Cours 5:
Electricity in biological systems

Cours “Physique de la Cellule” donné le 18.12.2020 M1 option Physique Médicale

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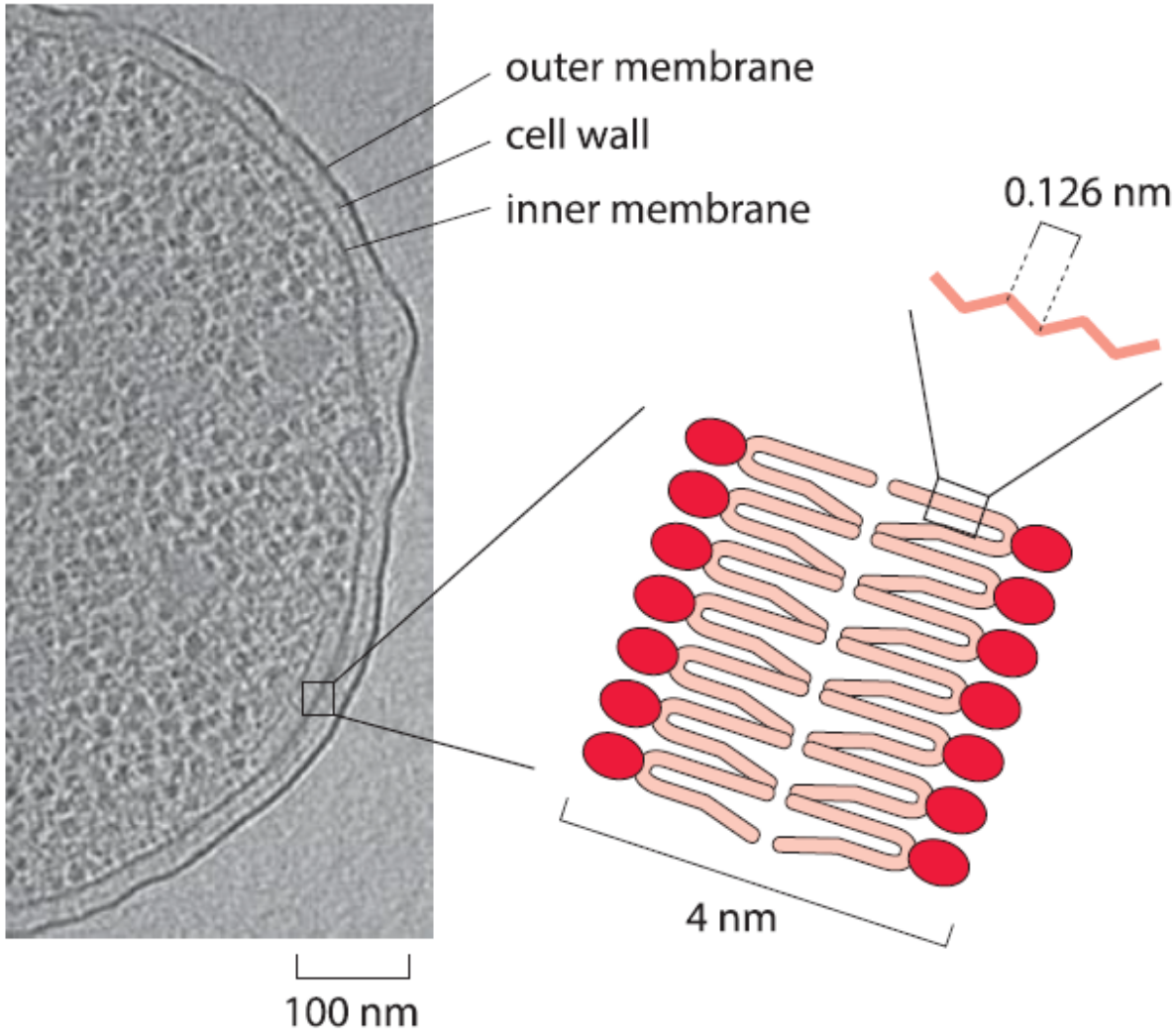
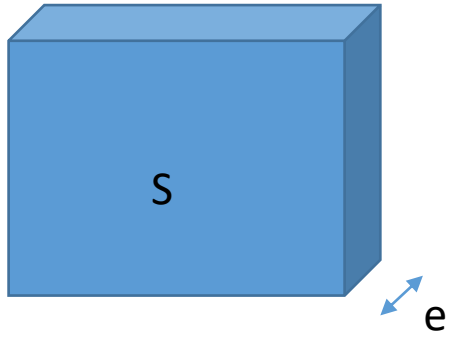
La membrane cytoplasmique: résistance



From "Cell Biology by the numbers", R. Philipps et al.



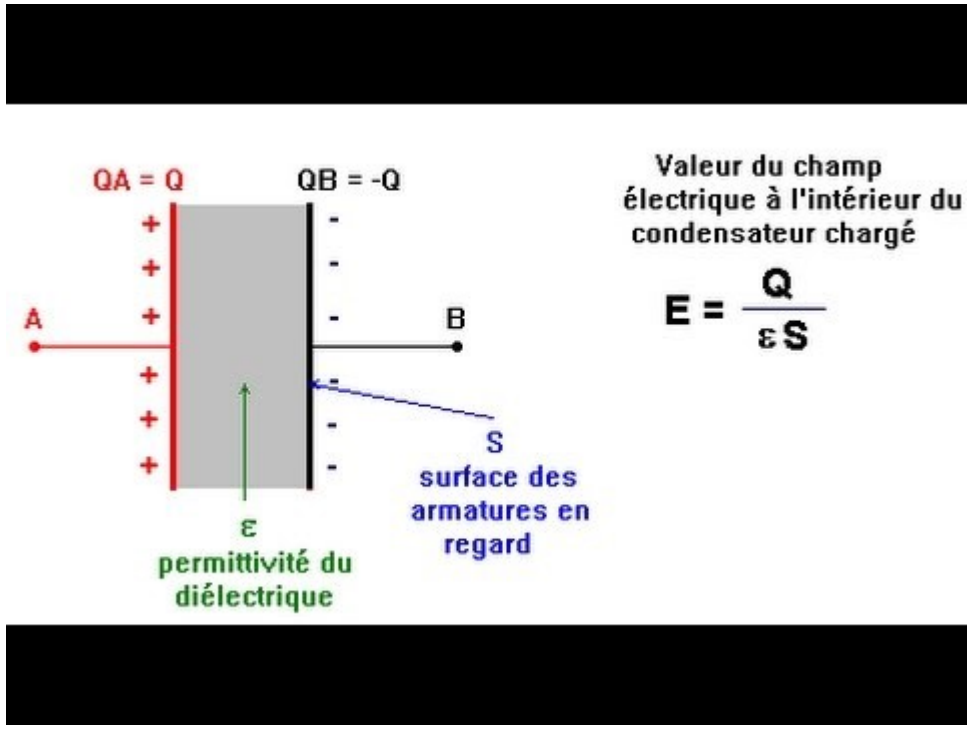
$$R = \frac{\rho e}{s} = \tilde{\rho} / S$$

Ω Ω.m Ω.m²

	Resistivité ρ (Ω.cm)
Membrane lipidique	10^{15}
Membrane cellulaire	10^{7} -10^{12}
Fluide extracellulaire	60
Eau de mer	20

La membrane cytoplasmique: capacitance

$$C = \frac{Q}{\Delta V}$$



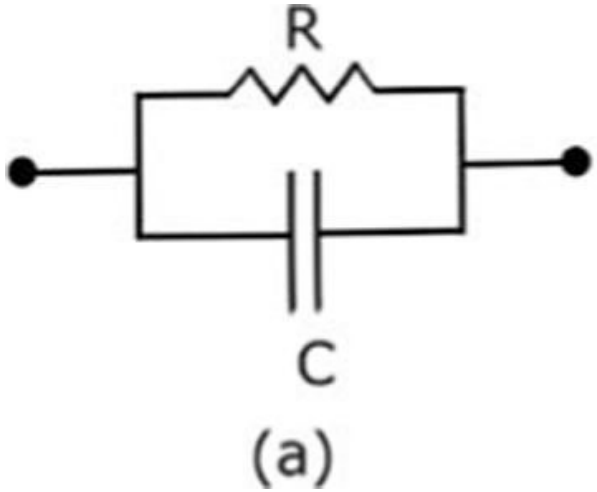
$$\rightarrow C = \frac{\varepsilon_0 \varepsilon S}{e}$$ en Farad

$$\rightarrow c = C/S$$ en Farad/m²

= 0.44 uF/cm²

→ Measured: 1 uF/cm²

Electrical model of membrane (without channels):



$\tau = RC = \tilde{\rho}c$= de 10 usec à 1 sec

Les porteurs de charge: les ions

Tableau 1: Concentrations, [Ion], des ions des milieux interne et externe d'une cellule musculaire squelettique de mammifère.

Ion	$[Ion]_{ext}$ (mM)	$[Ion]_{int}$ (mM)
Na^+	145	12
K^+	4	155
Ca^{2+}	1,5	10^{-7}
Cl^-	123	4,2

(Hille, 1992)

le

La perméabilité des membranes seules varie selon les molécules (Alberts *et al.*, 1983) :

- Les petites molécules apolaires diffusent rapidement (O_2, N_2)
- Les petites molécules polaires non chargées diffusent plus lentement (CO_2, H_2O, urée)
- Les grosses molécules polaires et chargées ne diffusent pratiquement pas (glucides)
- Les grosses molécules et les ions ne diffusent pas

