

Université Paris Sud - M1 parcours Physique Médicale  
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# Physique de la Cellule & des Tissus

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# Blood flow

Oxygenation

Hydrodynamics

Pressure

Vascular permeability

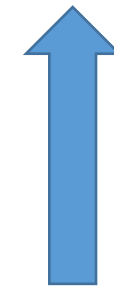
Neo-angiogenesis and oncotic pressure

# Dissolved Oxygen & Carried by Hemoglobin

Consommation O<sub>2</sub> au repos : 6.4 mL/sec. Or volume cardiaque en une seconde:70 mL/battement (~1 sec), donc on a ~90 mL O<sub>2</sub> / L de sang

Arterial oxygen capacity in adult (max): ~200 mL O<sub>2</sub> / L de sang

Dissolved O<sub>2</sub> in water at 37°C: 5,34 mL / L



Carbogen : 95% O<sub>2</sub>, 5% CO<sub>2</sub> 24,2 mL/L

# Oxygen diffusion

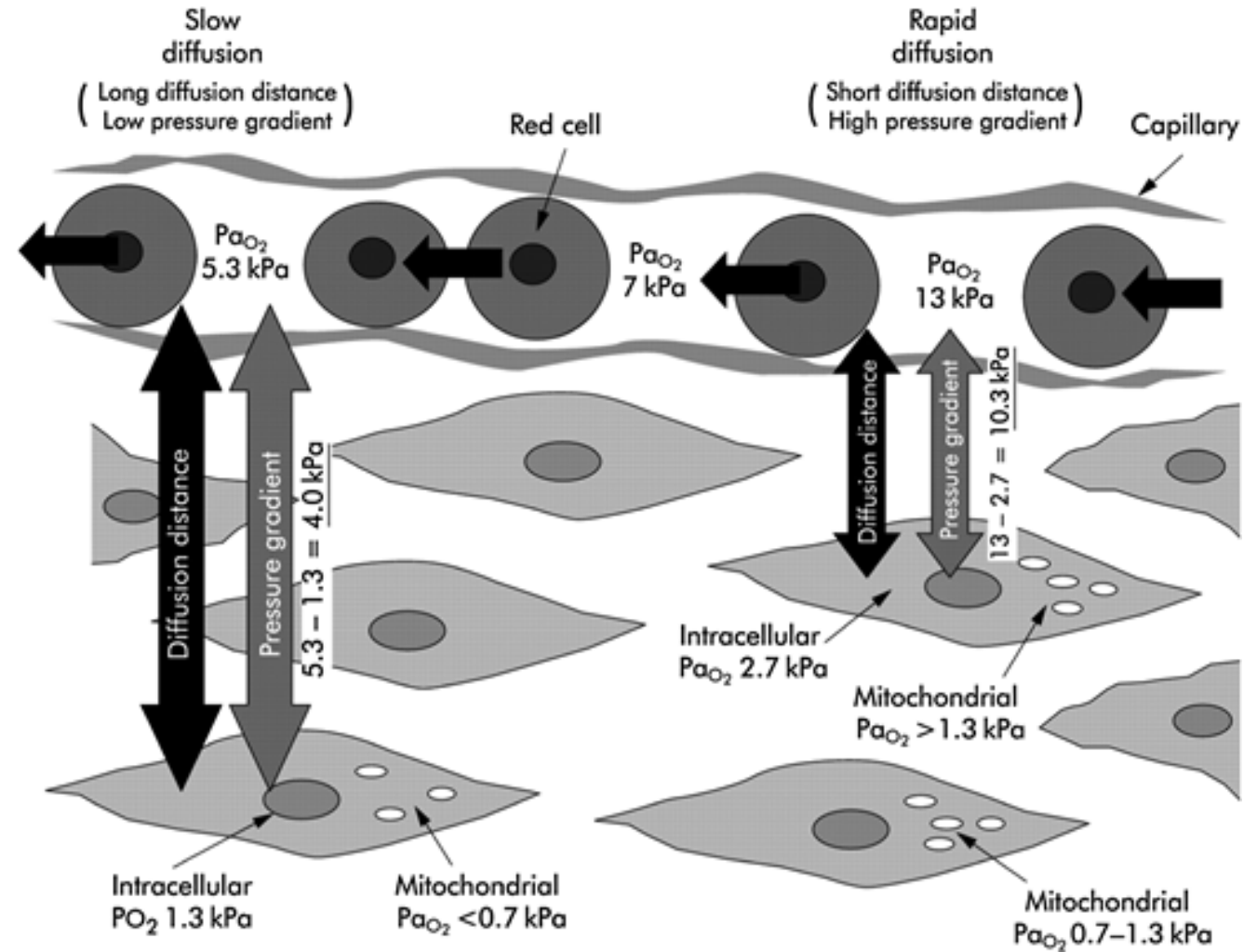
$$J = -D \frac{\partial C}{\partial x}$$

m<sup>2</sup>/sec

$$\text{Flux} = \frac{DA(C_1 - C_2)}{T}$$

Oxygen has to diffuse from capillary to target cell:

