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NARODOWA STRATEGIA SPÓJNOŚCI

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BIOPHYSICS

Prezentacja multimedialna współfinansowana przez Unię Europejską w ramach Europejskiego Funduszu Społecznego w projekcie pt.

„Innowacyjna dydaktyka bez ograniczeń - zintegrowany rozwój Politechniki Łódzkiej - zarządzanie Uczelnią, nowoczesna oferta edukacyjna i wzmacniania zdolności do zatrudniania osób niepełnosprawnych"

Transport (4)

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Department of Biophysics
Institute of Materials Science and Engineering
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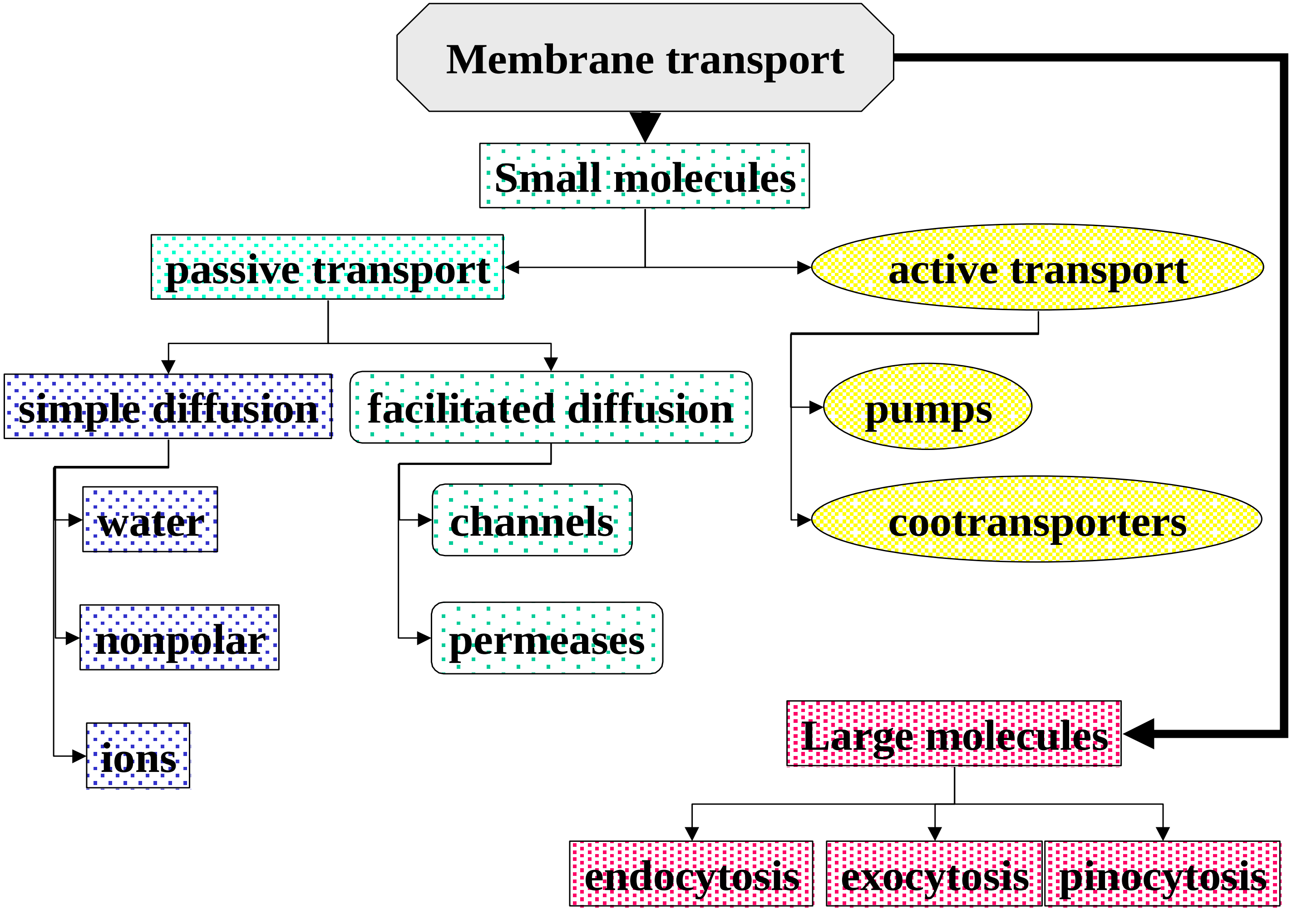
Membrane Transport Systems - general remarks

Transport of nutrients, ions, and excretory substances from one side to the other is a major function of the cell membrane.

A number of different systems have been developed to fulfill this function.

Generally, the permeation of small molecules across the membrane is quite different from molecules too large to penetrate membrane.

Membrane Transport Systems - general remarks



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Transport of Small Molecules - Passive transport

Depending on whether a cell pays for the transport (energetically) we talk about passive (free) and active transport

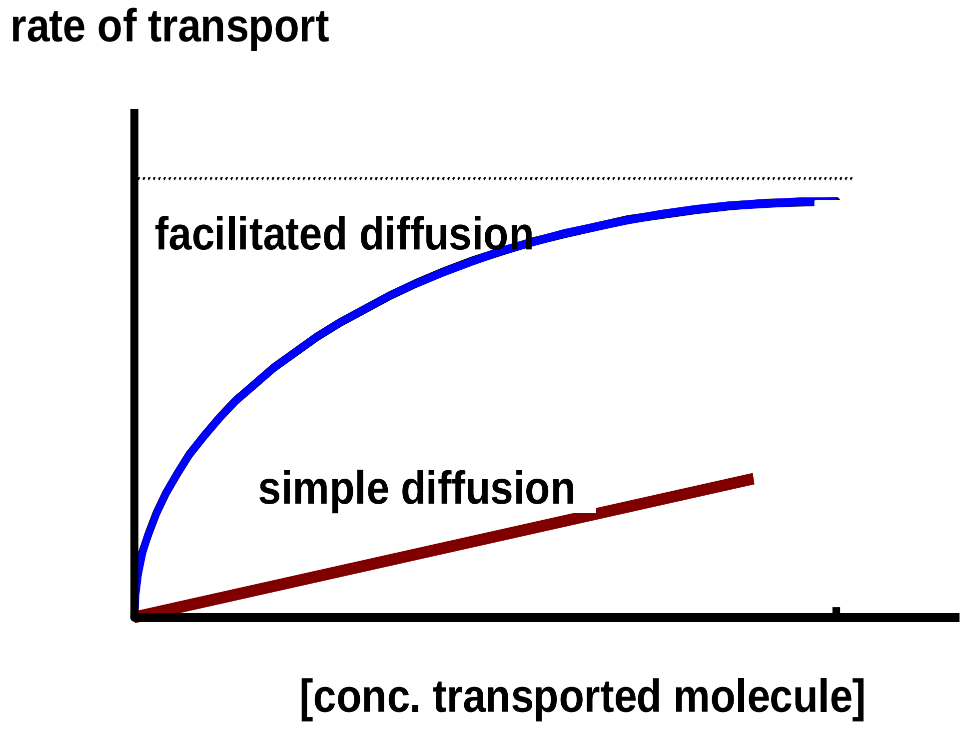
Passive transport:

Simple diffusion - the simplest form of transport is passive diffusion. It does not need any helpers.

Facilitated diffusion - Some molecules diffuse freely but with the help of another molecule.

Passive transport is always driven by a concentration gradient and undergo to Fick's Law:

$$dn/dt = -DS\,(dC/dL)$$



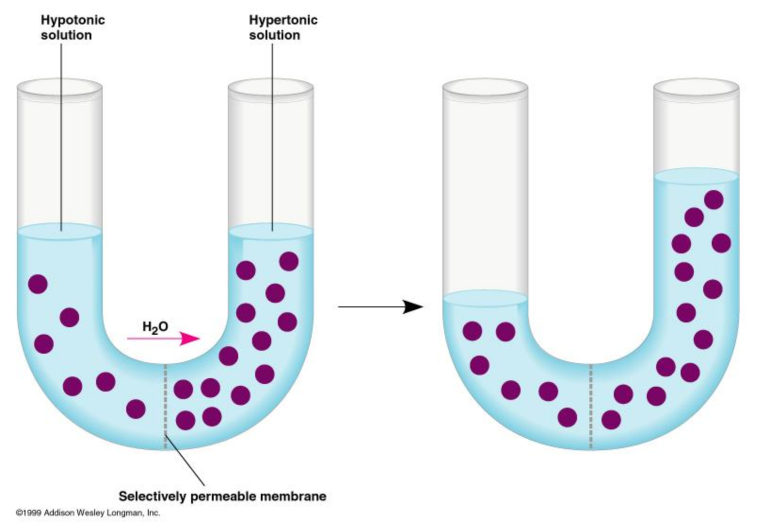
Transport of Small Molecules; Water Diffusion - Osmosis

Lipid membranes are semi-permeable; some substances pass through freely (water) some don't (ions)

Consider two water solutions, one rich in ions and the other not, which are separated by a semi-permeable membrane. Water can move across the membrane in both directions, but because ions attract water and impede its random diffusion, water is retarded on the ion-rich side, therefore the rate from the ion-rich side is less than the rate of ions permeating the membrane from the other side.