Les protéines membranaires: transport actif et passif de charge

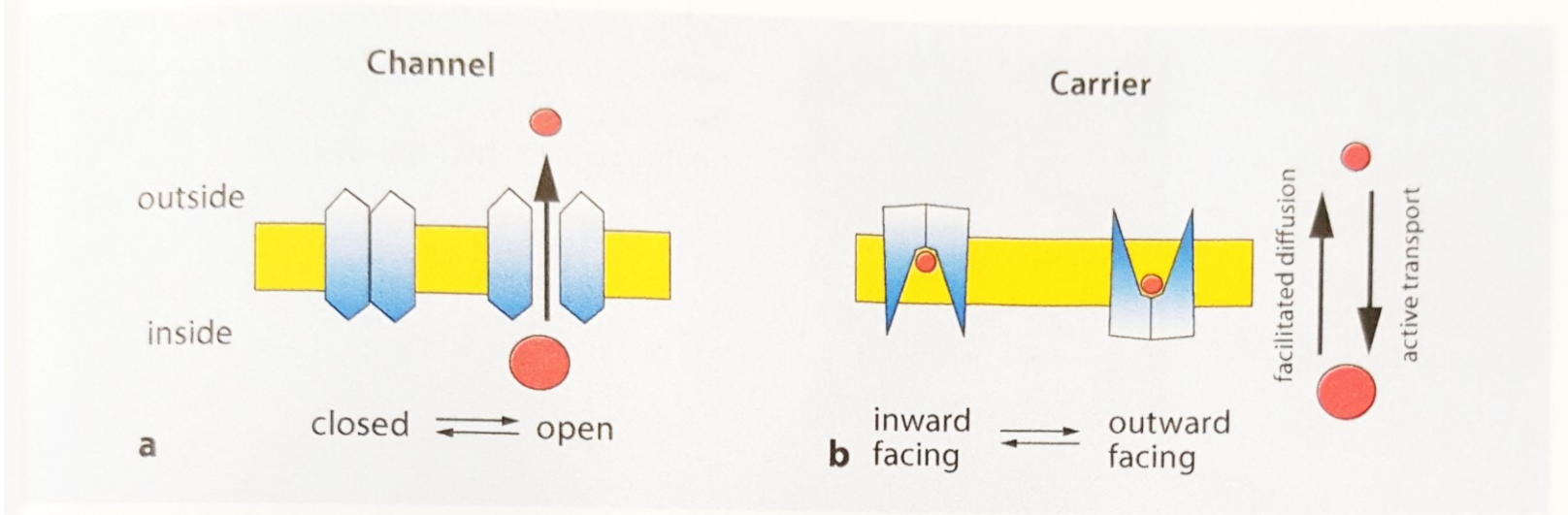


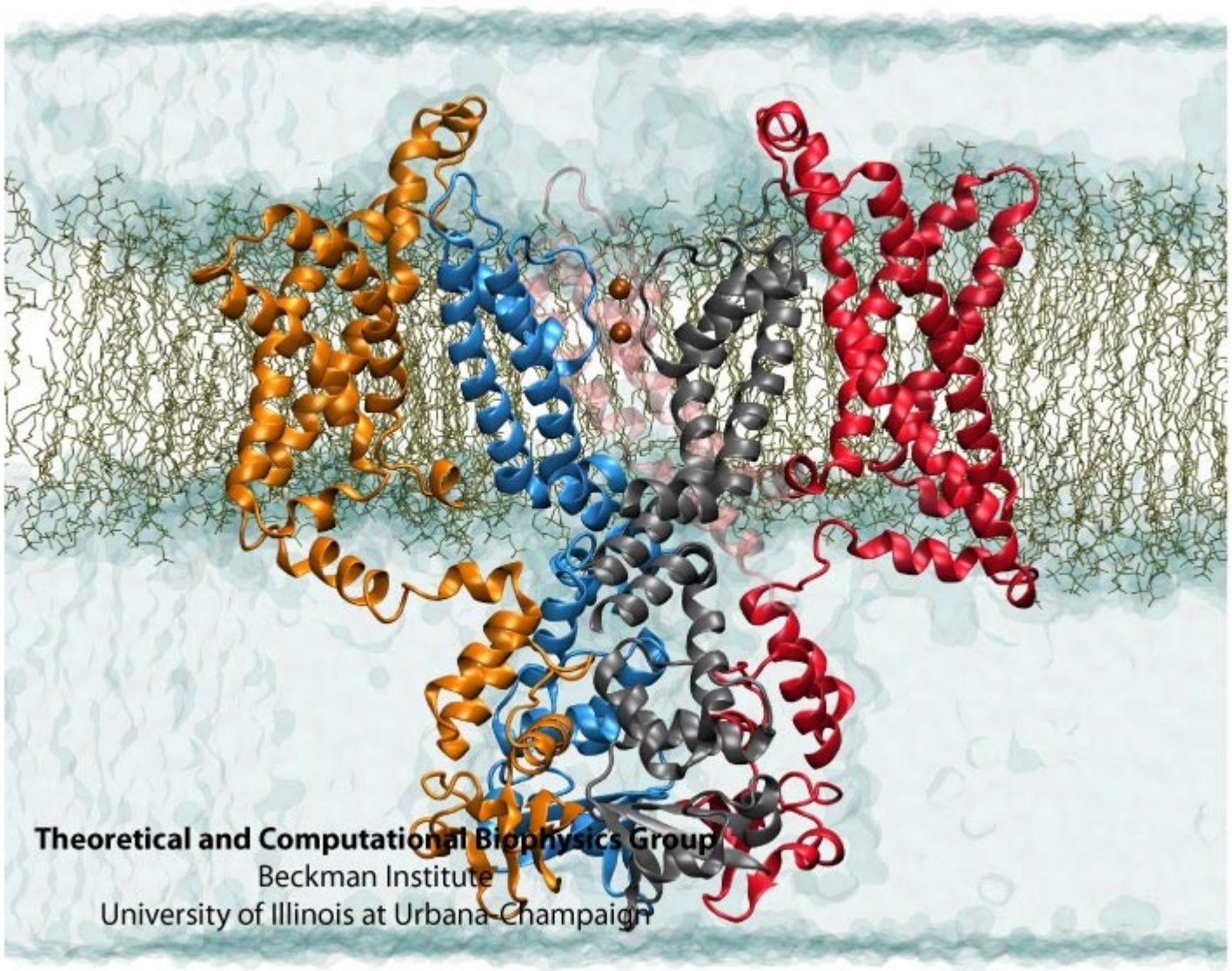
Fig. 1.2 Schematic illustration of a channel (**a**) and a carrier (**b**)

Table 1.1 Characteristic properties of channels and carriers

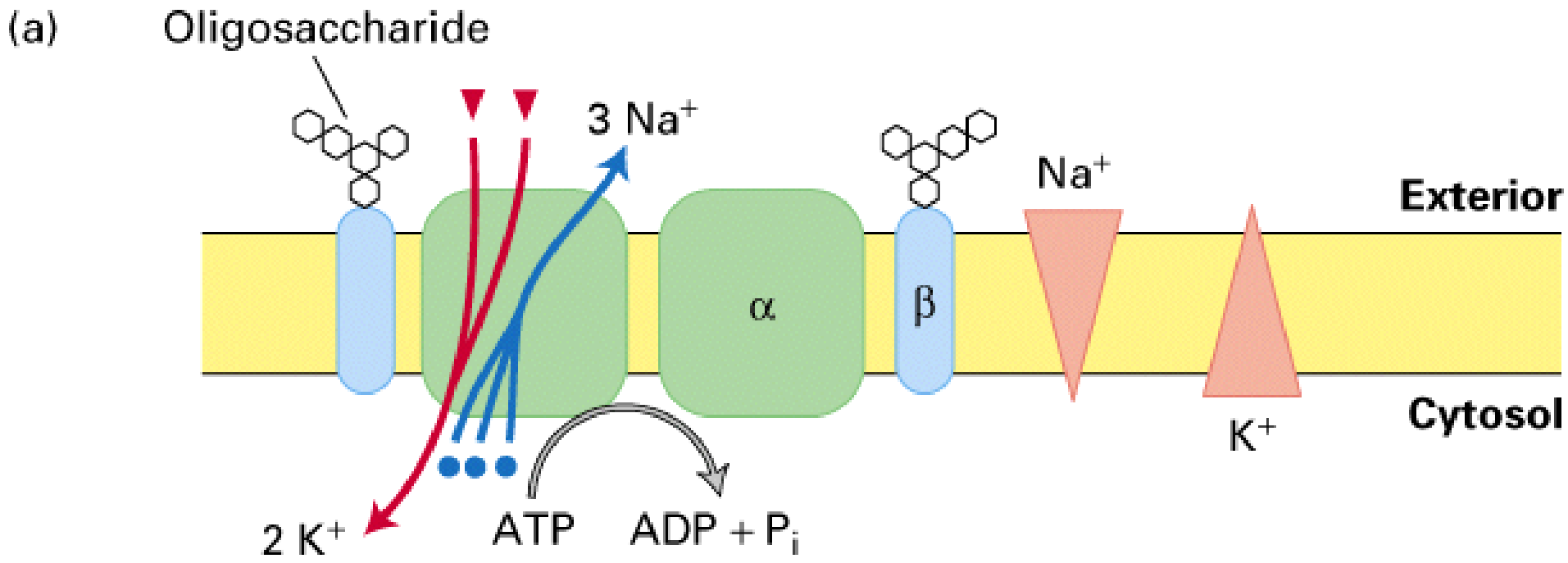
	Pores	Carriers		
Type of Transport	Ion Channels	Facilitated Diffusion	Primary Active Transport	Secondary Active Transport
Driving force	*Diffusion along a gradient*	*Diffusion along a gradient*	*Transport against a gradient utilizing*	
			Metabolic energy (ATP)	*Ion gradients*
Rate of Transport	$<10^8\ s^{-1}$	$<10^3\ s^{-1}$		
Conductance	*~1–300 pS*	*<< pS*		
Function	*Signalling function*	*Housekeeping function*		