- Reduce path length
- In cell culture : reduce medium thickness

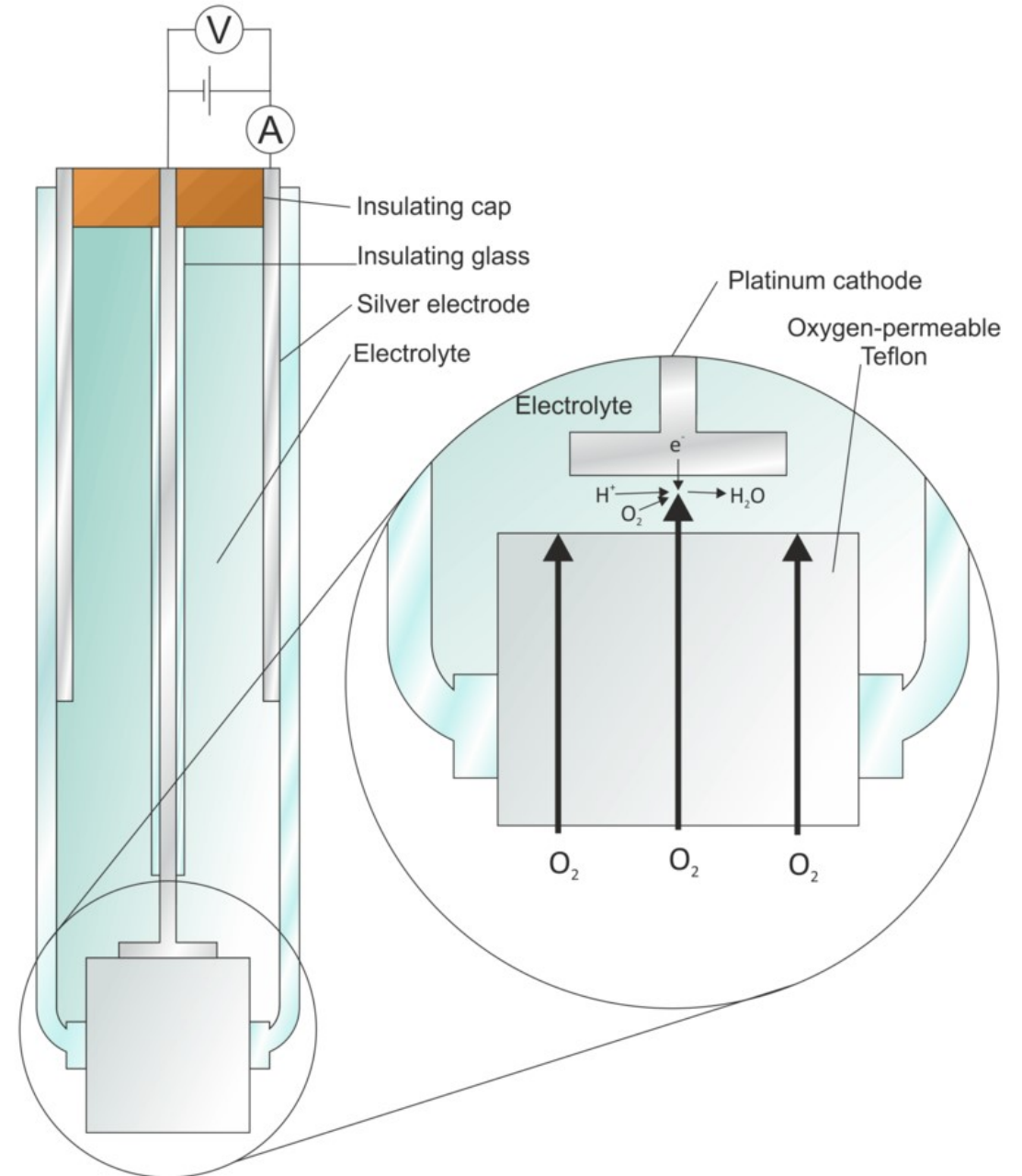


# How to measure dissolved O<sub>2</sub> : Clarke Electrode



Knowing the number of cells in suspension, O<sub>2</sub> kinetics gives the consumption rate per cell

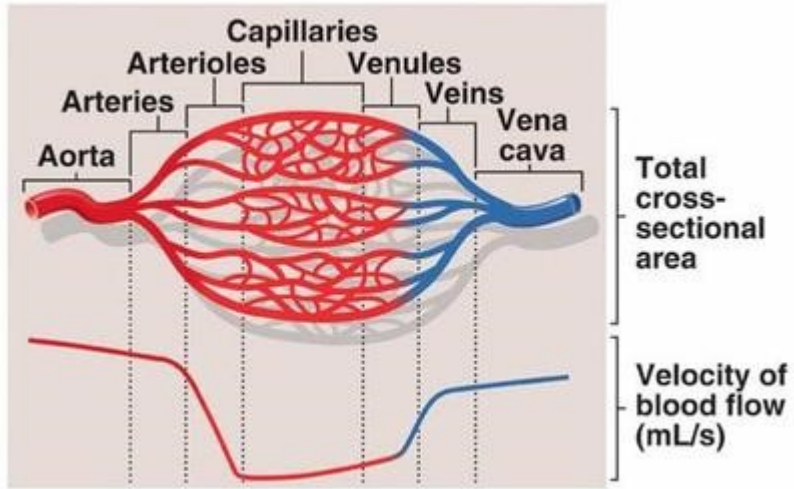
Exercice: estimez l'ordre de grandeur de la consommation d'O<sub>2</sub> par cellule ?