The net movement of water toward the ion-rich solution builds up hydrostatic pressure, called osmotic pressure, which at some point will counteract the attraction of ions.

The two sides will then be at equilibrium.

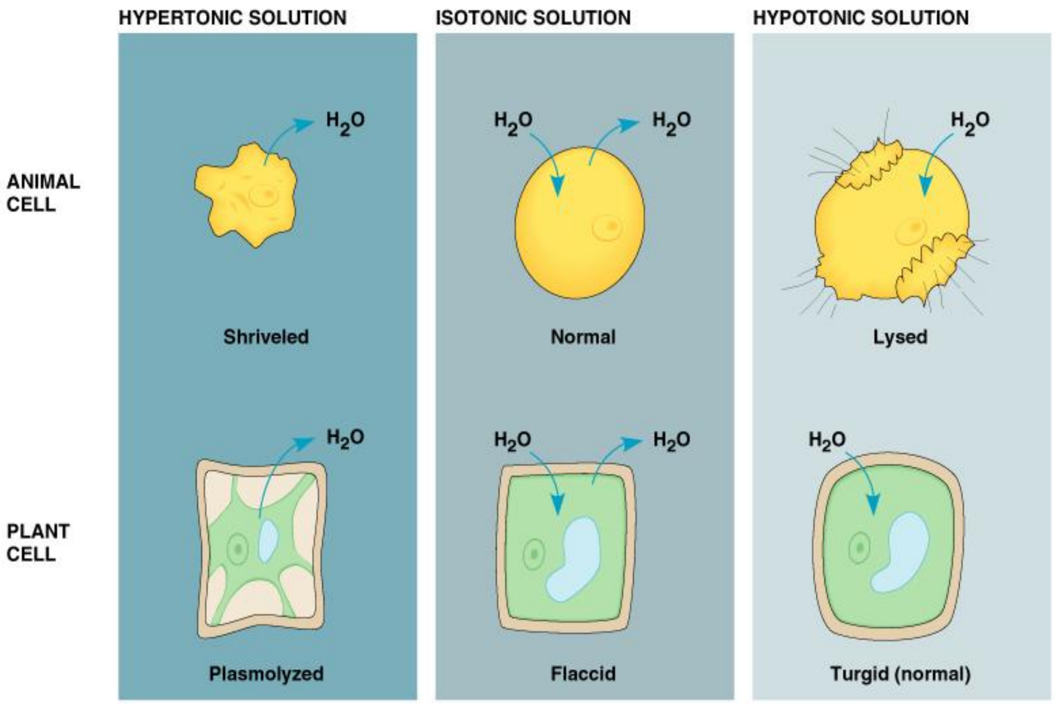


Transport of Small Molecules; Water Diffusion - Osmosis

We say, the more concentrated solution is hypertonic with respect to solution less rich in the impermeant substance. The water will always try to rush in to make the more concentrated solution less hypertonic.

The less concentrated solution is referred to as hypotonic, water will attempt to leave this compartment and thereby decrease concentration of impermeant solute.

When two compartments are equally concentrated they are isotonic with respect to each other, and there is no net diffusion of water.



Transport of Small Molecules; Uncharged Molecules Diffusion

Gases like CO_2, O_2, N_2, diffuse easily through membrane because they have no charge (partial or complete) to interact with water.

Hydrophobic molecules (oils) have also no trouble permeating membrane.

Ions do not penetrate because of charge and the solvation layer that would have to diffuse with them.

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Transport of Small Molecules; Facilitated Diffusion

Some molecules diffuse freely but with the help of another molecules.

In facilitated diffusion, however, the rate is limited by the availability of the helper molecules (carriers - channels or permeases). Once all the helpers are saturated, the increasing concentration of diffusing molecules will only increase a waiting line for the helper and will not increase rate of transport.

Such a saturation kinetics is characteristic of any event (transport, chemical reaction) that requires the help of other molecules.

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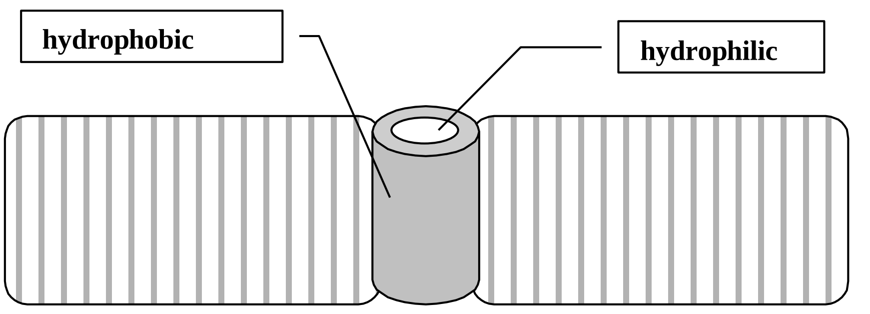
Transport of Small Molecules; Protein Channels

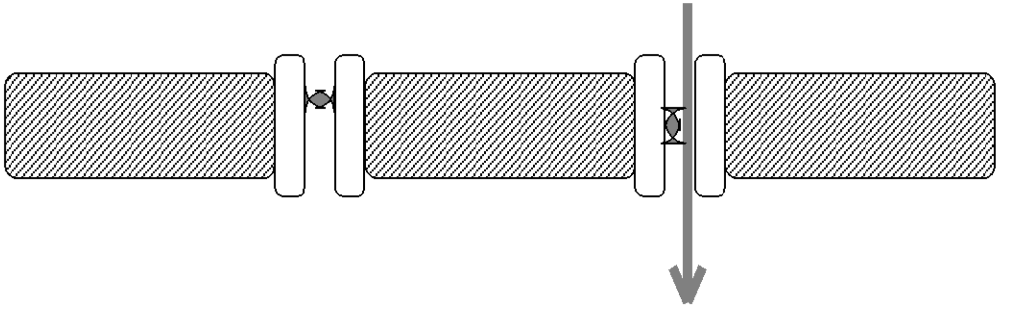
The simplest form of a helper-facilitator is an ion channel.

Channels are usually simple peptides or small proteins of which the outside surface is hydrophobic and the inside hydrophilic, e.g. gramicidin.



Gated channels

Gated channel



Some channels are more complex they have gates that open in response to a chemical (phosphorylation) or electrical (depolarization) stimulus.

Source: INTERNET

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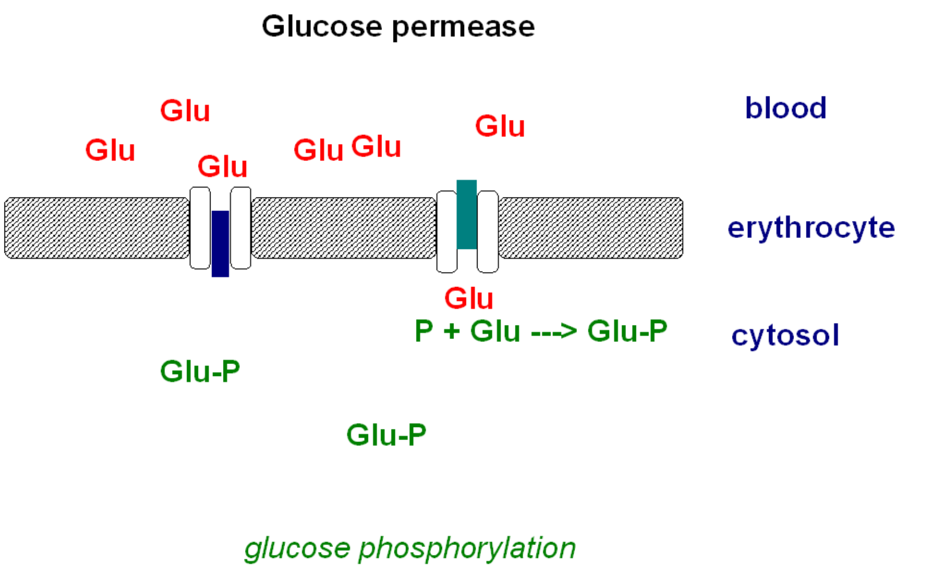
Transport of Small Molecules; Protein Permeases

More complex than channels are carrier proteins such as glucose permease in erythrocytes.

The transported molecule (glucose) moves down its concentration gradient. Once inside the cell, the molecule is transformed into another, impermeant species, thus lowering the inside concentration and maintaining the concentration gradient.