"Electrophysiology" J. Rettinger et al., Springer Verlag

Example 1: voltage gated potassium (K^+) channel

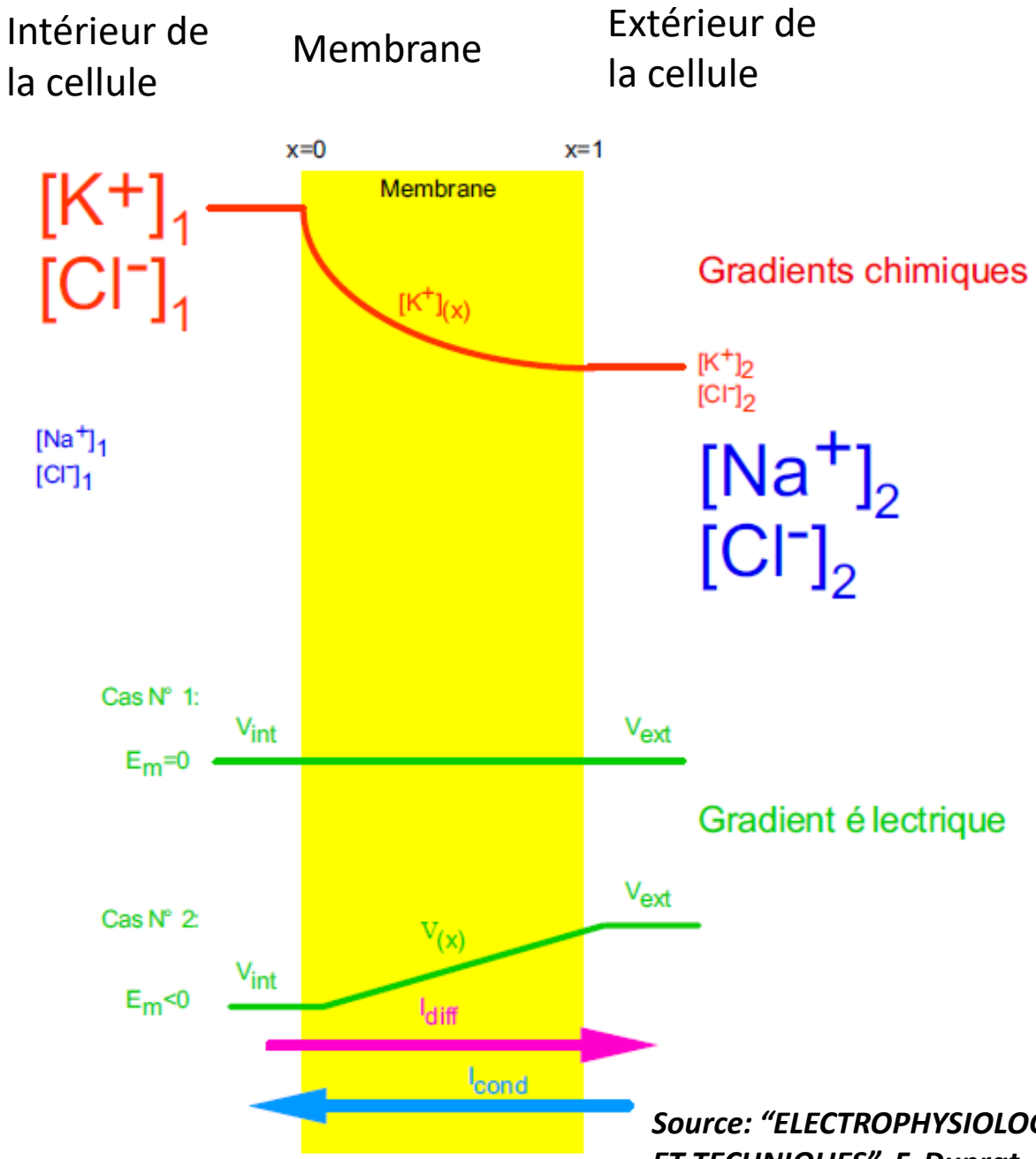


Example 2: Na+ K+ ATP-ase



Other examples: H^+ proton extrusion carriers to acidify stomach

A selectively permeable cell membrane generates a voltage gradient



Source: "ELECTROPHYSIOLOGIE: PRINCIPES ET TECHNIQUES", F. Duprat, INSERM

Equilibre de Nernst

$$J = \underbrace{D\nabla c}_{\text{Courant diffusif}} + \underbrace{\mu z e\, c\, \nabla\varphi}_{\text{Courant électrique}}$$

Einstein relation of mobility and diffusion coefficient:

$$\mu = D/k_B T$$

A l'équilibre: $J = 0$

I_{ion}: densité de courant de l'ion (A/cm^2)
z: valence de l'ion
F: constante de Faraday ($9{,}648.10^4$ C)
D: coefficient de diffusion de l'ion (cm^2/s), voir le Tableau 2
$[Ion]_{(x)}$: concentration de l'ion à la distance x (M)
x: distance dans le pore (cm)
R: constante des gaz parfaits ($8{,}315\ J.K^{-1}.mole^{-1}$) (1 J = 1 V.C)
T: température absolue (°K = °C + 273,16)

En intégrant de part et d'autre de la membrane:

$$\Delta\varphi_{Nernst} = \underbrace{\frac{kT}{ze}}_{\sim 25\ mV} \ln\left(\frac{c_e}{c_i}\right)$$

Tableau 3: Exemple de concentrations en ions (en mM) dans les milieux interne et externe et potentiels d'équilibre correspondants.

	Interne	Externe	$E_{ion} = 58 \log [Ion]_{ext} / [Ion]_{int}$
Na^+	14	140	+ 58 mV
K^+	160	3	- 100 mV
Ca^{++}	10^{-4}	1	+ 232 mV
Cl^-	14	150	- 60 mV

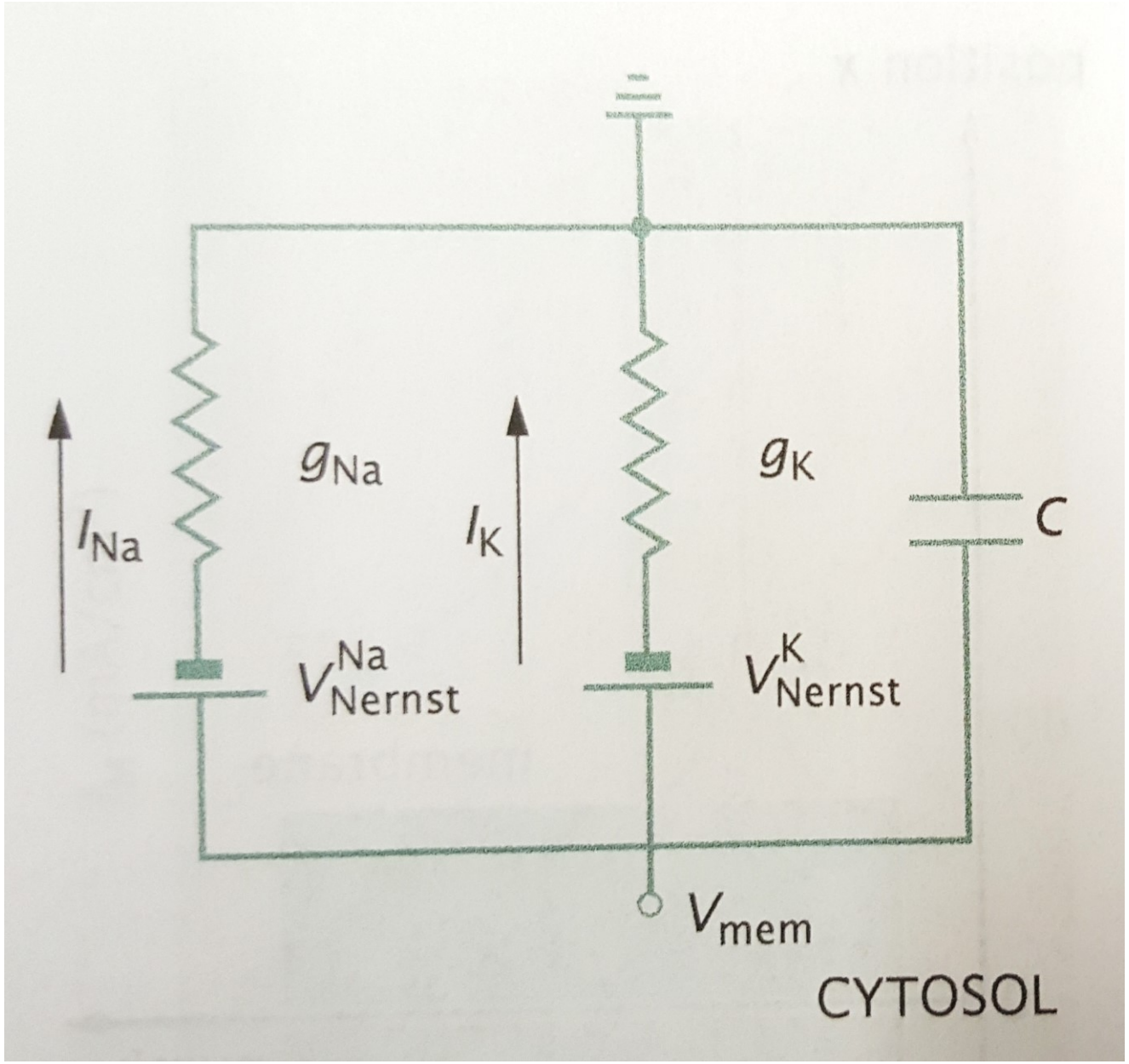
Nota: pour les ions Cl^-, le rapport des concentrations est inversé.

Source: "ELECTROPHYSIOLOGIE : PRINCIPES ET TECHNIQUES", F. Duprat, INSERM

but $$\Delta\varphi_{Cell\ membrane} = -90\ mV$$

for typical mamallian cell

Model of the cell membrane with pores (channels)