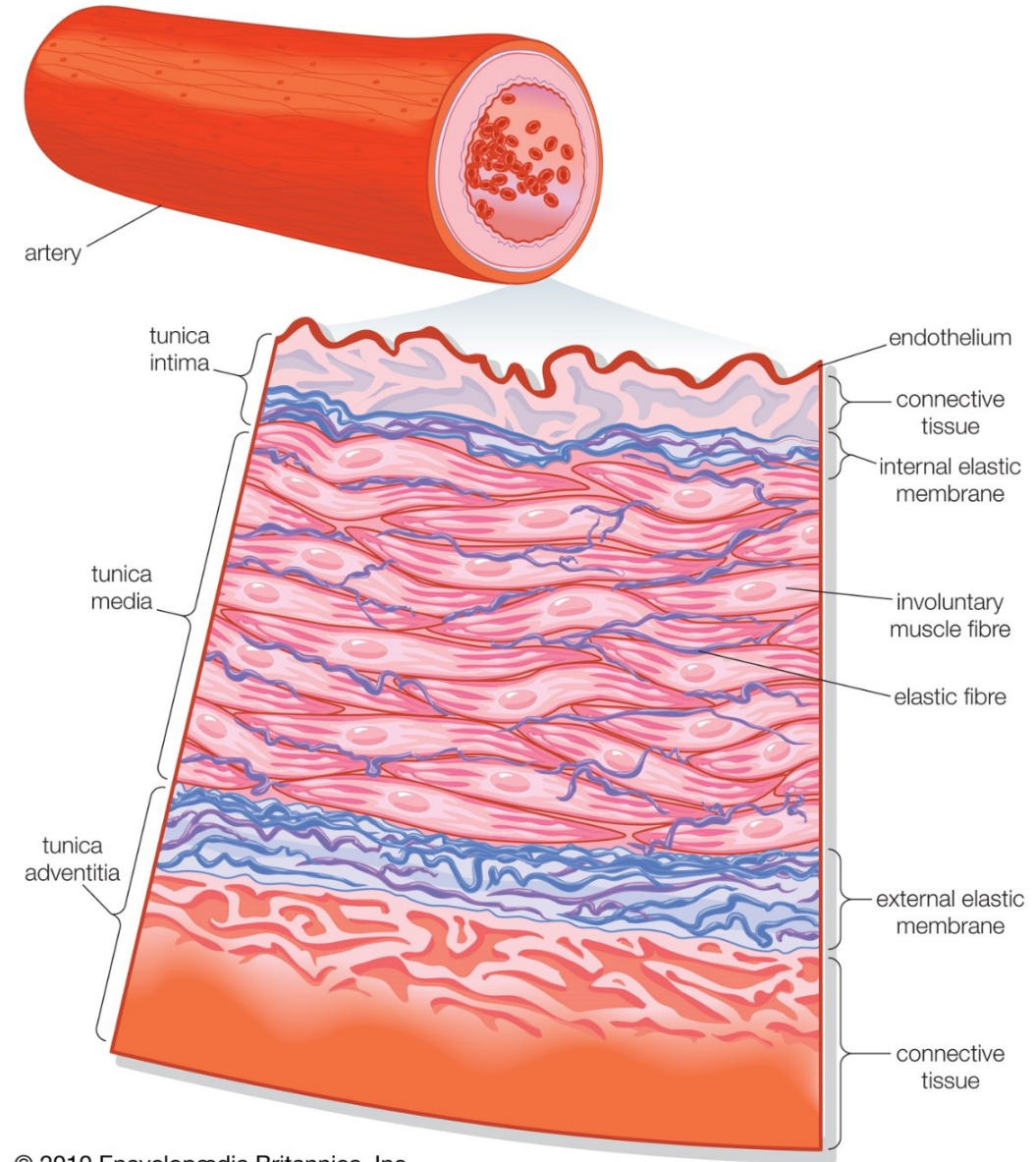
## Cell size and oxygen uptake

Cell	Diameter/volume <sup>a</sup> ( $\mu\text{m}/\text{pL}$ ) <sup>b</sup>	Protein Mass/cell (pg)	O <sub>2</sub> Consumption Rate in $\text{amol s}^{-1} \text{cell}^{-1}$ (OCR in units of $\text{amol s}^{-1} \text{ng-protein}^{-1}$ )		
			Mean	Std err (+/-)	n
<b>HL-60</b> Promyelocytic leukemia	10.7 $\mu\text{m}$ 0.64 pL	170 (13) <sup>c</sup>	<b>9.9</b> <sup>d e</sup> , (58) <sup>f</sup>	0.8	13
<b>HL-60</b> Retinoic acid differentiated	9.8 $\mu\text{m}$ 0.49 pL	180	<b>8.3</b> <sup>d e</sup> , (46) <sup>f</sup>	2.0	11
<b>HL-60</b> Retinoic acid differentiated Stimulated with PMA		180	<b>30.5</b> <sup>d e</sup> , (170) <sup>f</sup>	6.1	9
<b>U-937</b> Histocytic lymphoma	12.1 $\mu\text{m}$ 0.93 pL	110 (12) <sup>c</sup>	<b>3.7</b> <sup>d e</sup> , (34) <sup>f</sup>	0.3	14
<b>MDA-MB-231</b> Mammary adenocarcinoma	14.3 $\mu\text{m}$ 1.53 pL	295 (15) <sup>c</sup>	<b>16.8</b> <sup>d e</sup> , (56) <sup>f</sup>	1.2	13
<b>MCF-7</b> Mammary adenocarcinoma	14.8 $\mu\text{m}$ 1.70 pL	404 (29) <sup>c</sup>	<b>53</b> <sup>g h</sup> , <b>32.5</b> <sup>d e</sup> , (81) <sup>f</sup>	4 5.6	16 11
<b>MCF-7-p51</b> Mammary adenocarcinoma ( <i>GPx4</i> ) Ov erexpressor	15.2 $\mu\text{m}$ 1.84 pL	625 (45) <sup>c</sup>	<b>35</b> <sup>g h</sup> , <b>39.9</b> <sup>d e</sup> , (63) <sup>f</sup>	5 3.9	16 12