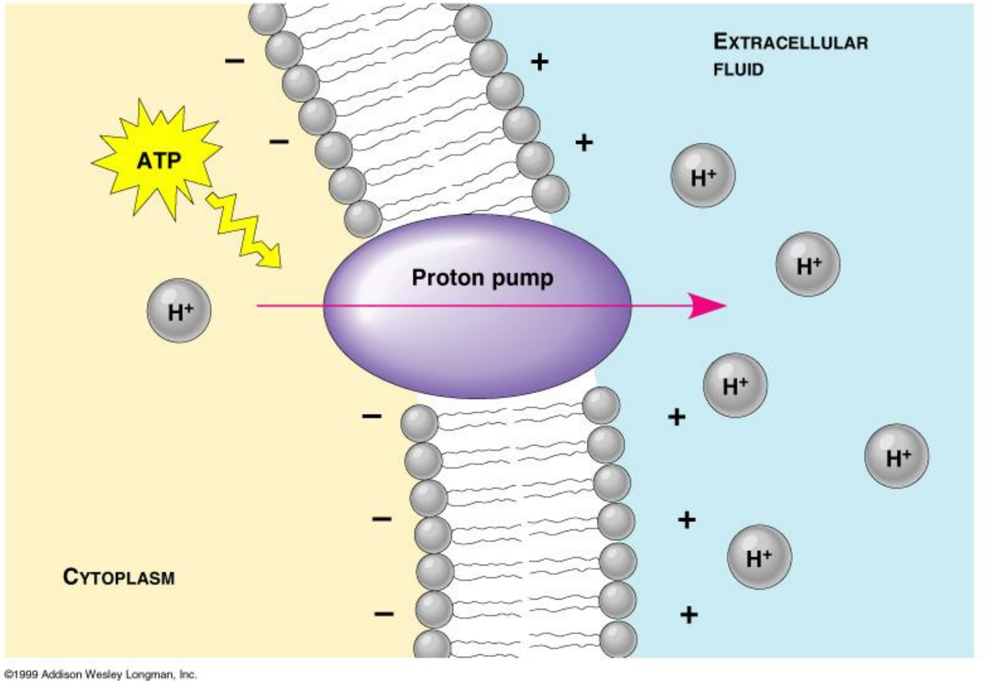


Source: INTERNET

Transport of Small Molecules; Active Transport

Often the transport has to happen in the direction opposite to the concentration gradient. In order to accomplish this, membranes have mechanisms able to pump the substance from the area of smaller concentration to a compartment with higher concentration. All these schemes cost the cell energy and thus are called active transport.

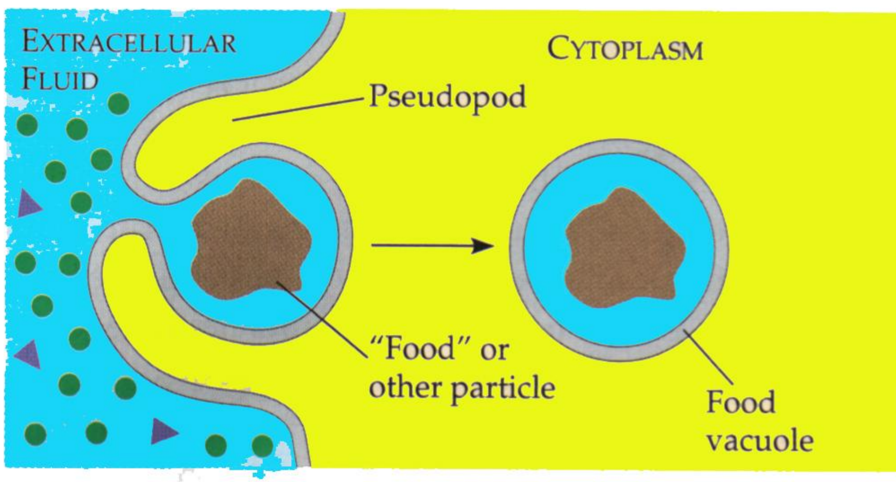
This pump is an ATPase, which means that the enzyme derives its energy from the hydrolysis of ATP.



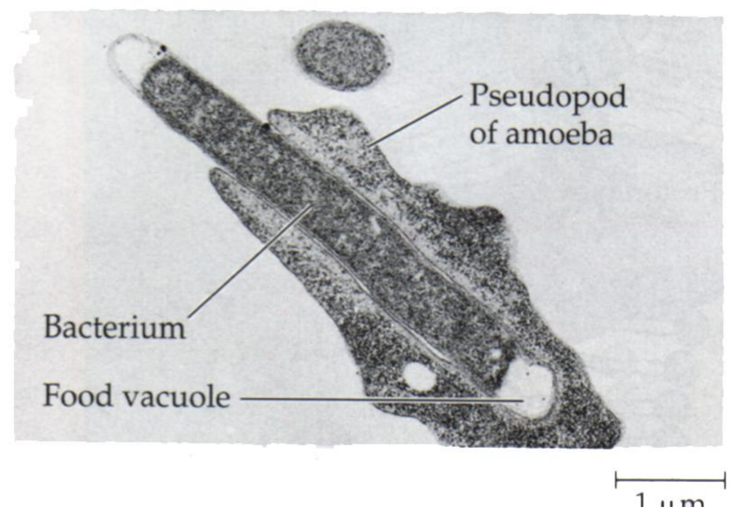
Transport of Large Molecules; Phagocytosis

Removal of foreign materials or dead cells by immune cells is a form of endocytosis.

For example, phagocytes are macrophages that line blood channels of liver (spleen) and eat up aging rbc's; monocytes penetrate inflamed tissue and remove the invading bacteria.



(a) Phagocytosis

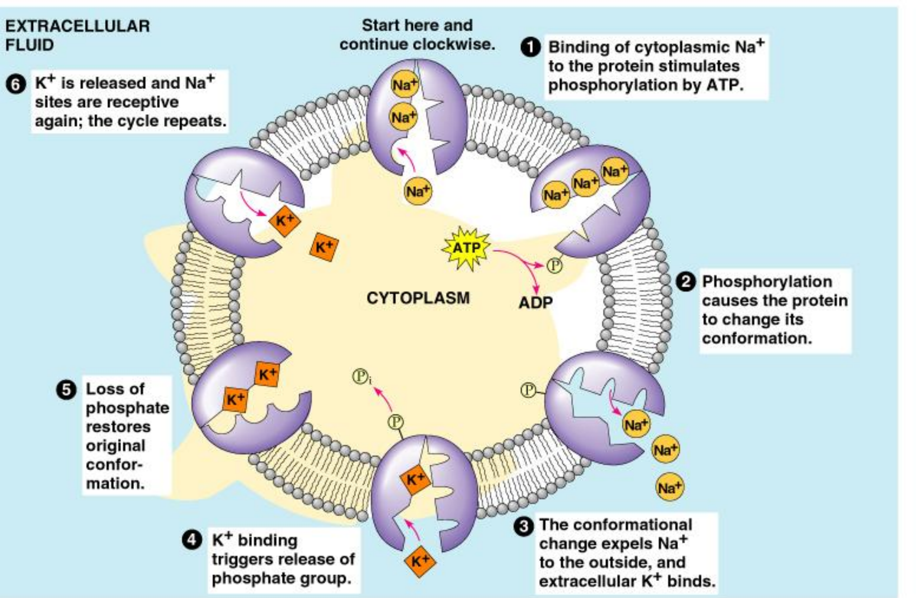


Transport of Small Molecules; Active Transport

The function of Na/K ATPase is to set up the electrochemical gradient of the membrane. It does so by pumping Na^+ out of the cell and pumping K^+ into the cell.

The net effect is to create a chemical potential consisting of two concentration gradients (for Na and for K), as well as electrical potential because three positive charges are pumped out while two positive charges are pumped in. A negative potential inside the cell is thus created.

Mechanism: inside of the cell, Na^+ binding triggers phosphorylation by ATP; conformational change and Na^+ release to outside of the cell; K^+ binding triggers dephosphorylation; inversion to inside of the cell; K^+ release.



