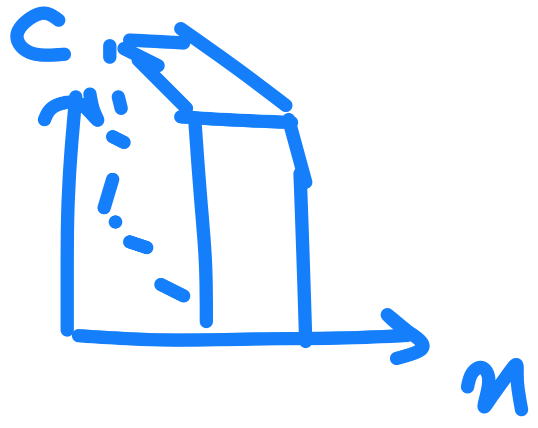
$$= D\,\frac{C_0 R}{R^2} \times \underbrace{4\pi R^2}_{A} = 4\pi C_0 D_0 R$$



Q2: The company hired you as a consultant engineer, they noticed that they need to double **the delivery rate** of insulin for their clinical trials per microbead. What should they do?

Let's review the examples and solutions in S.S approximation lectures part I and II $\cancelto{0}{\frac{\partial c}{\partial t}} = D\nabla^2 c$

1) Cartesian example



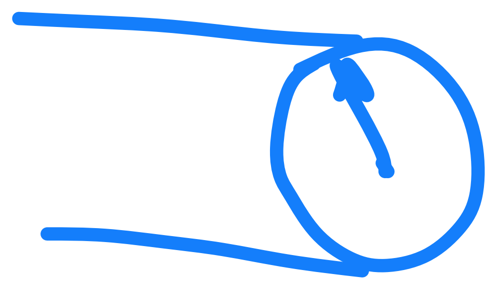
y, z symmetry $\Rightarrow$

$c(x) = c_1 x + c_2$

$J(x) = -Dc_1 \hat{x}$

$c_1, c_2 \rightarrow$ const

2) Cylindrical



θ, z symmetry $\Rightarrow$

$c(r) = c_1 \ln(r) + c_2$

$\vec{J}(r) = -c_1 \frac{D}{r} \hat{r}$

3) spherical

θ, ϕ symmetry $\Rightarrow$

$c(r) = c_2 - c_1 \frac{1}{r}$

$\vec{J} = -\frac{Dc_1}{r^2} \hat{r}$

Pause point I I

Example Implications of these equations in cell biology

Diffusion limited reactions: In fast reactions, the rate can be limited by how quickly molecules reach the reaction site, known as diffusion-limited reactions. These depend on the diffusion rate, not the chemical process itself. Examples include reactions in solutions, between molecules and cells, and on surfaces.

reaction time $\ll$ Diffusion time

Example 2: In this simplified analysis, let's consider the diffusion of molecules toward a reacting, central molecule. We assume that the reaction rate is limited by diffusion. The diffusing molecules, or ligands, are assumed to be much smaller than the central molecule, or receptor, what is the rate of reaction (mol/second) if the Radius of the central molecule is R?

Solution

1) $C(r) = C_2 - \frac{C_1}{r} \quad \left| \begin{array}{l} C(r \to \infty) = C_0 \\ C(r = 0) = 0 \end{array} \right. \quad B.C \Rightarrow C(r) = C_0\left(1 - \frac{R}{r}\right)$

2) $J = +DC_0\frac{R}{r^2} \rightarrow \frac{\text{total mass in}}{\text{time}} = J \times A = 4\pi R D C_0$