# The blood vessels

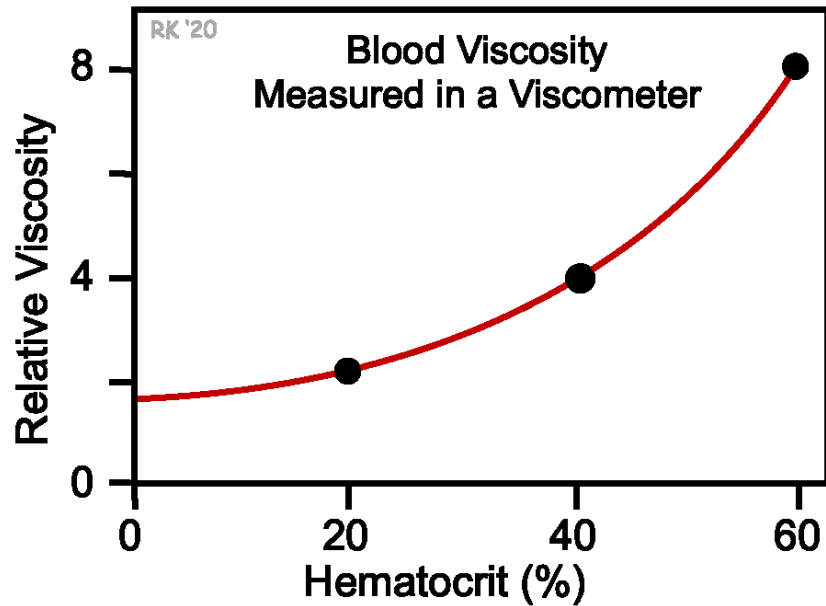


	Aorta	Artery	Arteriole	Precap sphincter	Capillary	Venule	Vein	Vena cava
Diameter	25 mm	4 mm	30 $\mu$	35 $\mu$	8 $\mu$ 20 $\mu$	5 mm	30 mm	
Wall thickness	2 mm	1 mm	20 $\mu$	30 $\mu$	1 $\mu$ 2 $\mu$	0.5 mm	1.5 mm	
Endothelium	█	█	█	█	█	█	█	
Elastic tissue	▨	▨	▨	▨	▨	▨	▨	
Smooth muscle	▨	▨	▨	▨	▨	▨	▨	
Fibrous tissue	▨	▨	▨	▨	▨	▨	▨	



<https://nursekey.com/cardiovascular-anatomy-and-physiology/>

# Reynolds number of blood flow in vessels



Viscosity  
blood:  
~4 mPa.sec

$$Re = \frac{\rho u L}{\mu}$$

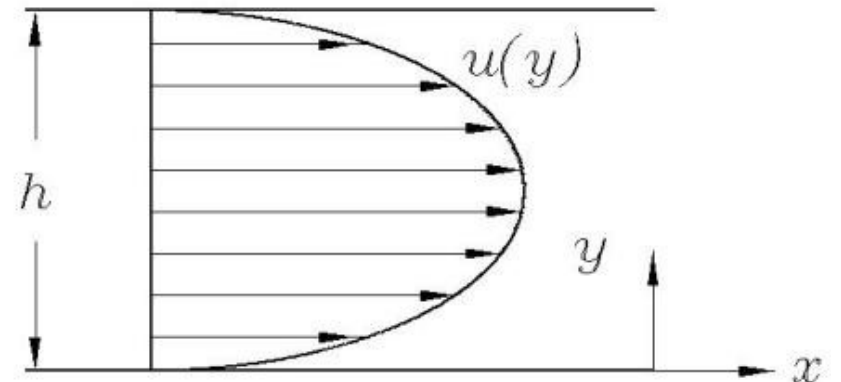
Density (kg/m<sup>3</sup>)      Flow speed  
 Typical dimension of flow setup  
 Viscosity (Pa.sec)