Transport of Small Molecules; Coupled Transport

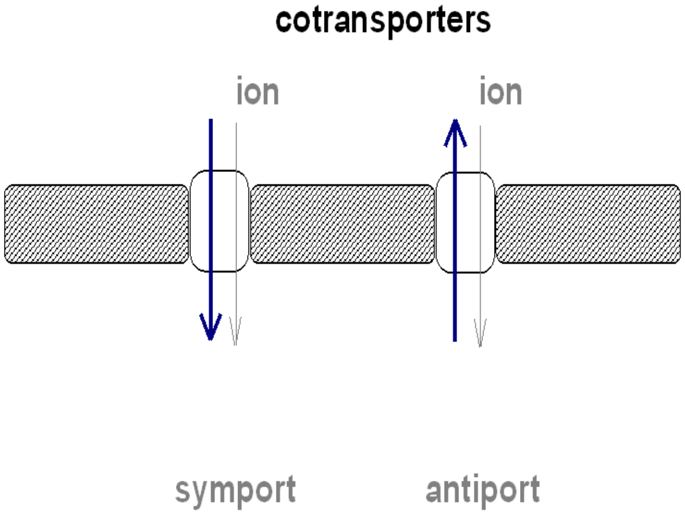
Two molecules travel together, one as a passenger, the other as a driver. The driver diffuses down its electrochemical gradient, but it cannot do so unless it has the passenger.

ATP is not directly involved, but it sets up the electrochemical gradient used to propel the driver.

Symport

The passenger and the driver are transported in the same direction.

Na-glucose symport takes place in the intestine, from the gut lumen to the insides of the cells lining the gut.



Source: INTERNET

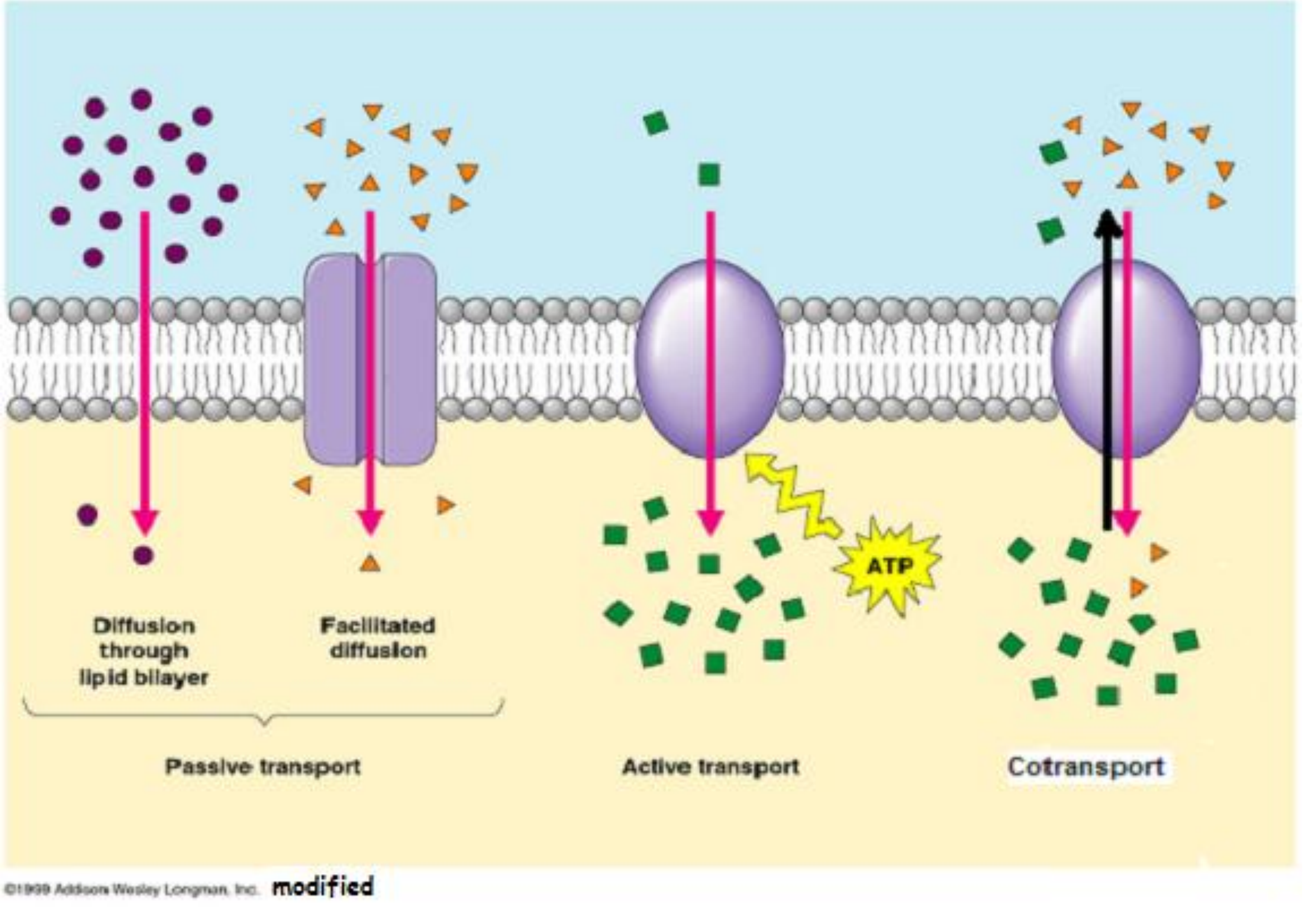
Antiport

The driver and passenger travel in opposite directions.

Ca-Na antiport takes place in cardiac muscle.

Very popular are proton-driven pumps: Na-H antiport, Ca-H antiport, sucrose-H antiport in plant vacuoles.

Transport of Small Molecules; Short Summary



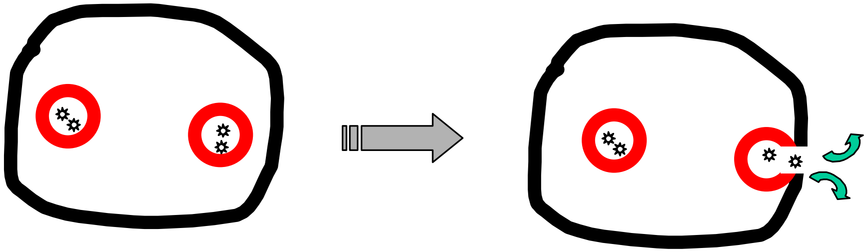
Transport of Large Molecules; Exo- and Endocytosis

Membranes transport molecules too big to permeate the membrane by engulfing the substance and forming internal vesicles.

Uptake of substances by such a mechanism is called endocytosis; the secretion is called exocytosis.

In exocytosis, the transport vesicle fuses with the plasma membrane, making the inside of the vesicle continuous with the outside of the cell.

Exocytosis is used in secretion of protein hormones (insulin), serum proteins, extracellular matrix (collagen).



exocytosis

Source: INTERNET

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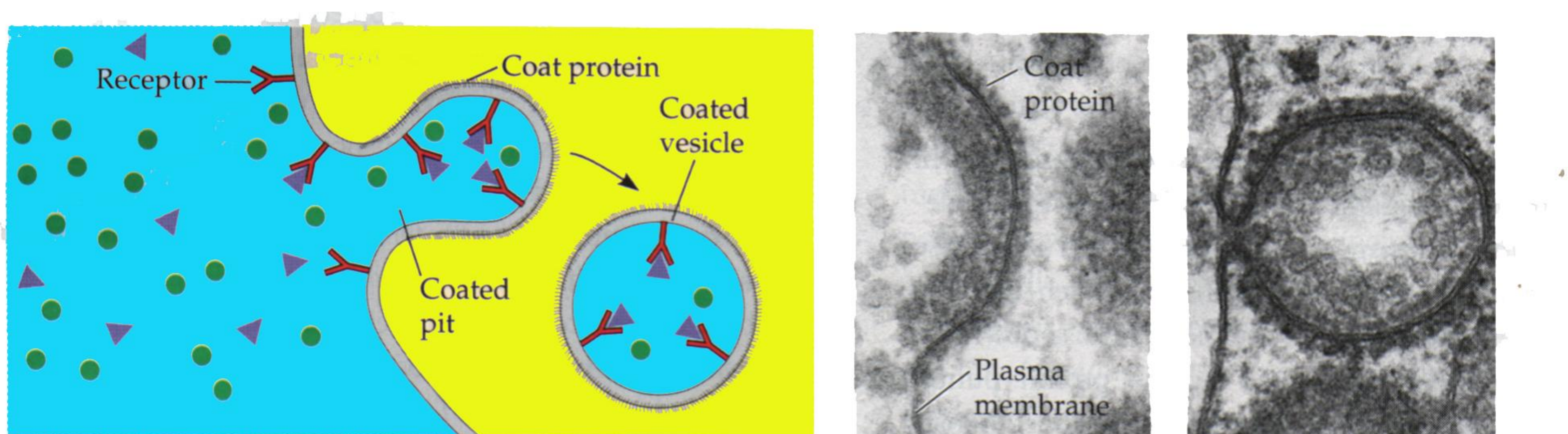
Transport of Large Molecules; Endocytosis

Endocytosis occurs mainly in animal cells, as plants have rigid cell walls.

Mechanism: the cell forms pseudopodia that engulf macromolecules; the pseudopodia fuse, and the membrane pinches off, forming an internal vesicle; the vesicle fuses with the lysosome; release.