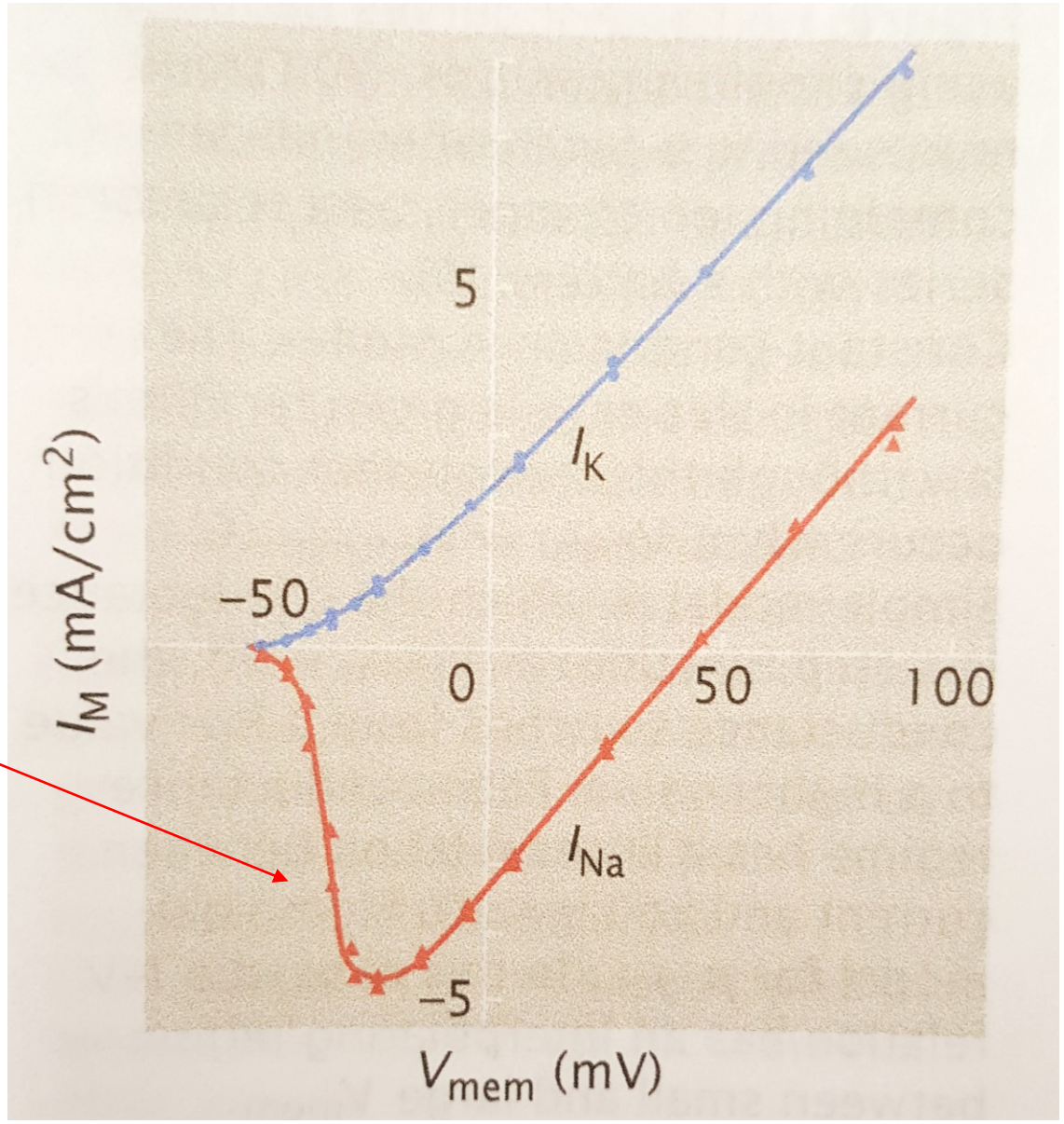


From "Physical Biology of the Cell", R. Philipps et al.

The conductivity of ion channels depends on voltage: voltage-gated

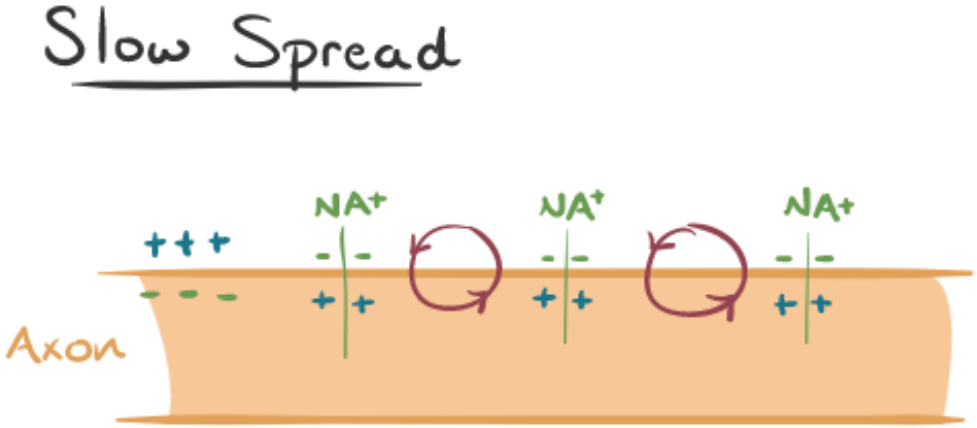
Strongly non-linear part

$$g_{\mathrm{Na}} = g_{\mathrm{Na}}^{\mathrm{open}} \frac{1}{1 + e^{\beta q(V^* - V_{\mathrm{mem}})}}.$$

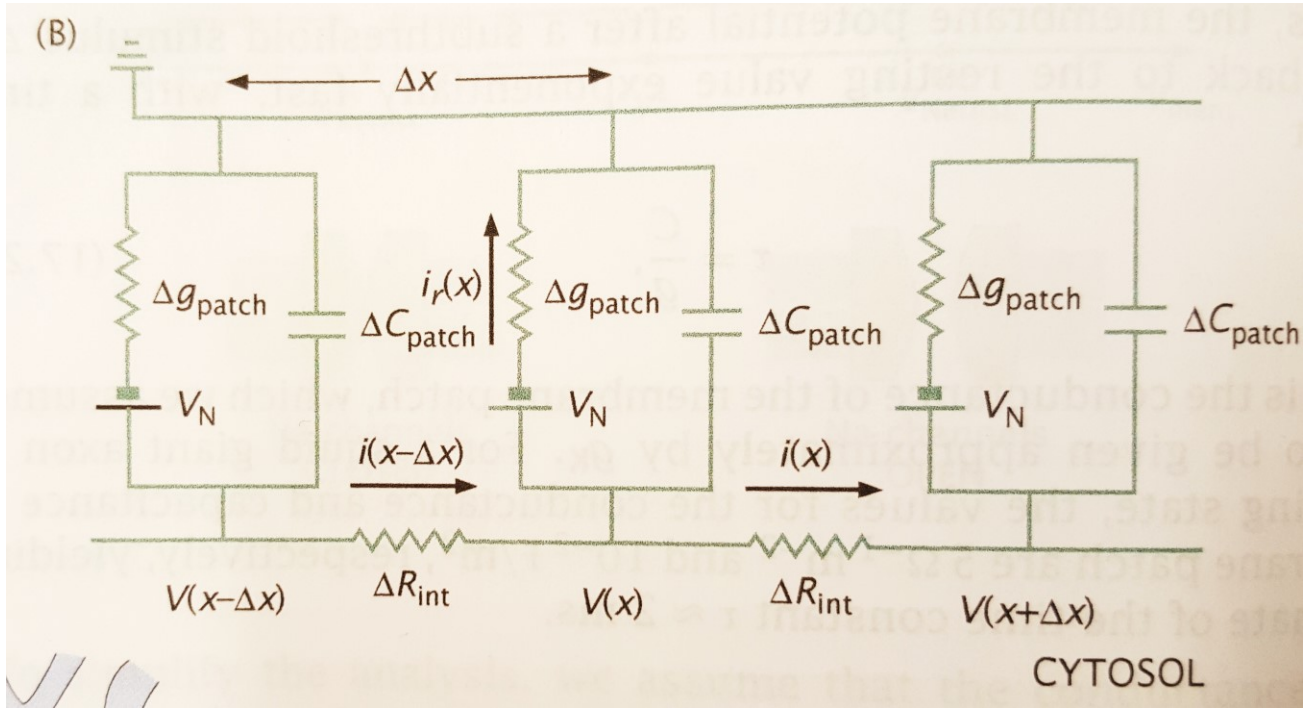


From "Physical Biology of the Cell", R. Philipps et al.

Voltage-gated channels give rise to electrotonic spread of action potential in neurons



Circuit model of action potential – time independent



$$\frac{dV(x)}{dx} = -\frac{\Delta R_{int}}{\Delta x} i(x),$$

$$\frac{di(x)}{dx} = -\frac{\Delta g}{\Delta x}[V(x) - V_{Nernst}].$$

$$\Delta R_{int} = \rho \Delta x / (\pi d^2/4)$$

$$\Delta g_{patch} = g \pi d \Delta x,$$

$$\frac{d^2V(x)}{dx^2} = \frac{1}{\lambda^2}[V(x) - V_{Nernst}],$$

$$\lambda = \sqrt{\frac{d}{4\rho g}}$$

From "Physical Biology of the Cell", R. Philipps et al.

Circuit model of action potential – time dependent

Include capacitive currents

$$i(x-\Delta x,t)-i(x,t)=\Delta g^{\mathrm{Na}}_{\mathrm{patch}}[V(x,t)-V^{\mathrm{Na}}_{\mathrm{Nernst}}]$$
$$+\Delta g^{\mathrm{K}}_{\mathrm{patch}}[V(x,t)-V^{\mathrm{K}}_{\mathrm{Nernst}}]+\Delta C_{\mathrm{patch}}\frac{\partial V(x,t)}{\partial t},$$

Time-dependent cable equation:

$$\lambda^2\frac{\partial^2 V(x,t)}{\partial x^2}-\tau\frac{\partial V(x,t)}{\partial t}=\frac{g_{\mathrm{Na}}(V(x,t))}{g_{\mathrm{K}}}[V(x,t)-V^{\mathrm{Na}}_{\mathrm{Nernst}}]+[V(x,t)-V^{\mathrm{K}}_{\mathrm{Nernst}}],$$

with

$$g_{\mathrm{Na}}=g^{\mathrm{open}}_{\mathrm{Na}}\frac{1}{1+e^{\beta q(V^*-V_{\mathrm{mem}})}}.$$

From "Physical Biology of the Cell", R. Philipps et al.