Re < 1 : laminar flow

1 < Re < 1000 : intermediate

Re > 1000 : turbulent

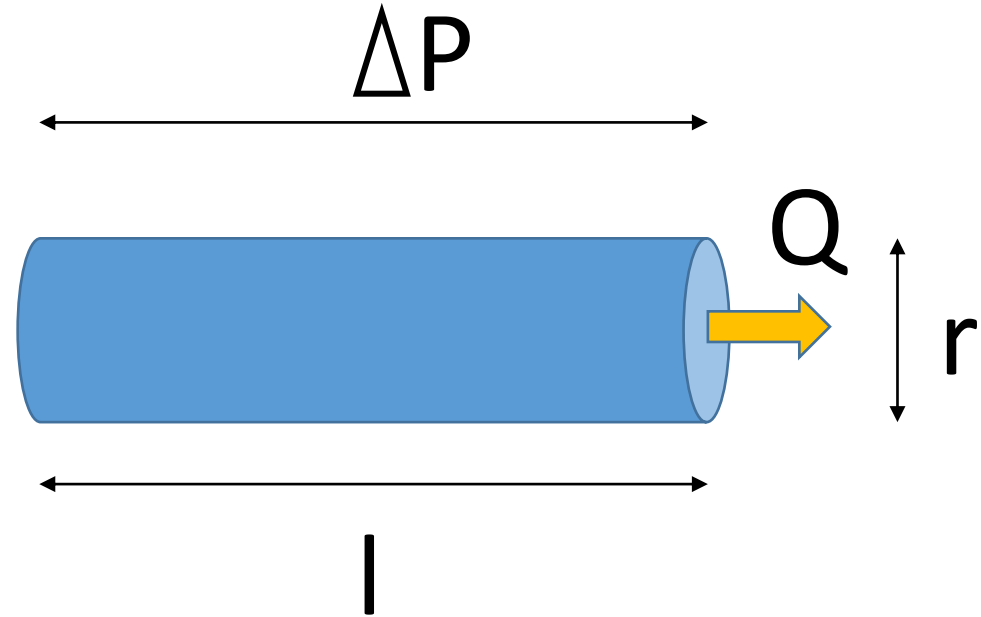
Exercice: Compute Reynolds number in pulmonary artery



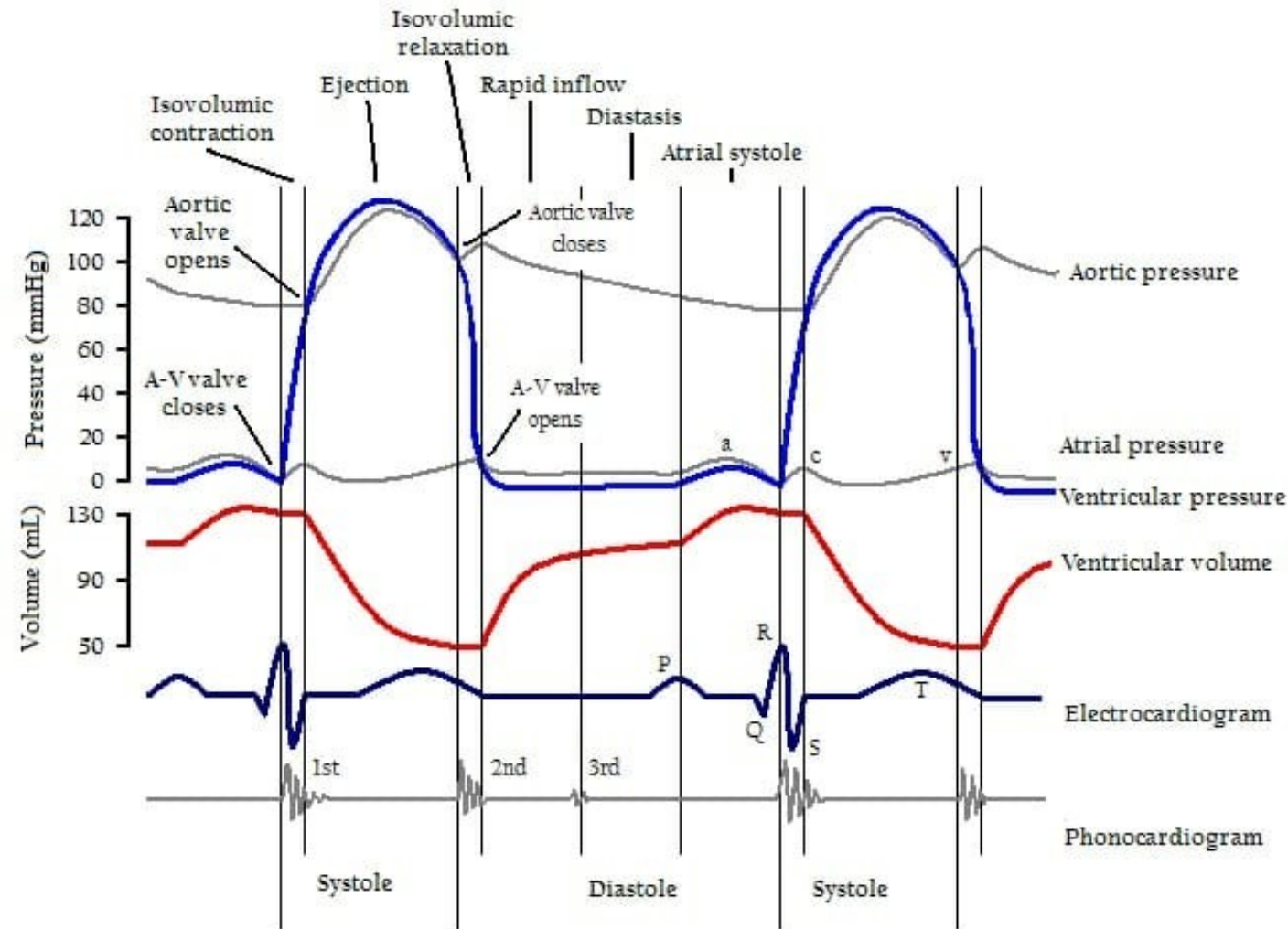
# Poiseuille : low Reynolds number flow in a cylindrical pipe

Q	Flow rate
$\Delta P$	Pressure
r	Radius
$\eta$	Fluid viscosity
l	Length of tubing

$$Q = \frac{\pi \Delta P r^4}{8 \eta l}$$



# Le problème de la vascularisation: trouver un chemin nourrissant toutes les cellules en minimisant le $\Delta P$ nécessaire



le  $\Delta P$  nécessaire = la pression générée par la pompe cardiaque

# Where does the major load loss occurs ?

Typical blood speed in capillaries : 0.3 mm/sec

Total length of capillaries in body: 80 000 km (!)