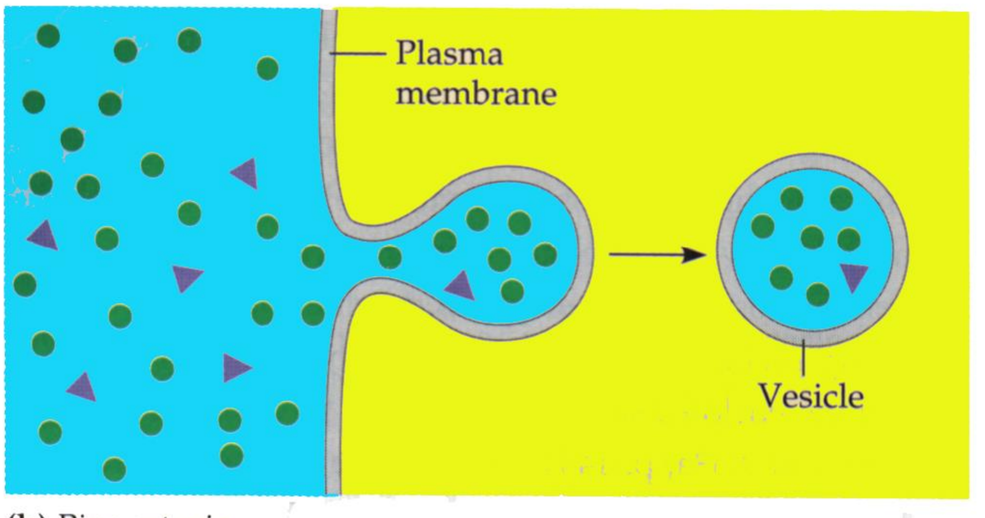
Receptor-mediated endocytosis



(c) Receptor-mediated endocytosis

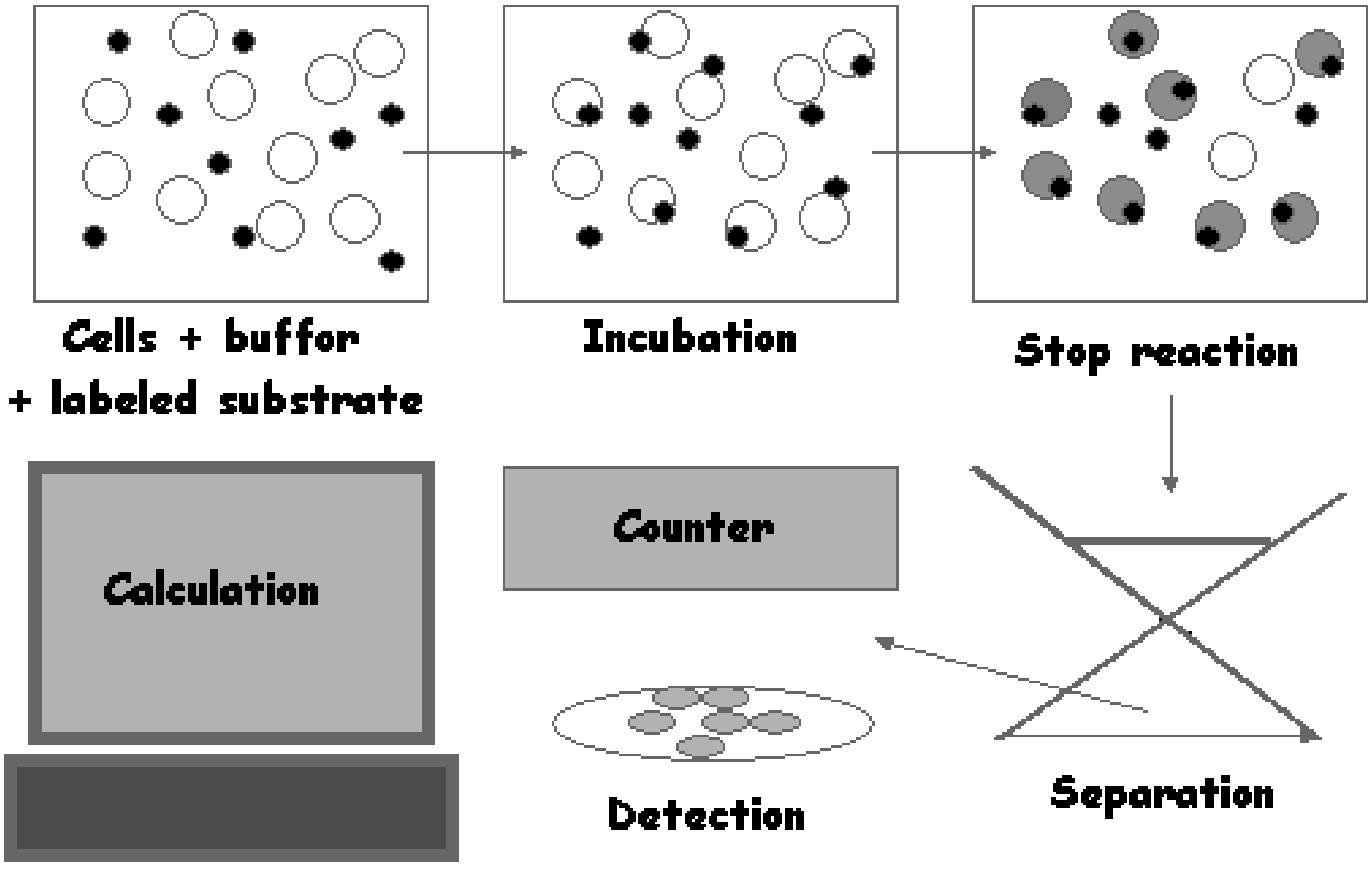
Transport of Large Molecules; Pinocytosis

Pinocytosis is a nonspecific uptake of extracellular solution. Whatever is in the solution is taken up by the cell.



(b) Pinocytosis

Experimental Examination of Transport Systems



Mathematical Modelling of Amino Acid Transport

Gen. Physiol. Biophys. (1988), 7, 475—494 475

Mathematical Modelling of the Transport of Low Molecular Weight Solutes Across Biological Membranes. The Transport of Leu, His and Glu into Human Blood Platelets

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Mathematical Modelling of Amino Acid Transport

$$S_i^1 + B_j \underset{k_{ij}^{-1}}{\overset{k_{ij}^1}{\rightleftharpoons}} T_{ij} \underset{k_{ij}^{-2}}{\overset{k_{ij}^2}{\rightleftharpoons}} S_i^2 + B_j$$

$$k_{ij}^1 = Na_1^+ k_{ij}^*$$

$$k_{ij}^{-2} = Na_2^+ k_{ij}^*$$

$$k_{ij}^1 \gg k_{ij}^{-2} \qquad j = 1, \dots, r-1$$

$$k_{ij}^1 \gg k_{ij}^{-2} \qquad j = r, \dots, p-1$$

$$k_{ij}^{-1} = k_{ij}^2 = k_j \qquad j = 1, \dots, p-1$$

$$S_i^1 + B_j \underset{k_j}{\overset{k_{ij}^1}{\rightleftharpoons}} T_{ij} \underset{k_{ij}^{-2}}{\overset{k_j}{\rightleftharpoons}} S_i^2 + B_j$$

$$\xleftrightarrow{\;k_{il}\;}$$

$$i = 1, \dots, m;\ j = 1, \dots, p-1;\ l = p, \dots, n$$

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Mathematical Modelling of Amino Acid Transport

$$\frac{\mathrm{d}\,B_j(t)}{\mathrm{d}\,t} = -B_j(t)\sum_{i=1}^{m}(k_{ij}^{1}S_i^{1} + k_{ij}^{-2}S_i^{2}(t)) + 2k_j\sum_{i=1}^{m}T_{ij}(t)$$

$$\frac{\mathrm{d}\,S_i^{2}(t)}{\mathrm{d}\,t} = \sum_{j=1}^{p-1}(k_j T_{ij}(t) - B_j(t)k_{ij}^{-2}S_i^{2}(t)) + \sum_{l=p}^{n}k_{il}(S_i^{1} - S_i^{2}(t))$$

$$\frac{\mathrm{d}\,T_{ij}(t)}{\mathrm{d}\,t} = B_j(t)(k_{ij}^{1}S_i^{1} + k_{ij}^{-2}S_i^{2}(t)) - 2k_j T_{ij}(t)$$

It can be easily seen that the system (6—8) includes first integrals

$$B_j(t) + \sum_{i=1}^{m}T_{ij}(t) = B_j^{0}$$

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Mathematical Modelling of Amino Acid Transport

$$\frac{\mathrm{d}\,B_j(t)}{\mathrm{d}\,t} = -B_j(t)\sum_{i=1}^{m} k_{ij}^{1} S_i^{1} + 2k_j\left(B_j^{0} - B_j(t)\right)$$