Result: a propagating spike when above threshold potential

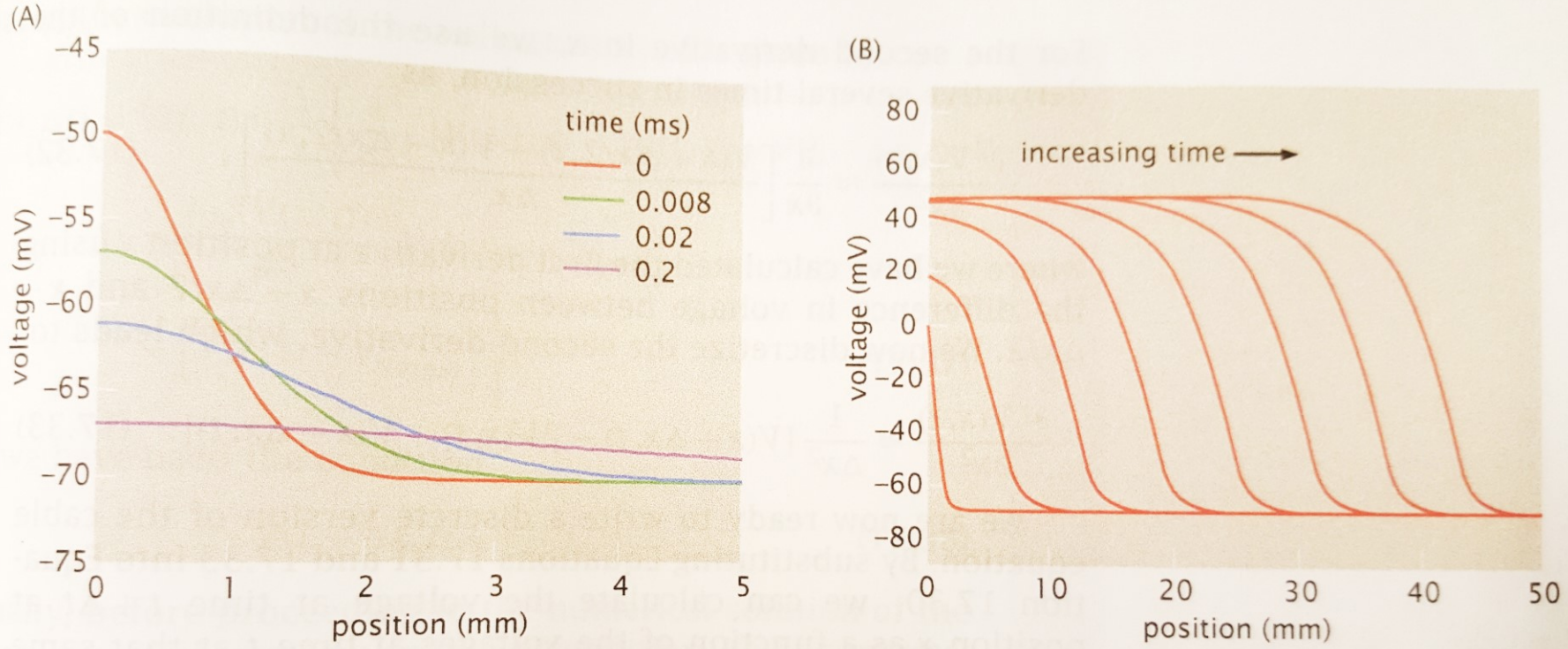
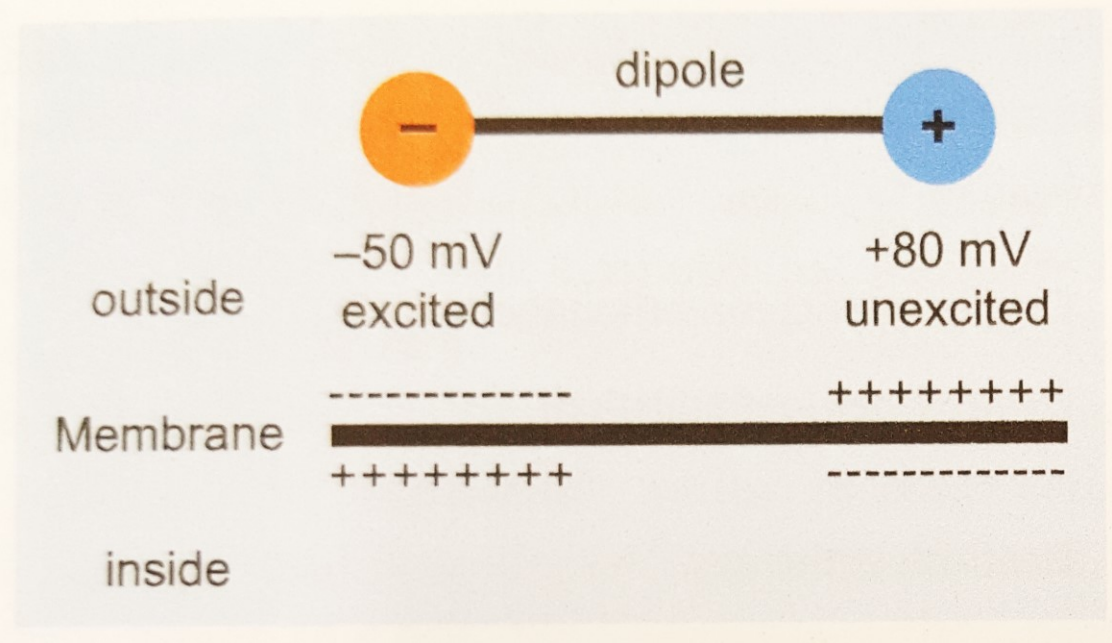
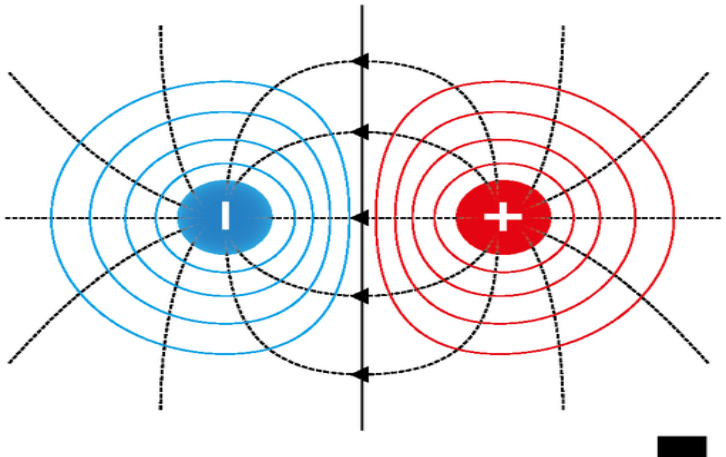


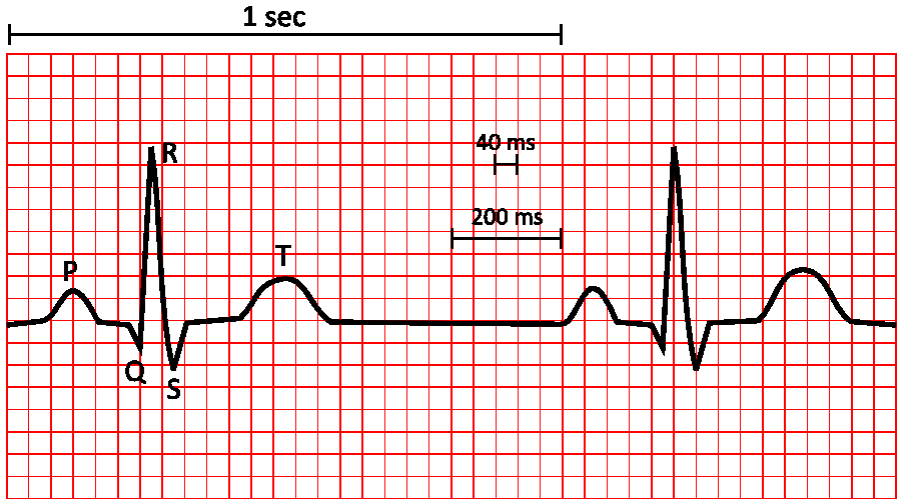
Figure 17.20: Numerical solutions to the time-dependent cable equation, Equation 17.30, using $\lambda = 9.1$ mm, $\tau = 2$ ms, $V^{Na}_{Nernst} = 54$ mV, $V^{K}_{Nernst} = -75$ mV, and $V^* = -40$ mV. The initial membrane voltage is a Gaussian spike above the resting membrane potential, $V(x, 0) = \Delta V e^{-(x/\sigma)^2} + V_{mem}$, of amplitude ΔV and width $\sigma = 1$ mm. The resting potential V_{mem} is related to the Nernst potentials of Na^+ and K^+ by Equation 17.17. (A) Solution when the initial voltage spike is subthreshold, showing a decaying signal. (B) When the initial voltage spike is above the threshold, a propagating front solution is obtained. The snapshots in the propagating front are shown at 200 ms intervals.

From "Physical Biology of the Cell", R. Philipps et al.

Dipoles created by contractile wave of the heart







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Dipoles created by contractile wave of the heart

Table 3.1 Electromedical techniques

For diagnosis		For therapy	
Electrodermatography		Cardiac resynchronization therapy (CRT)	
Electrogastrography (from surface or intragast.)		Electroshock (defibrillation)	
Electrocochleography		Electrosleeptherapy	
Electrocardiography (from surface or intracard.)	ECG	Elektroneuraltherapy (electroacupuncture)	
Electroencephalography	EEG	Electrogymnastics	
Electroneurography (conduction pattern)	ENG	Electrocoagulation	
Electrospinography		(Electronarcosis) (Electrotetanustherapy)	*No longer used because of uncontrolled damage*
Electrooculography Electroretinography Electronystagmography	EOG		
Electromyography	EMG		

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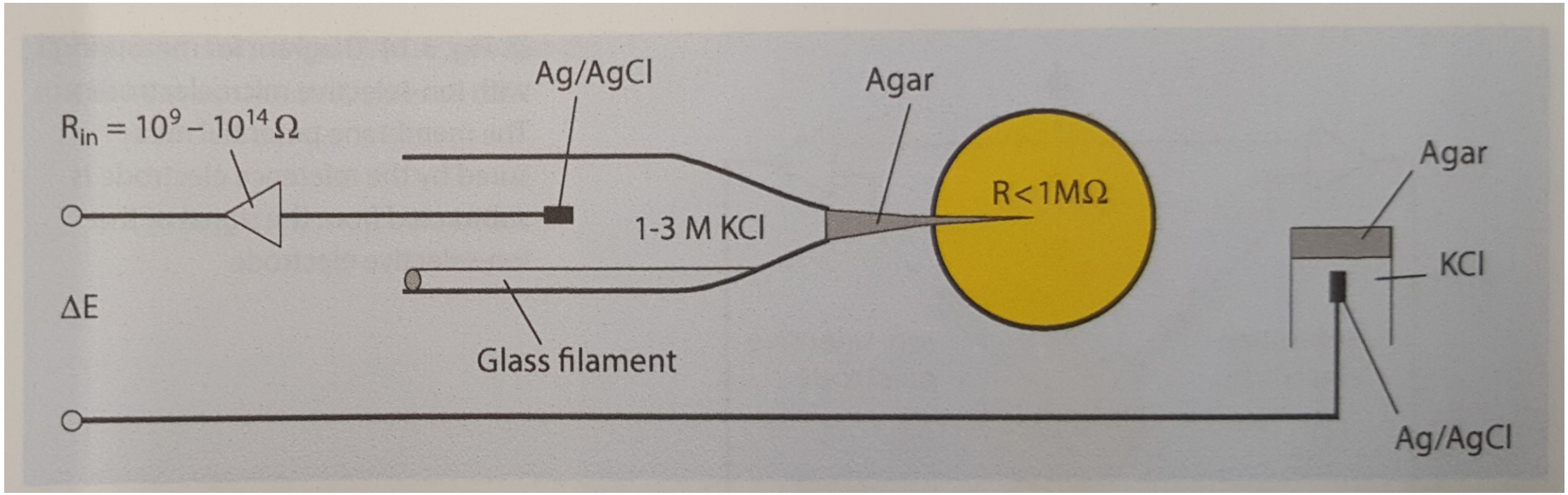
How to measure membrane potential, depolarization ?