Exercice : calculer la perte de charge dans les capillaires



Une équation simple relie pression osmotique et concentration dans le cas de solutions diluées, connue sous le nom de loi de Van't Hoff :

$$\pi = CRT$$

$\pi$  : pression osmotique en Pa.

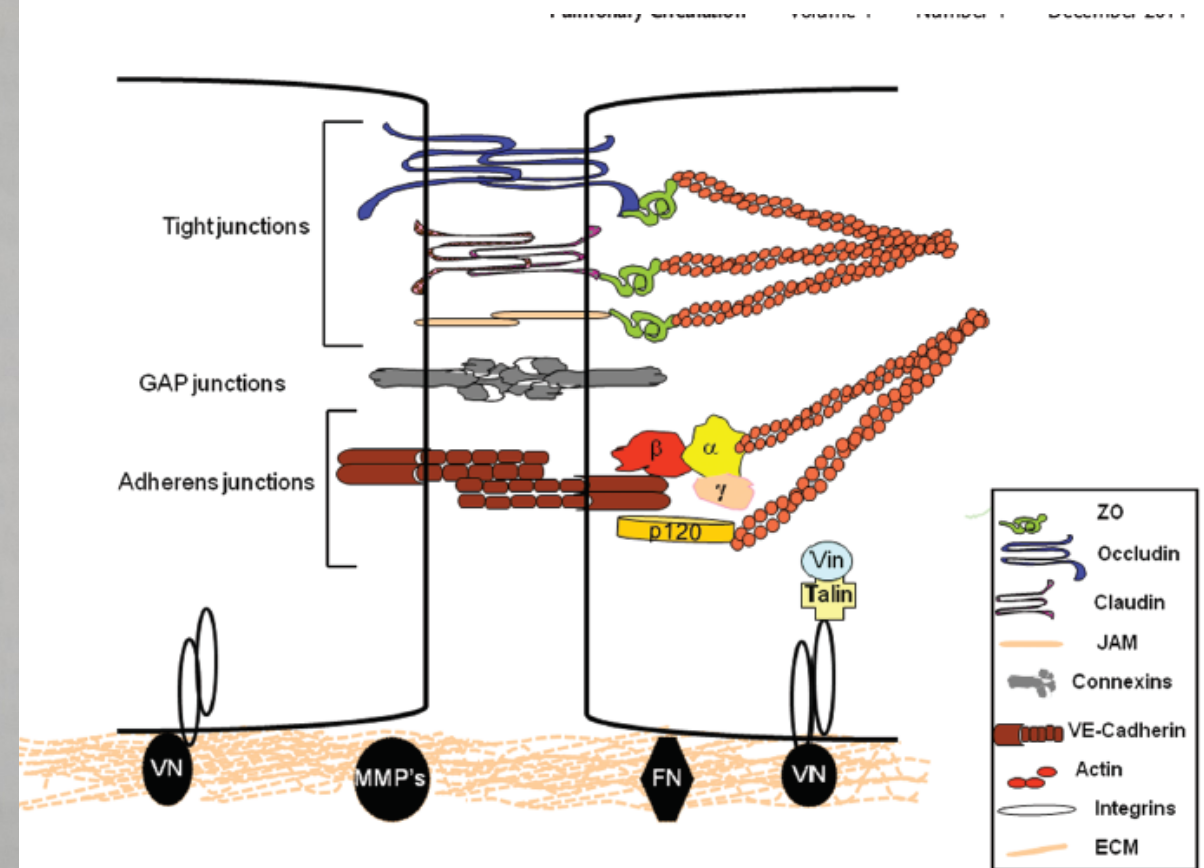
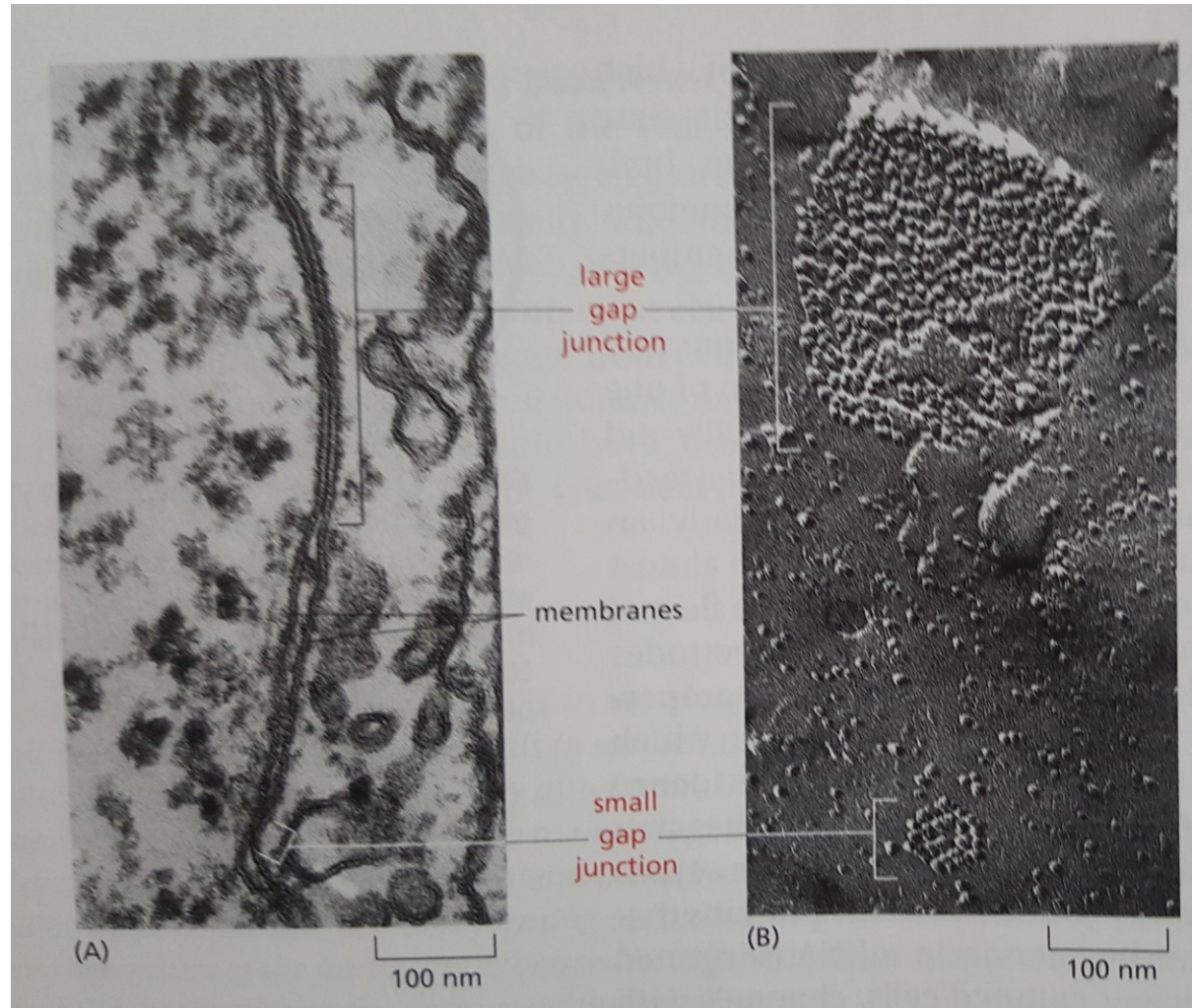
$C$  : concentration en mol · m<sup>-3</sup>