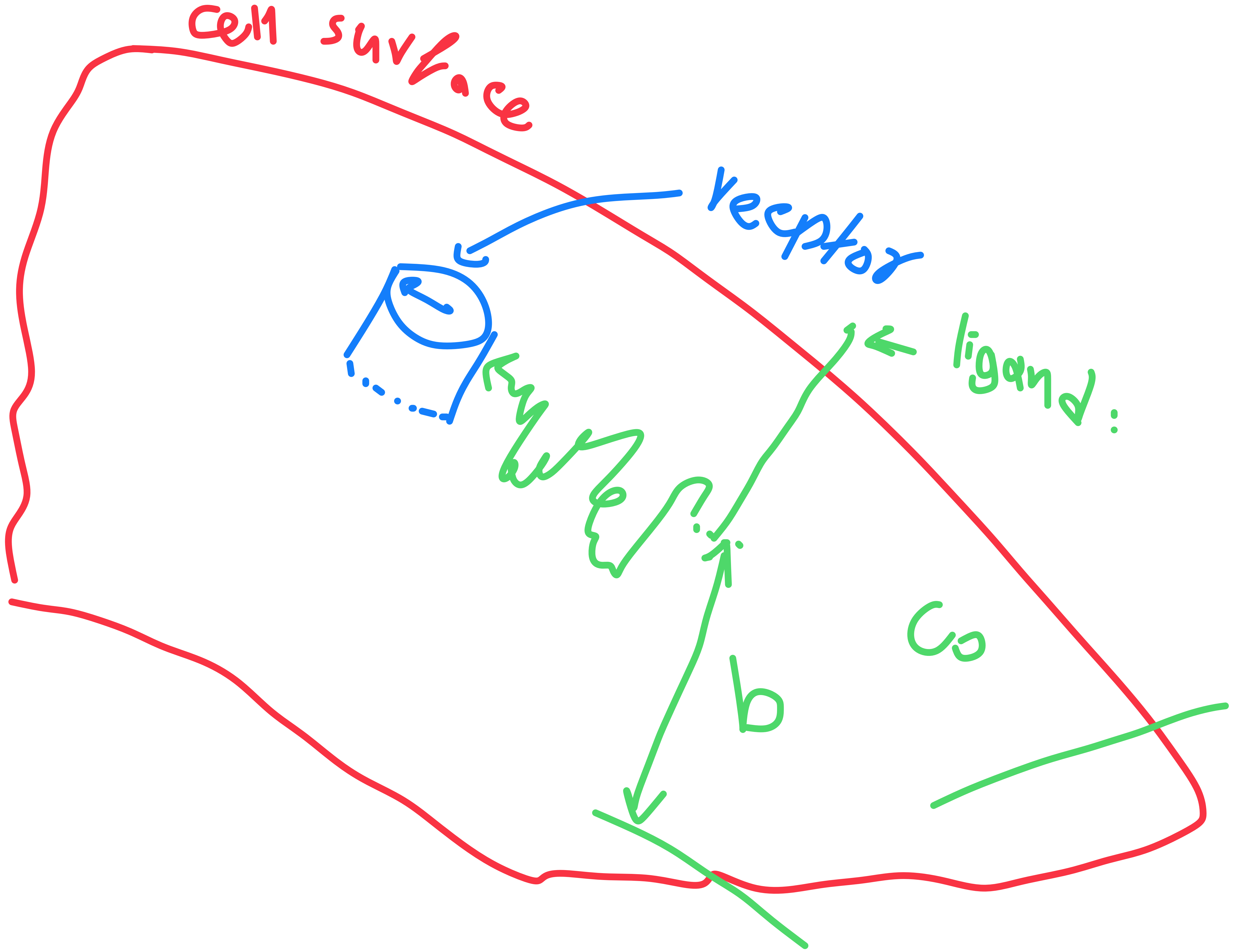
3) $\text{reaction rate} \equiv K C_0 \Rightarrow K = 4\pi R D$

radius of receptor

diffusion of ligand

Central molecule

Example 3: Diffusion-Limited Binding on a Cell Surface: Another case of diffusion-limited reactions is when two molecules on the cell surface bind to each other. This situation occurs quite frequently in biological systems. For example, receptor–ligand binding may cause the receptor to bind to a signaling protein, which forms a ternary complex. This type of binding initiates a cascade of events within the cell that leads to alterations in cell function.



Solution: cylindrical in 2D $\Rightarrow \frac{\partial C}{\partial z} = 0$

$$C(r) = c_1 \ln(r) + C_2 \quad \Bigg| \begin{array}{l} C(r=b) = C_0 \\ C(r=R_R) = 0 \end{array}$$

$$C(r) = C_0 \frac{\ln\left(\frac{r}{R_R}\right)}{\ln\left(\frac{b}{R_R}\right)}$$

$$\Rightarrow J_r A\Big|_{r=R_R} = 2\pi R_R \frac{D}{\ln\left(\frac{b}{R_R}\right)} \frac{1 \times C_0}{R_R}$$

$$= C_0 \frac{2\pi D}{\ln\left(\frac{b}{R_R}\right)}$$

Discuss: use these ypical biological numbers and calculate K for diffusion limited ligand binding to receptor:

$R_R \approx 1\ nm$

$D_{membrane} \approx 10^{-10}\ \frac{cm^2}{s}$

$b \approx 100\ nm$

Now, what if the receptor is 50 times bigger? (giant receptor)

Question