The solution to this equation is

$$B_j(t) = B_j^{0}\,\frac{\sum_{i=1}^{m} k_{ij}^{1} S_i^{1}\exp\left(-\left(\sum_{i=1}^{m} k_{ij}^{1} S_i^{1} + 2k_j\right)t\right) + 2k_j}{\sum_{i=1}^{m} k_{ij}^{1} S_i^{1} + 2k_j}$$

Substituting Eq. (11) into Eq. (8) we obtain

$$T_{ij}(t) = \frac{k_{ij}^{1} S_i^{1} B_j^{0}}{\sum_{i=1}^{m} k_{ij}^{1} S_i^{1} + 2k_j}\left(1 - \exp\left(-\left(\sum_{i=1}^{m} k_{ij}^{1} S_i^{1} + 2k_j\right)t\right)\right)$$

Mathematical Modelling of Amino Acid Transport

$$S_i^2(t) = S_i^{02}\exp\left(-\sum_{l=p}^{n} k_{il}t\right) + S_i^1\left(1 - \exp\left(-\sum_{l=p}^{n} k_{il}t\right)\right) +$$

$$+\sum_{j=1}^{p-1}\left[\frac{k_{ij}^1 k_j S_i^1 B_j^0\left(\exp\left(-\left(\sum_{i=1}^{m} k_{ij}^1 S_i^1 + 2k_j\right)t\right) - \exp\left(-\sum_{l=p}^{n} k_{il}t\right)\right)}{\left(\sum_{i=1}^{m} k_{ij}^1 S_i^1 + 2k_j\right)\left(\sum_{i=1}^{m} k_{ij}^1 S_i^1 + 2k_j - \sum_{l=p}^{n} k_{il}\right)} + \frac{k_{ij}^1 k_j S_i^1 B_j^0\left(1 - \exp\left(-\sum_{l=p}^{n} k_{il}t\right)\right)}{\sum_{l=p}^{n} k_{il}\left(\sum_{i=1}^{m} k_{ij}^1 S_i^1 + 2k_j\right)}\right]$$

$$S_i^{2u}(t) = S_i^{02}\exp\left(-\sum_{l=p}^{n} k_{il}t\right) +$$

$$+\left(\sum_{l=p}^{n} k_{il}S_i^1 + \sum_{j=1}^{p-1}\frac{k_{ij}^1 k_j S_i^1 B_j^0}{2k_j + \sum_{i=1}^{m} k_{ij}^1 S_i^1}\right)\left(\frac{1 - \exp\left(-\sum_{l=p}^{n} k_{il}t\right)}{\sum_{l=p}^{n} k_{il}}\right)$$

Mathematical Modelling of Amino Acid Transport

$$\frac{\mathrm{d}\,S_i^{2u}(t)}{\mathrm{d}\,t} = \sum_{l=p}^{n} k_{il}(S_i^l - S_i^{02})\exp\left(-\sum_{l=p}^{n} k_{il}\,t\right) + \sum_{j=1}^{p-1} \frac{k_{ij}^l k_j S_i^l B_j^0 \exp\left(-\sum_{l=p}^{n} k_{il}\,t\right)}{2k_j + \sum_{i=1}^{m} k_{ij}^l S_i^l}$$

$$V_i = \frac{\mathrm{d}\,S_i^{2u}}{\mathrm{d}\,t} = K_{Di}(S_j^l - S_i^{02}) + \sum_{j=1}^{p-1} \frac{V_{\max ij} S_i^l}{\sum_{i=1}^{m} S_i^l + K_{Mij}}$$

where V_i is the rate of concentration change of the i-th solute inside the cell;

$$V_{\max ij} = k_j B_j^0 \exp\left(-\sum_{l=p}^{n} k_{il}\,t\right)$$

is the maximal transport rate mediated by the j-th system;

$$K_{Mij} = \frac{2k_j}{k_{ij}^l}$$

is the Michaelis constant for the j-th system, and

$$K_{Di} = \sum_{l=p}^{n} k_{il}\exp\left(-\sum_{l=p}^{n} k_{il}\,t\right)$$

Mathematical Modelling of Amino Acid Transport

$$\lim_{t \to \infty} \frac{\mathrm{d} S_i^2(t)}{\mathrm{d} t} = \lim_{t \to \infty} \frac{\mathrm{d} S_i^{2u}(t)}{\mathrm{d} t} = 0$$

$$\lim_{t \to \infty} S_i^{2u}(t) = \lim_{t \to \infty} S_i^2(t) = S_i^1 + \sum_{j=1}^{p-1} \frac{k_{ij}^1 k_j S_i^1 B_j^0}{\left(\sum_{i=1}^{m} k_{ij}^1 S_i^1 + 2k_j\right) \sum_{l=p}^{n} k_{il}}$$

$$\sum_{l=p}^{n} k_{il} (S_i^{02} - S_i^1) = \sum_{j=1}^{p-1} \frac{k_{ij}^1 k_j S_i^1 B_j^0}{2k_j + \sum_{i=1}^{m} k_{ij}^1 S_i^1}$$

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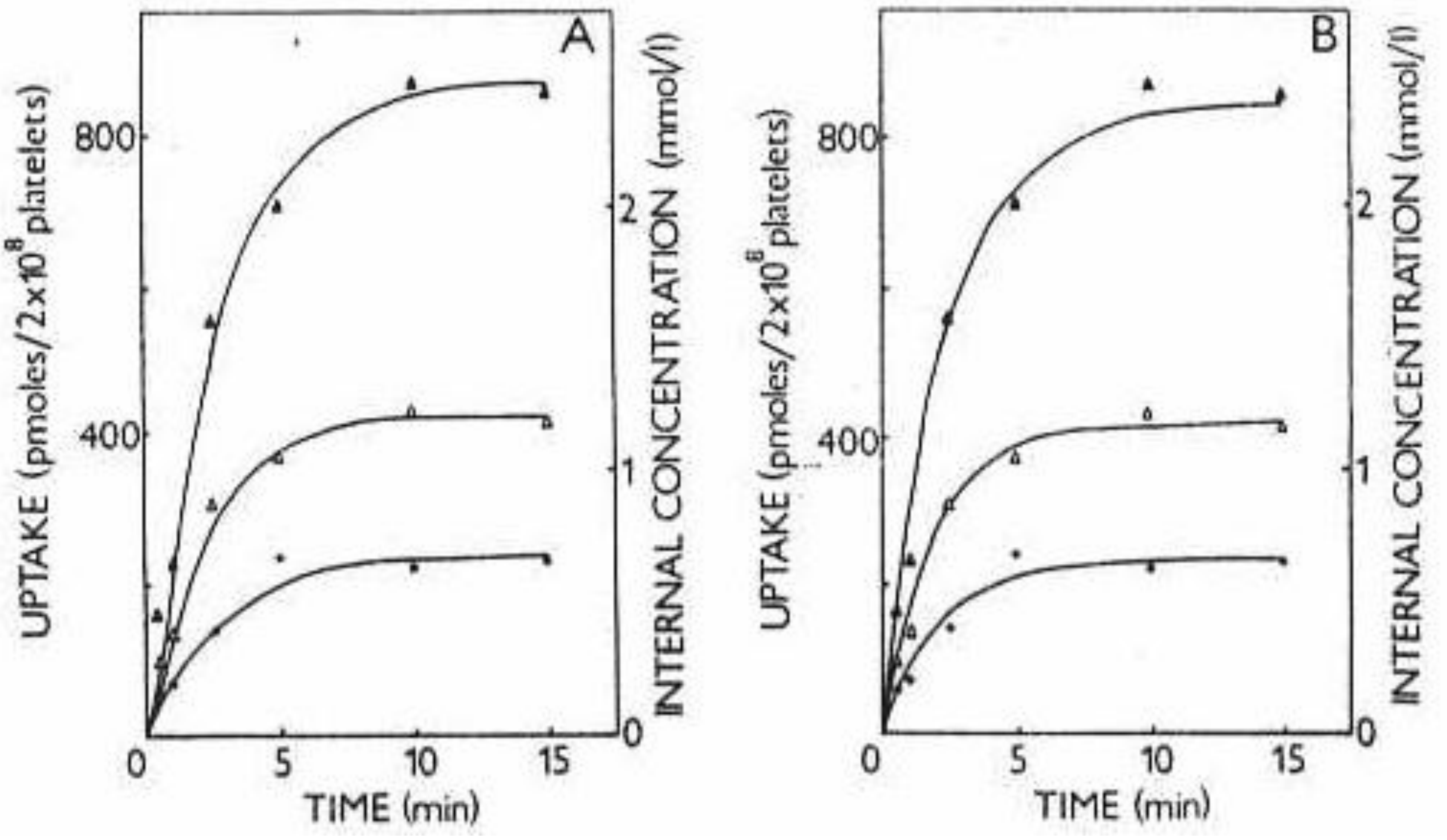
Mathematical Modelling of Amino Acid Transport