$$C = \frac{\text{concentration en kg} \cdot \text{m}^{-3}}{\text{masse en mol kg} \cdot \text{mol}^{-3}}$$

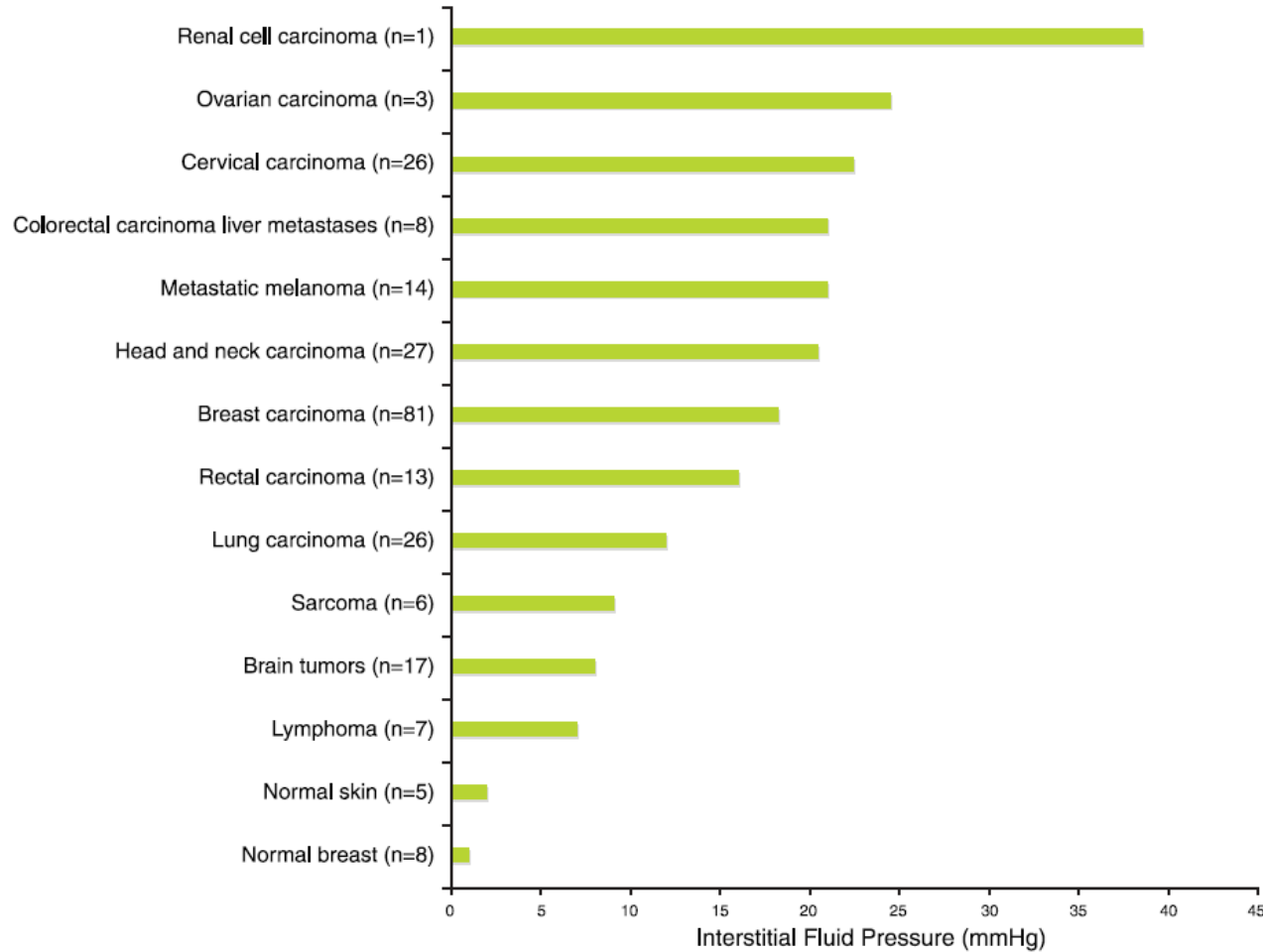
$R$  : constante molaire des gaz parfaits = 8,314 J · mol<sup>-1</sup> · K).