$AgCl + e^- \rightleftharpoons Ag + Cl^-$



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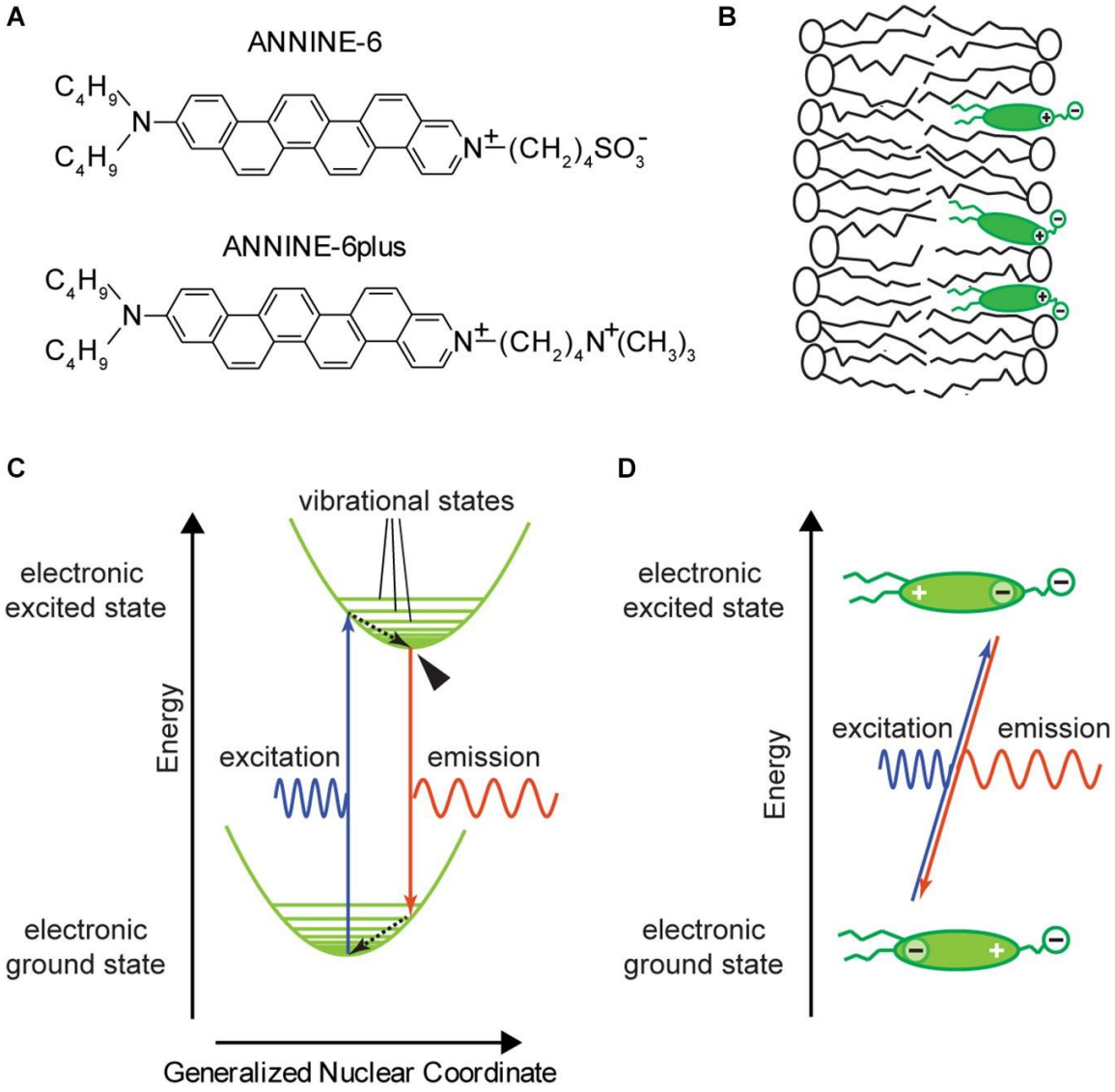
Transmembrane potential and ion concentrations can be measured with fluorescent probes

Calcium sensitive dye: Fluo4-AM

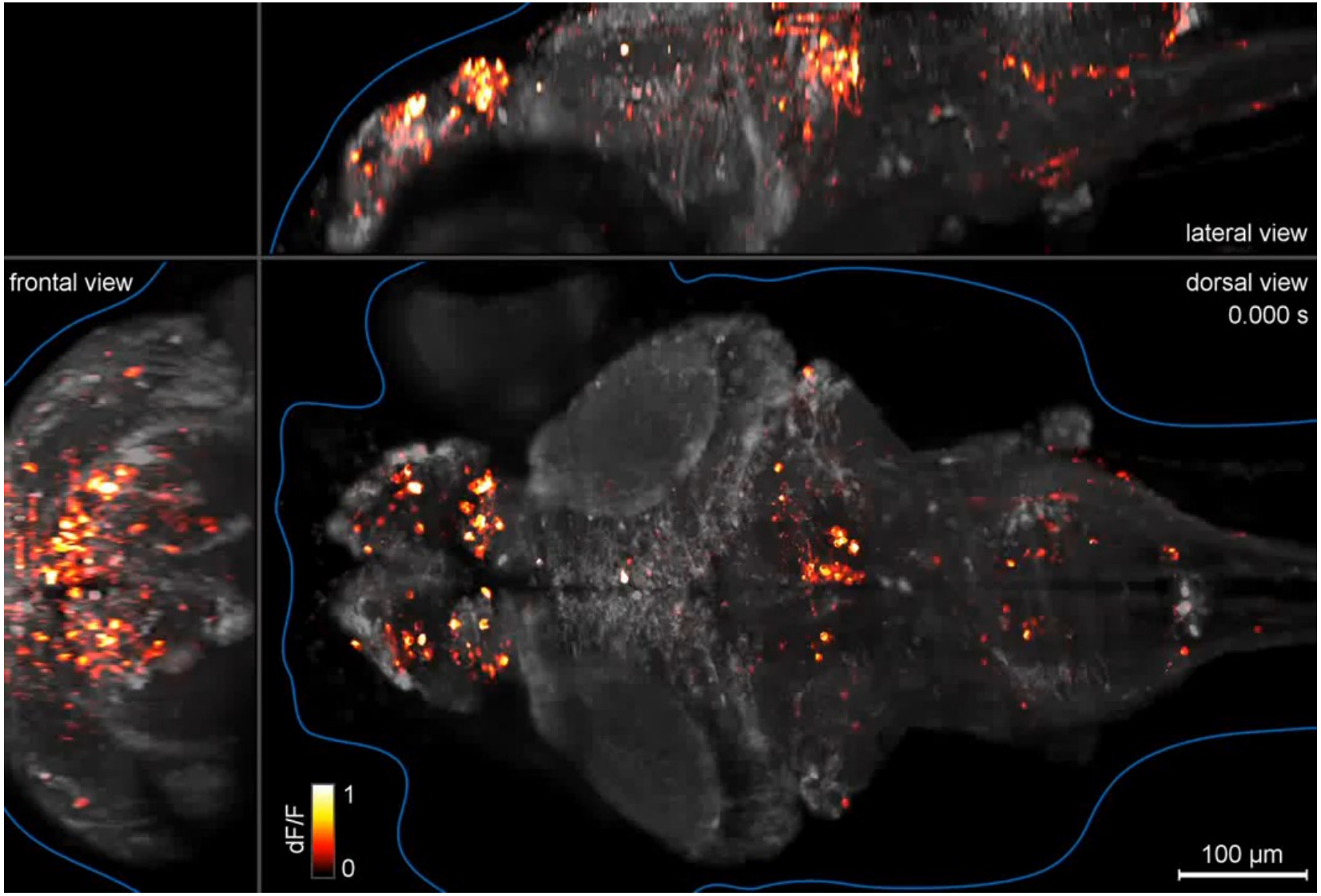
Voltage sensitive dye: ANNINE-6

Can also be genetically encoded:

Example GCamp

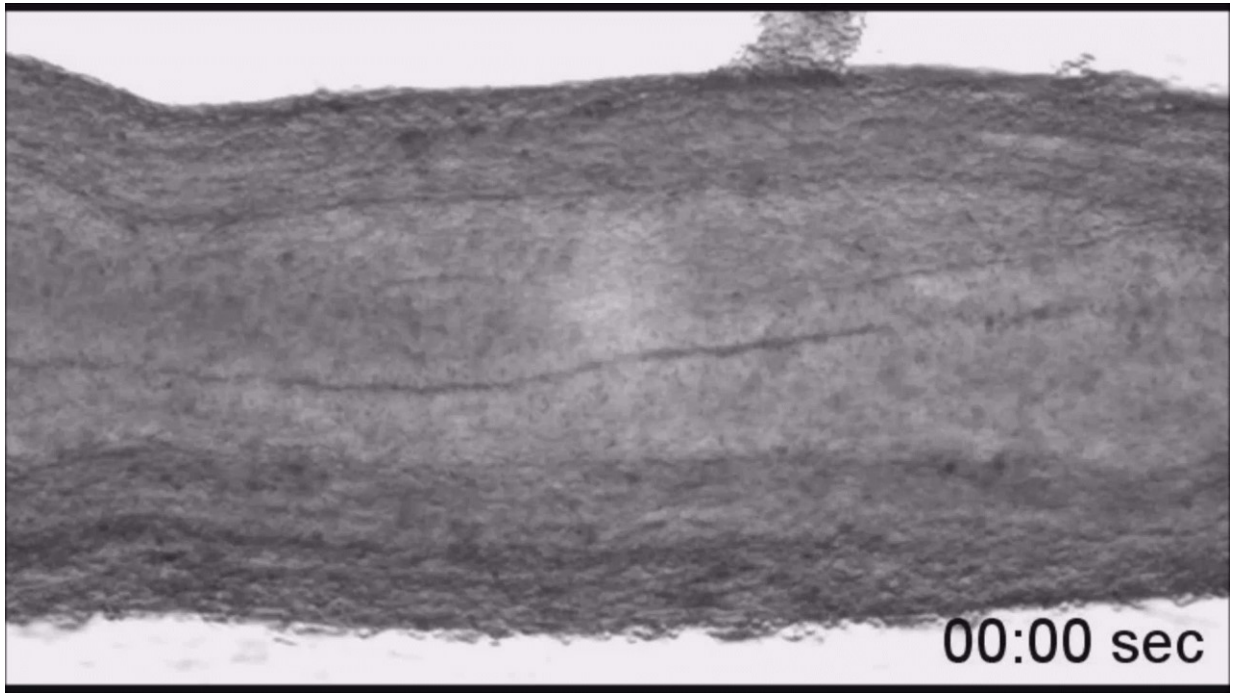


Example: electrical activity in the zebrafish brain (neurons)