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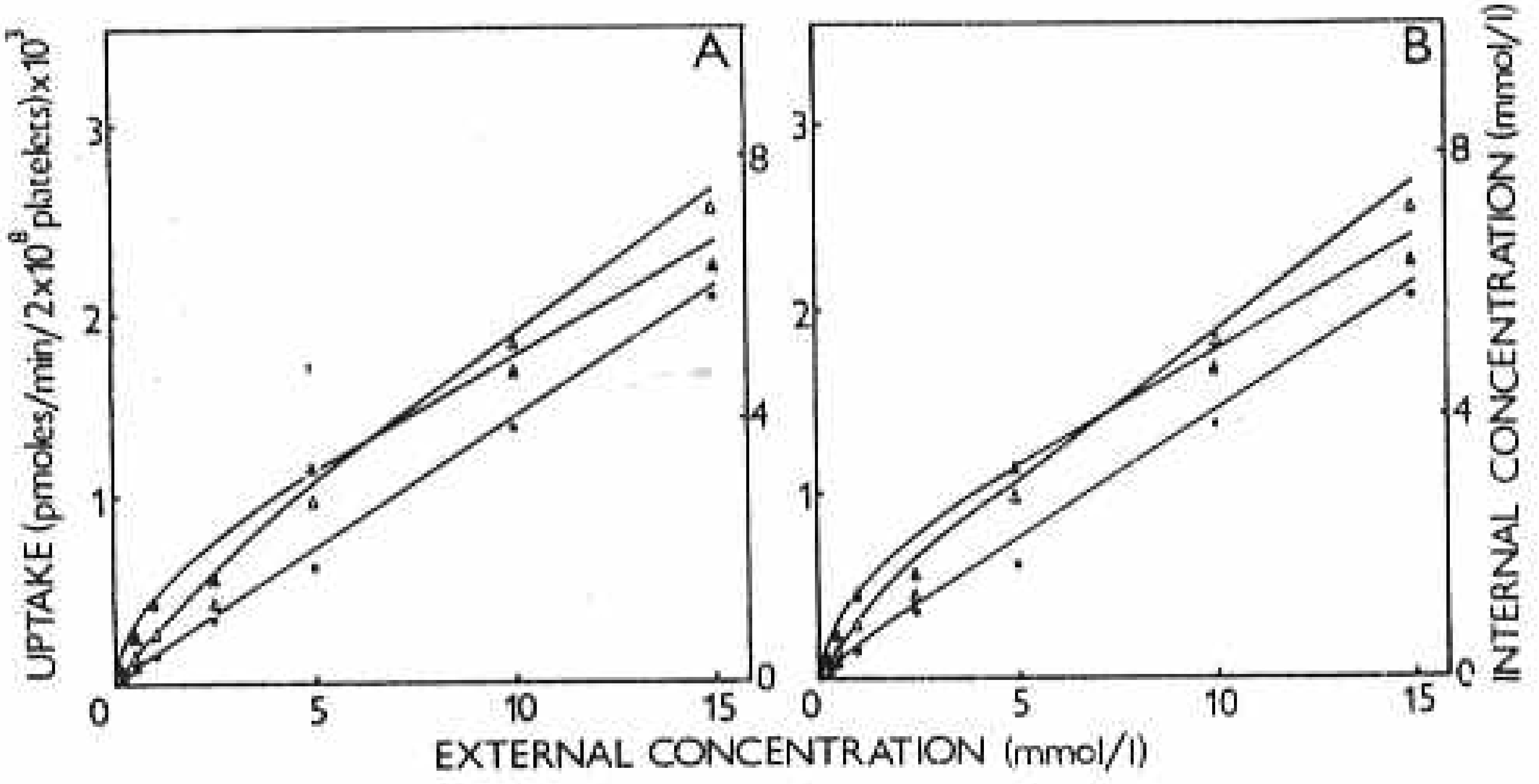

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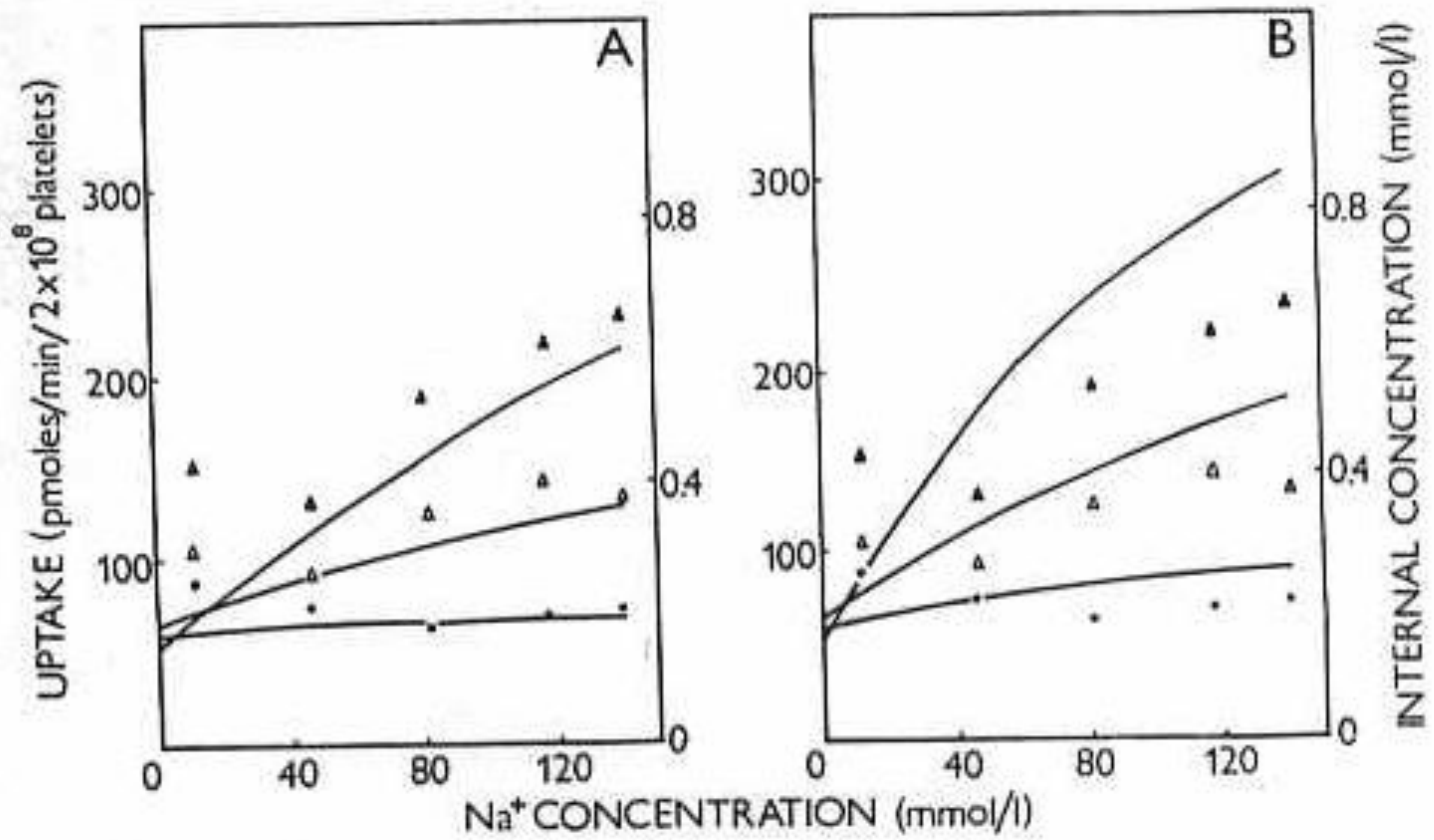