$T$  : température en °K.

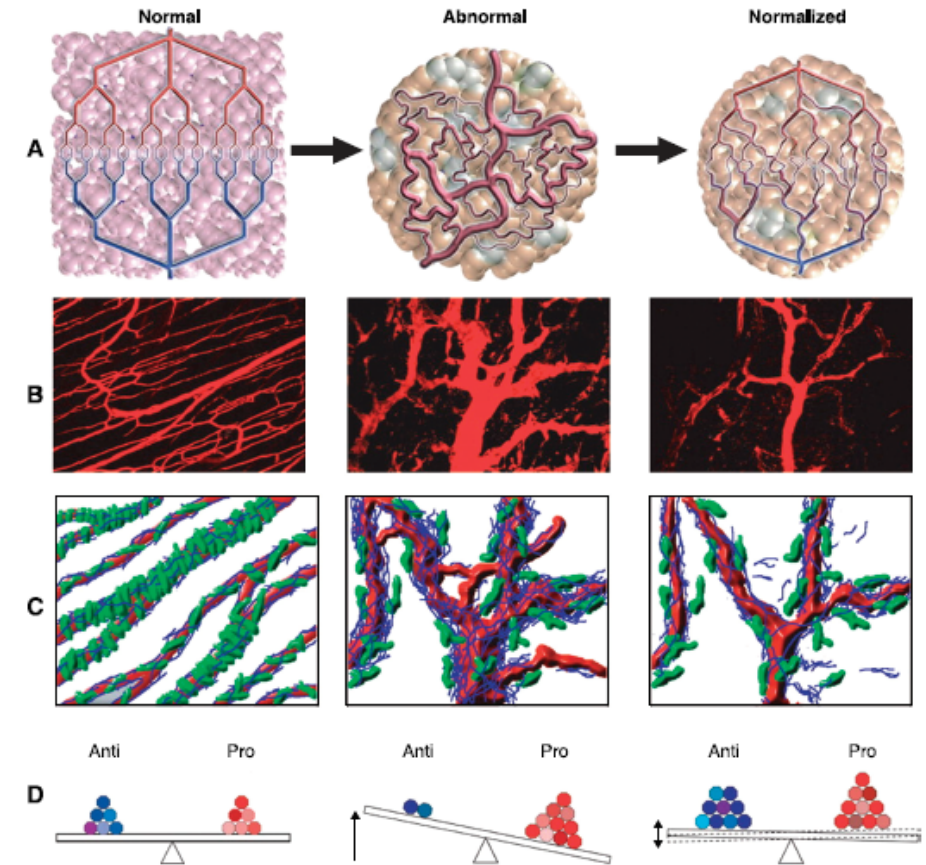
# Les vaisseaux sanguins ont une perméabilité sélective



# Les tumeurs cancéreuses se néovascularisent et sont caractérisées par une surpression interstitielle



**FIGURE 3** Aggregate data from published (and our own ongoing) studies of interstitial fluid pressure (IFP) measured in a variety of human tumors and normal tissues, demonstrating the principle that IFP is grossly elevated in human solid tumors.



**FIGURE 4** Proposed role of vessel normalization in the response of tumors to antiangiogenic therapy. *A*: tumor vasculature is structurally and functionally abnormal. It is proposed that antiangiogenic therapies initially improve both the structure and the function of tumor vessels. However, sustained or aggressive antiangiogenic regimens may eventually prune away these vessels, resulting in a vasculature that is both resistant to further treatment and inadequate for the delivery of drugs or oxygen. *B*: dynamics of vascular normalization induced by VEGFR2 blockade. On the left is a two-photon image showing normal blood vessels in skeletal muscle; subsequent images show human colon carcinoma vasculature in mice at day 0 and day 3 after administration of VEGFR2-specific antibody. *C*: diagram depicting the concomitant changes in pericyte (red) and basement membrane (blue) coverage during vascular normalization. *D*: these phenotypic changes in the vasculature may reflect changes in the balance of pro- and antiangiogenic signaling in the tissue. [From Jain [143], with permission.]

*Fin*

*(pour aujourd'hui)*