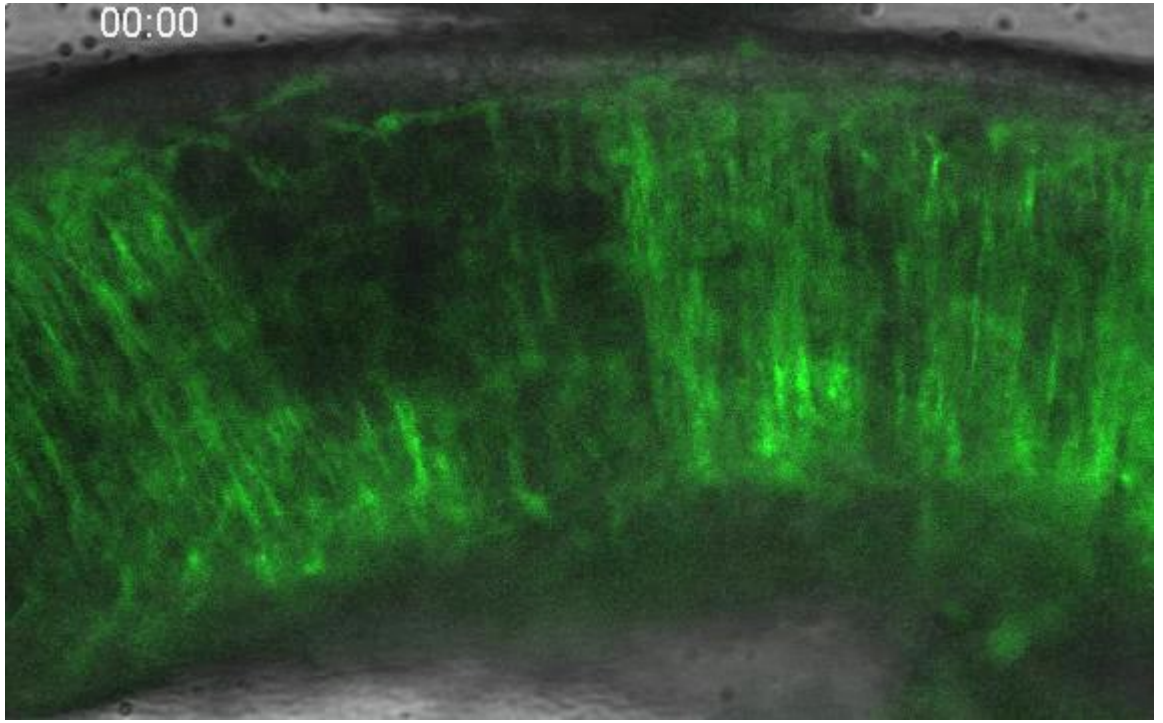


Laboratoire J. Perrin,
Université Paris 6

The heart and the intestine: electro-mechanical inter-cellular depolarization / calcium waves in smooth muscle



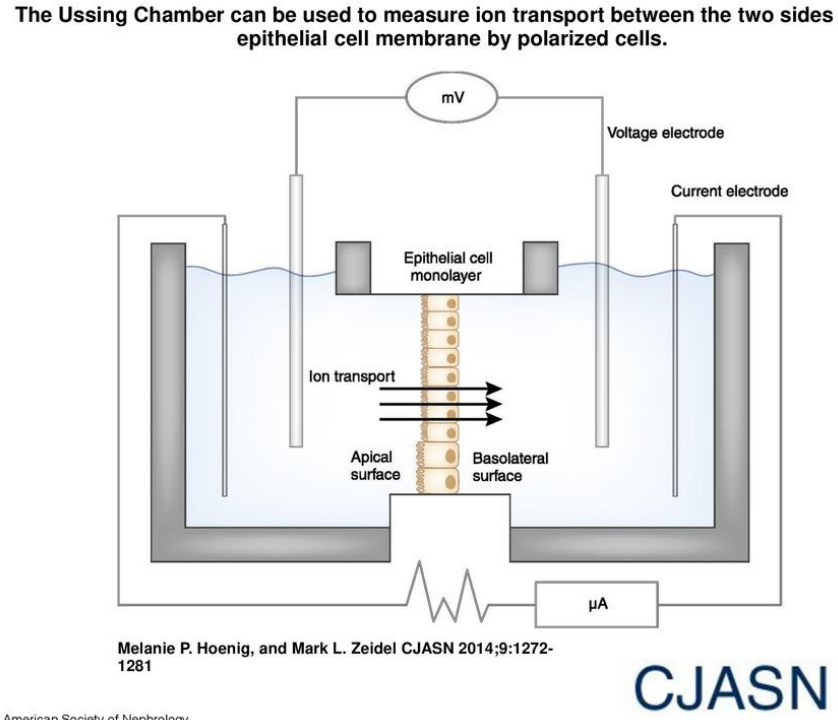
Chevalier et al., Sc. Rep 2017



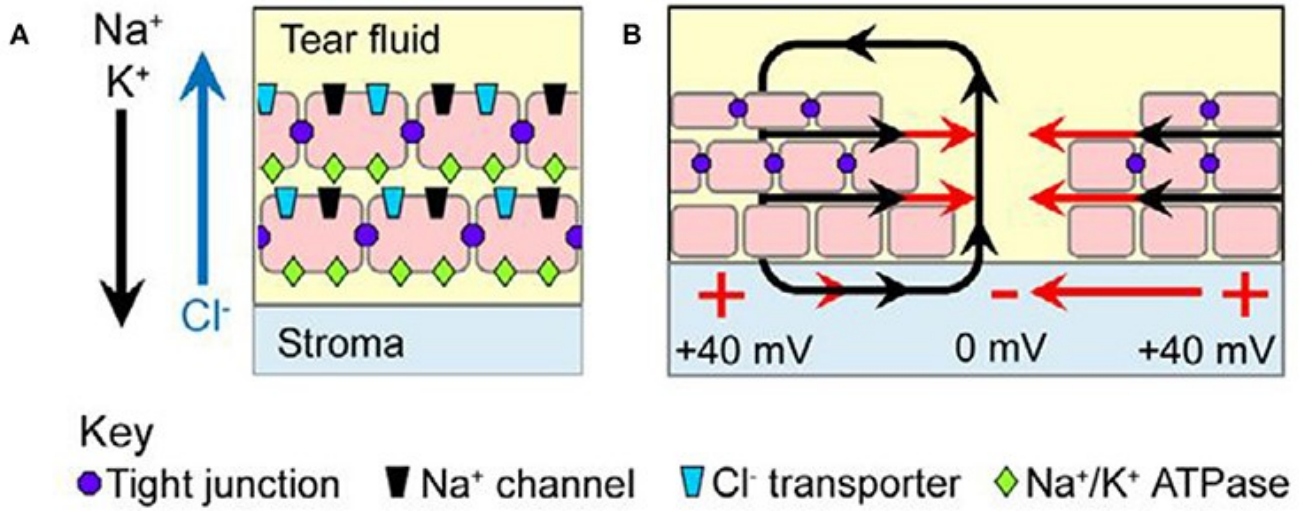
Huycke et al., Cell 2019

Supracellular electricity: Epithelia develop trans-epithelial potentials (TEP)

Rôle dans la fermeture de blessure de l'épithélium:

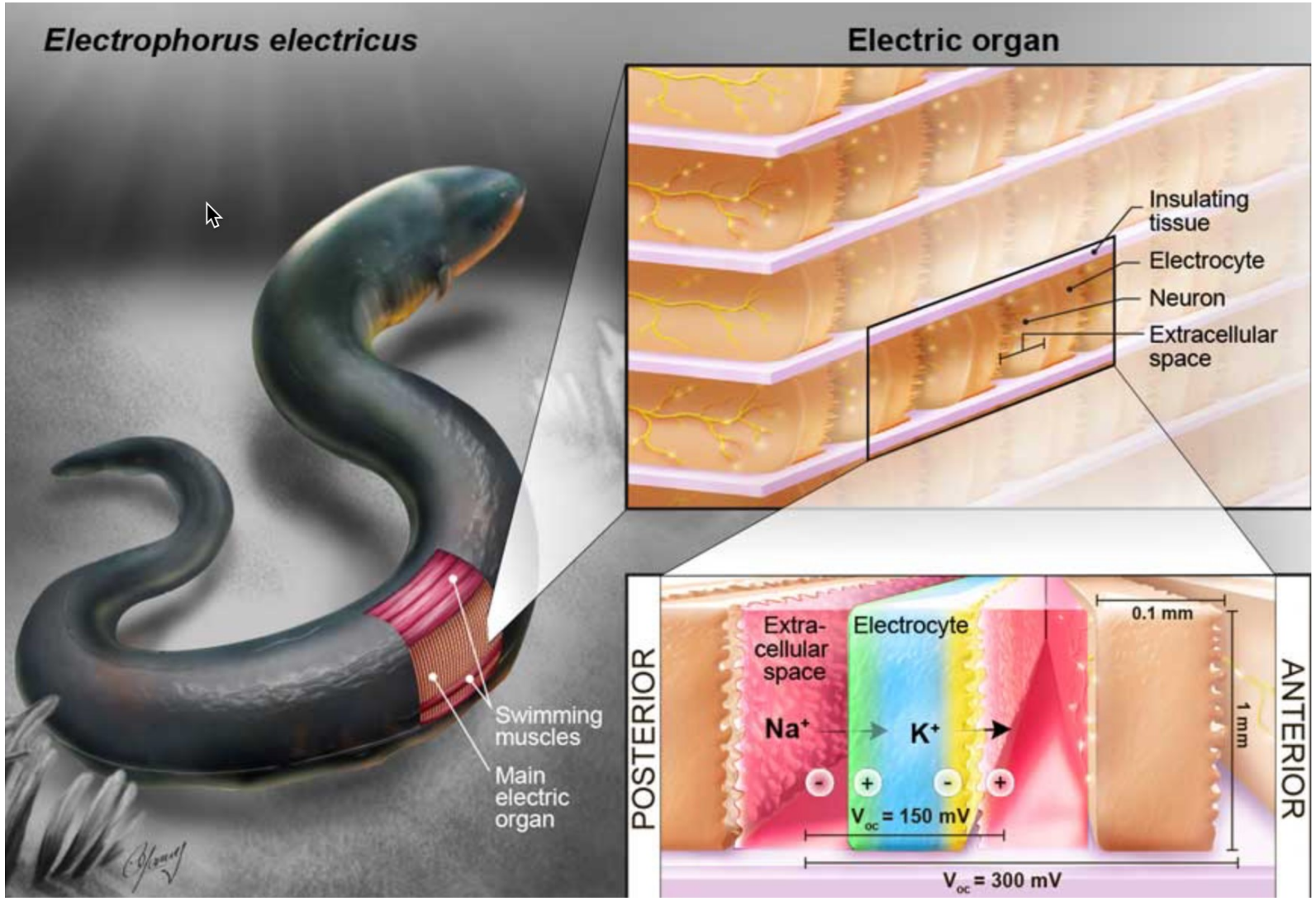


Ussing chamber

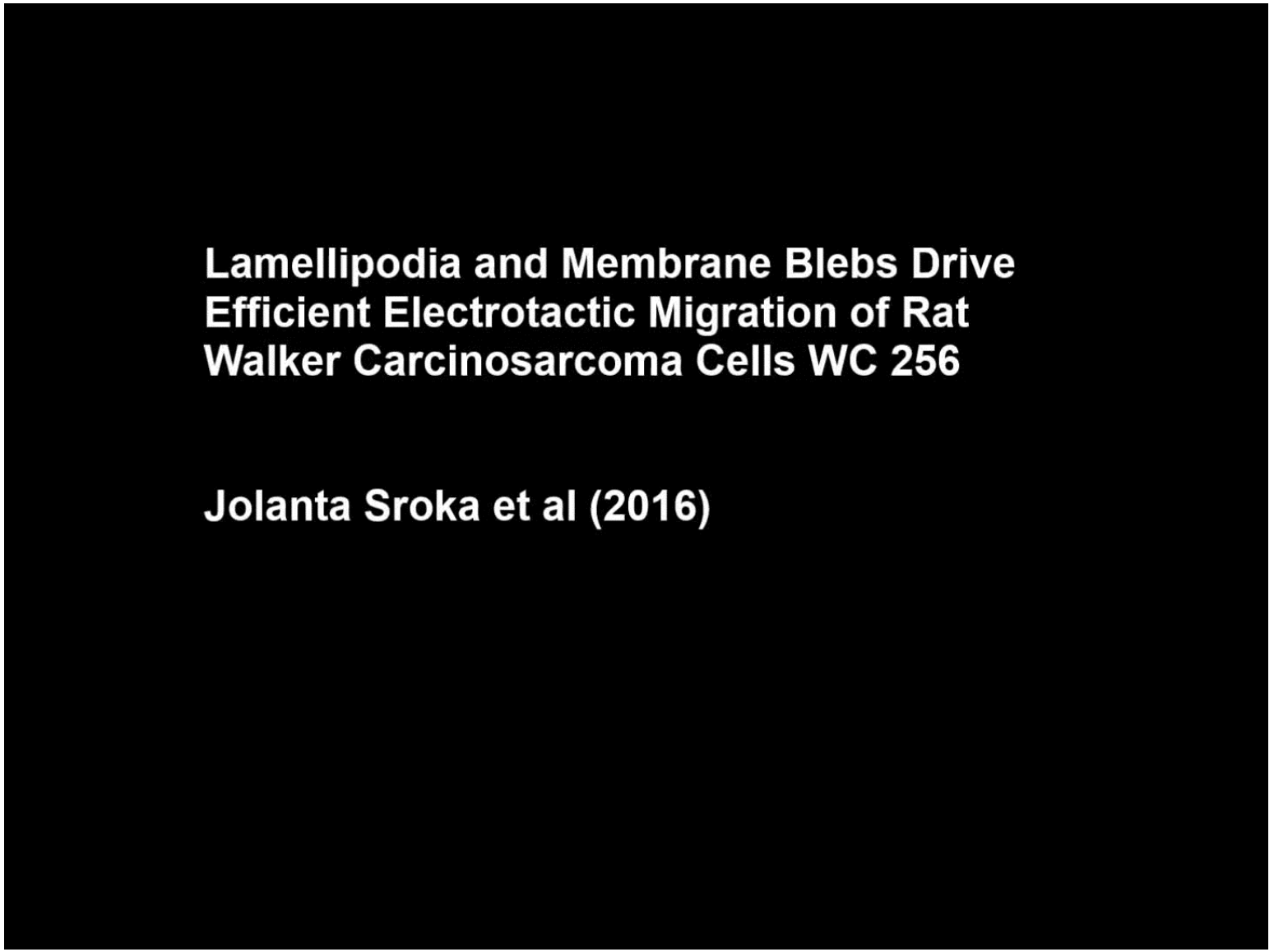


→ Rôle pour définir la polarité de l'épithélium

Charge transporters across membrane drive electric eel voltage



Galvanotactic cell migration



Potentiel trans-membranaire, prolifération et cancer

Aujourd'hui on:

- Étudie les propriétés électrophysiologiques de cellules cancéreuses
- L'effet de drogues altérant le potentiel transmembranaire (bloqueur ou activateur de canaux ioniques) sur le développement du cancer

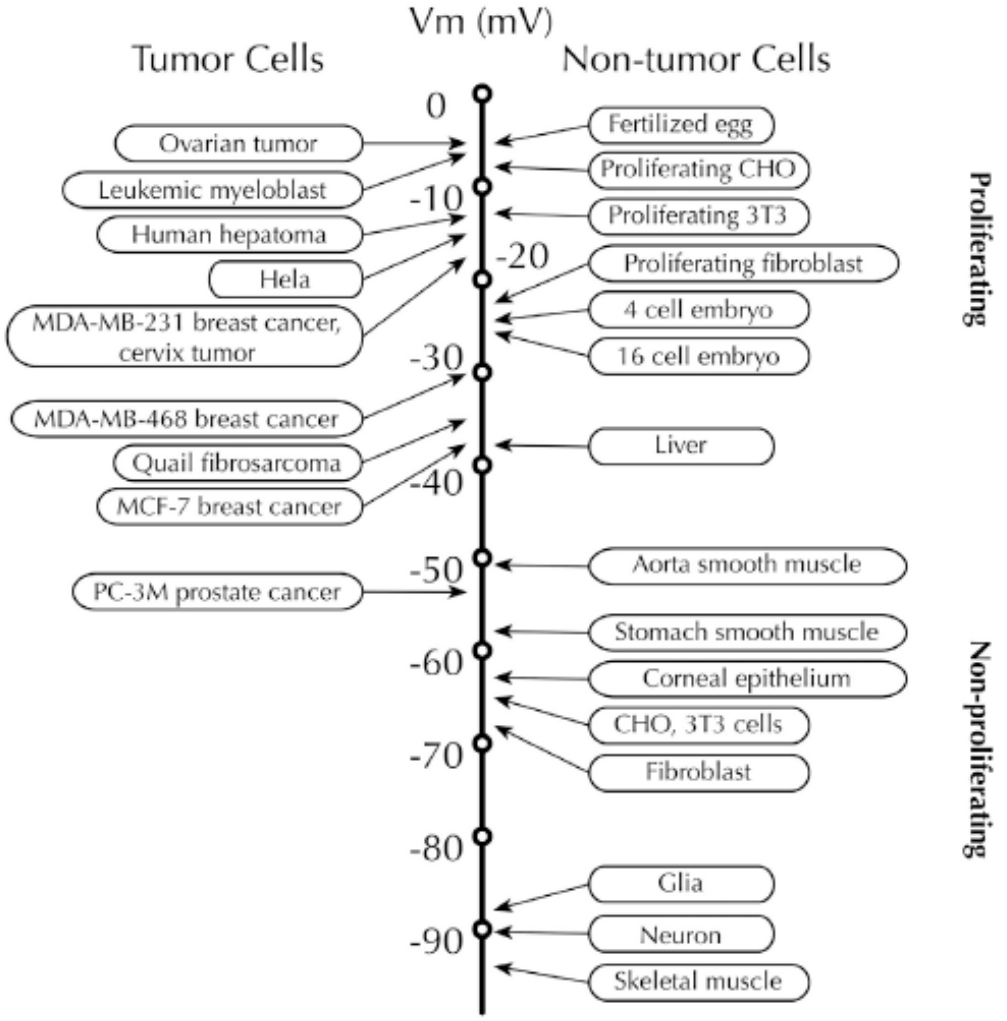


FIGURE 1 | Membrane potential (V_m) scale. Rapidly proliferating cancer cells possess depolarized V_m, while the V_m of quiescent cells is generally more negative. Proliferative somatic cells are also depolarized, suggesting that V_m is functionally instructive in cell development (Levin, 2007b). Scale adapted from Binggeli and Weinstein (1986), with additional data from Fraser et al. (2005); Mycielska et al. (2005); Yang et al. (2012).

Conclusions

- Toutes les cellules présentent **un potentiel transmembranaire** résultant de la perméabilité variable de **canaux ioniques** et de l'activité de **transporteurs**

- Les canaux sont **voltage-gated**, résultant en une conductance non-linéaire

- Ceci donne lieu à la propagation de **potentiels d'action** dans les neurones, mais aussi **d'ondes calcium dans le cœur, l'intestin, dans les épithélium** etc.

- On utilise la différence de potentiel générée par ces signaux dans le milieu extracellulaire pour mesurer **électrocardiogramme, encéphalogramme** etc.

- On peut mesurer Vmem par **électrophysiologie** et par des **teintures voltamétriques**

- Les propriétés électriques des tissus sont fondamentales pour **la régénération**, **la fermeture de blessures**, le **développement embryonnaire**

- Les cellules migrent dans des champs électriques: **galvanotaxie**

- Les cellules embryonnaires /souches et cancéreuses sont plus dépolarisés que les cellules différencies. On commence seulement à étudier **l'électrophysiologie des tumeurs.**