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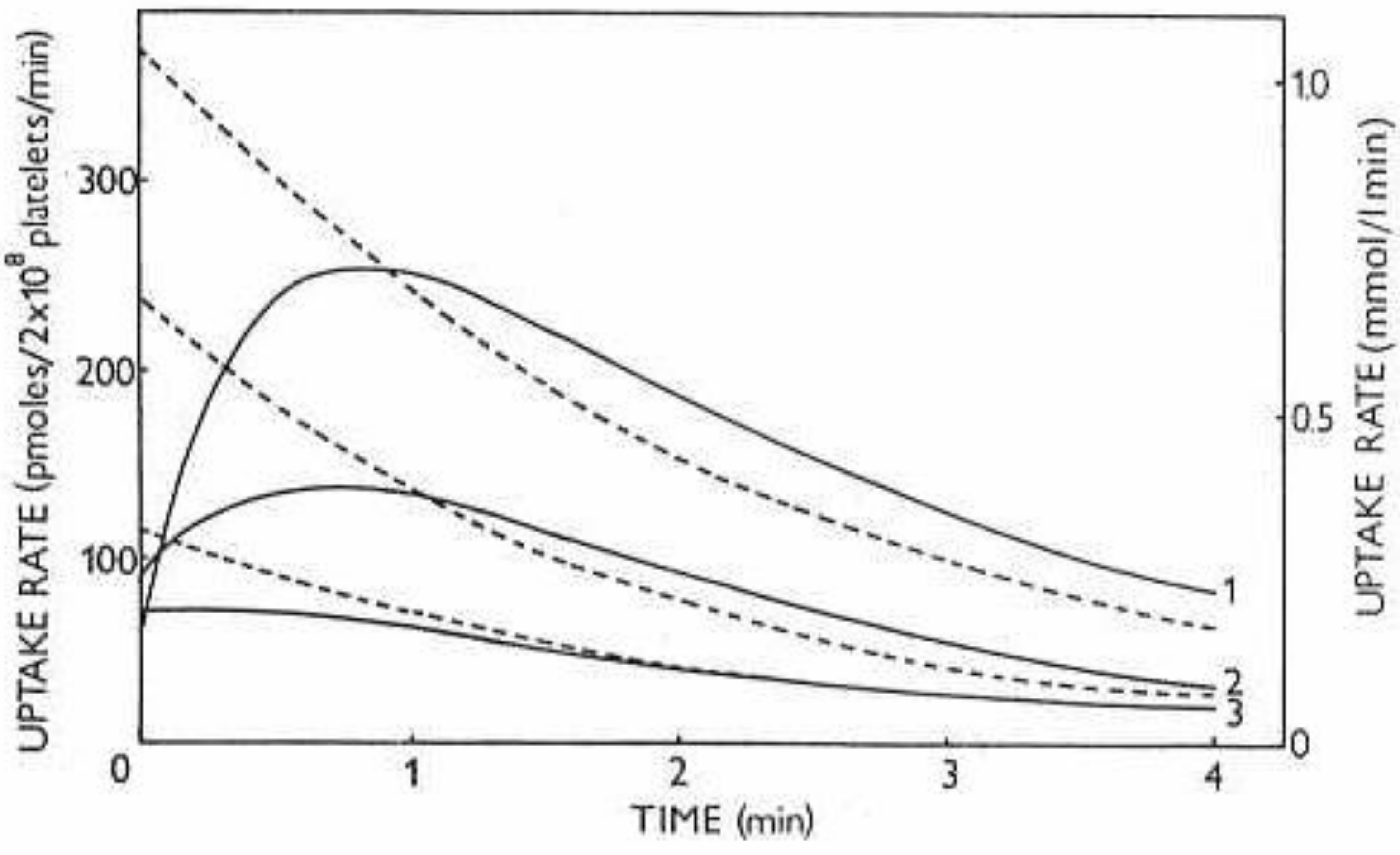

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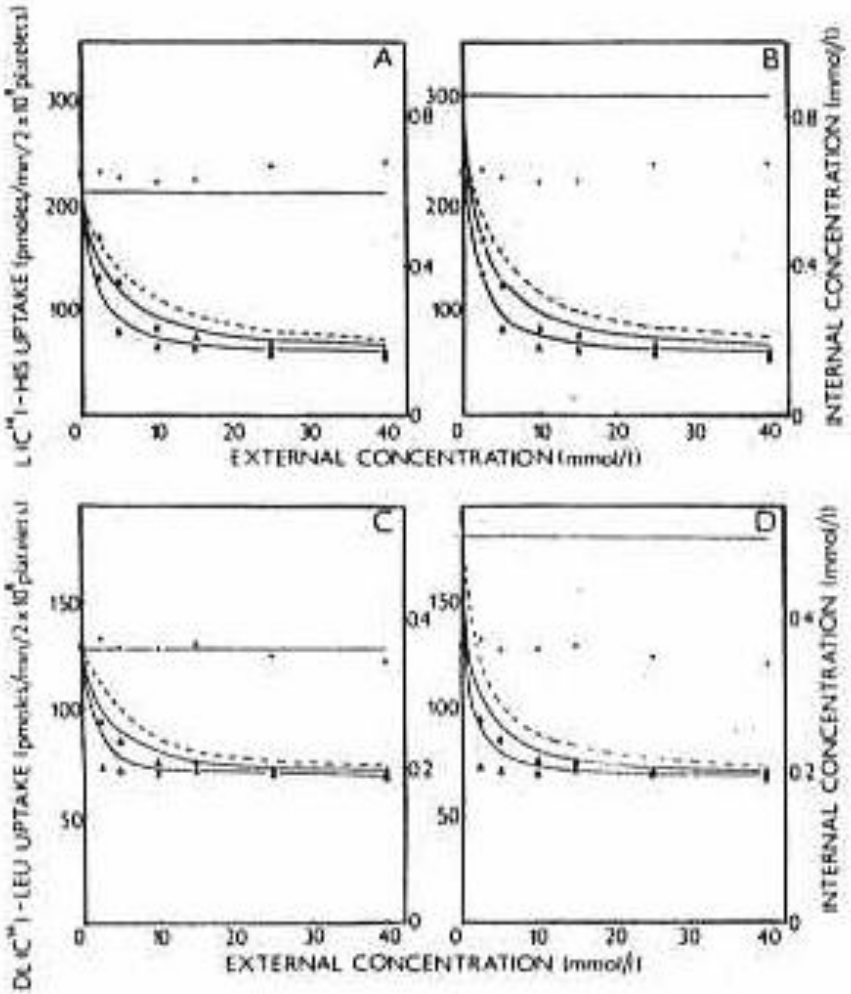

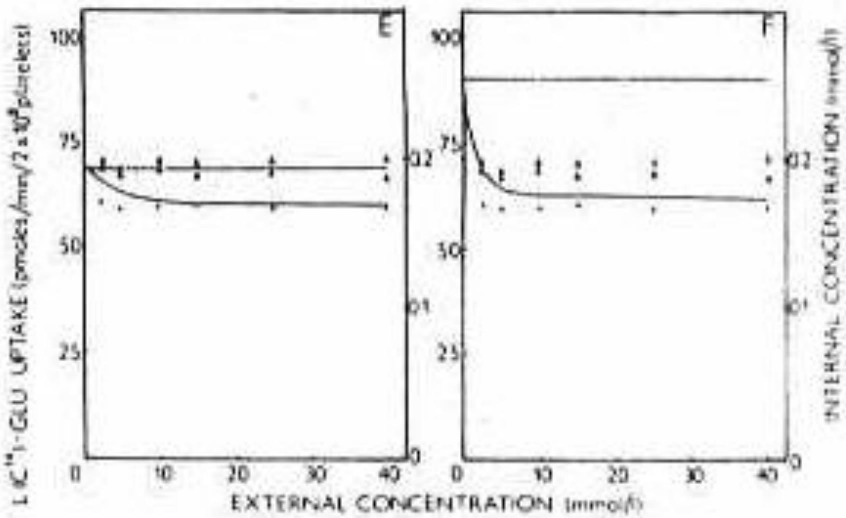

Mathematical Modelling of Amino Acid Transport

	L-Leu	L-His	L-Glu
	exact solution		
k_{11}^{1}	3.92×10^{-2}	4.20×10^{-2}	1.22×10^{-2}
k_1	8.92×10^{-3}	9.58×10^{-3}	2.93×10^{-3}
k_{12}	9.65×10^{-3}	7.18×10^{-3}	8.20×10^{-3}
B_1^0	2.512	3.142	1.368
R	0.987	0.989	0.982
	simplified solution		
k_{11}^{1}	3.90×10^{-2}	4.19×10^{-2}	1.22×10^{-2}
k_1	8.90×10^{-3}	9.52×10^{-3}	2.92×10^{-3}
k_{12}	9.63×10^{-3}	7.45×10^{-3}	8.13×10^{-3}
B_1^0	2.502	3.116	1.362
B	2.7×10^{4}	3.3×10^{4}	1.5×10^{4}
K_D	2.59	2.12	2.28
K_M	0.456	0.454	0.479
V_{max}	5.97	8.45	1.10
R	0.981	0.983	0.979

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BIOPHYSICS

Prezentacja multimedialna współfinansowana przez Unię Europejską w ramach Europejskiego Funduszu Społecznego w projekcie pt.

„Innowacyjna dydaktyka bez ograniczeń - zintegrowany rozwój Politechniki Łódzkiej - zarządzanie Uczelnią, nowoczesna oferta edukacyjna i wzmacniania zdolności do zatrudniania osób niepełnosprawnych"