Facilitated Transport.
Instructor: Nam Sun Wang

Process Description. In **facilitated transport**, a carrier molecule C binds to the substrate S to form a carrier-substrate complex CS at the outer side of the cell membrane. The complex diffuses by Fick's diffusion from the outer side of the membrane toward the inner side of the membrane, where the substrate is released into the cell cytoplasm and the free carrier C is regenerated. The free carrier shuttles back, again by Fick's diffusion, toward the outer side of the membrane, where it picks up another substrate; and the cycle is repeated. The following "reaction mechanism" describes this process.

$$C_e + S_e \xleftrightarrow{\quad K \quad} CS_e \longrightarrow \text{diffusion across cell membrane} \longrightarrow CS_i \xleftrightarrow{\quad K \quad} C_i + S_i$$

$$C_e \longleftarrow \text{diffusion across cell membrane} \longleftarrow C_i$$
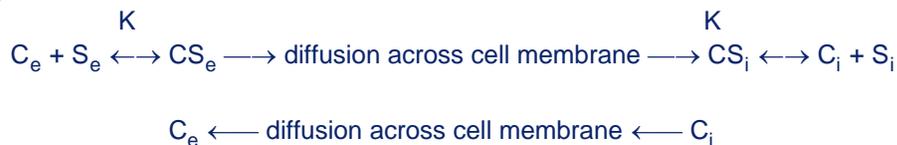
Alternate Process description with more intermediate steps.

$$C_e + S_e \xleftrightarrow{\quad K \quad} \text{intermediate} \rightarrow CS_e \longrightarrow \text{diffusion across cell membrane} \longrightarrow CS_i \leftarrow \text{intermediate} \xleftrightarrow{\quad K \quad} C_i + S_i$$

Underlying Ideas.

1. Flux of a chemical species across cell membrane via Fick's diffusion.

$$\text{flux} = \frac{D}{\delta} \cdot \left(c_e - c_i \right) \quad \text{... in mole/s·m}^2$$

where   D   ... Diffusivity of a chemical species

$\quad\quad\quad \delta$ ... thickness of cell membrane

$\quad\quad\quad c_e$ ... concentration of the chemical species at the outer cell membrane (extracellular)

$\quad\quad\quad c_i$ ... concentration of the chemical species at the inner cell membrane (intracellular)

We apply Fick's diffusion to both the complex and the free carrier.

$$\text{flux}_{CS} = \frac{D_{CS}}{\delta} \cdot \left(CS_e - CS_i \right) \quad \text{... flux of the carrier-substrate complex}$$

$$\text{flux}_C = \frac{D_C}{\delta} \cdot \left(C_e - C_i \right) \quad \text{... flux of the free carrier}$$

2. At quasi-steady state or equilibrium, the net in-flux of the carrier-substrate complex CS is balanced by the net out-flux of the free carrier C.

$$\text{flux}_{CS} = - \text{flux}_C$$

3. The carrier can take on two forms: complex with the substrate and free. We assume that the binding event is reversible and fast; thus, it is described by an equilibrium constant K, which is related to the affinity of the carrier molecule for the substrate molecule. The extent of complex depends on the substrate concentration.

$$CS \longleftrightarrow C + S$$

$$K = \frac{C \cdot S}{CS}$$

4. The total number of the carrier molecules is conserved. Strictly speaking, **the concentration of the carrier species is not conserved**, and we cannot simply add up concentrations from an arbitrary number of locations, say, at the inner and outer membrane. For example, we miss by a factor of 2 if we simply add up concentrations at the inner and outer cell membrane.

$$C_{total} \cdot Area \cdot \delta = \int_0^\delta CS(x) \cdot Area \, dx + \int_0^\delta C(x) \cdot Area \, dx$$

Because of Fick's diffusion, the concentration profiles for CS and C within the cell membrane are linear.

$$CS(x) = CS_e - \left(CS_e - CS_i\right) \cdot \frac{x}{\delta}$$

$$C(x) = C_e - \left(C_e - C_i\right) \cdot \frac{x}{\delta}$$

Substituting CS(x) and C(x) into the integral yields,

$$C_{total} = \frac{1}{2} \cdot \left(CS_e + CS_i + C_e + C_i\right)$$

Another way of thinking is that the different forms of carrier (free unassociated form C and associated form CS) are conserved.

$$C_{total} = CS_{average} + C_{average} \qquad where \qquad CS_{average} = \frac{CS_e + CS_i}{2} \qquad C_{average} = \frac{C_e + C_i}{2}$$

Derivation. Below, we express the above ideas mathematically and let Mathcad crank out the answer.

Given

Steady-state in- and out- fluxes.
$$flux = \frac{D_{CS}}{\delta} \cdot \left(CS_e - CS_i\right) \qquad flux = -\frac{D_C}{\delta} \cdot \left(C_e - C_i\right)$$

Definition of dissociation constant.
$$K = \frac{C_e \cdot S_e}{CS_e} \qquad K = \frac{C_i \cdot S_i}{CS_i}$$

Conservation of different forms.
$$C_{total} = \frac{1}{2} \cdot \left(CS_e + CS_i + C_e + C_i\right)$$

The above 5 equations allows us to solve for 5 variables, which are flux (which is what we are really after) and the different forms of carrier species (which are what we do not want to see appearing on the RHS of flux=?).

$$\text{Find}\left(CS_e, C_e, CS_i, C_i, \text{flux}\right) \rightarrow \begin{bmatrix} 2\cdot C_{total}\cdot S_e\cdot \dfrac{\left(D_C\cdot K + D_{CS}\cdot S_i\right)}{\left(S_i\cdot K\cdot D_C + S_i\cdot K\cdot D_{CS} + 2\cdot D_C\cdot K^2 + S_e\cdot D_C\cdot K + 2\cdot S_e\cdot D_{CS}\cdot S_i + S_e\cdot \dots\right)} \\[1em] 2\cdot\left(D_C\cdot K + D_{CS}\cdot S_i\right)\cdot C_{total}\cdot \dfrac{K}{\left(S_i\cdot K\cdot D_C + S_i\cdot K\cdot D_{CS} + 2\cdot D_C\cdot K^2 + S_e\cdot D_C\cdot K + 2\cdot S_e\cdot D_{CS}\cdot \dots\right)} \\[1em] 2\cdot C_{total}\cdot \dfrac{\left(D_C\cdot K + S_e\cdot D_{CS}\right)}{\left(S_i\cdot K\cdot D_C + S_i\cdot K\cdot D_{CS} + 2\cdot D_C\cdot K^2 + S_e\cdot D_C\cdot K + 2\cdot S_e\cdot D_{CS}\cdot S_i + S_e\cdot D_C\dots\right)} \\[1em] 2\cdot K\cdot C_{total}\cdot \dfrac{\left(D_C\cdot K + S_e\cdot D_{CS}\right)}{\left(S_i\cdot K\cdot D_C + S_i\cdot K\cdot D_{CS} + 2\cdot D_C\cdot K^2 + S_e\cdot D_C\cdot K + 2\cdot S_e\cdot D_{CS}\cdot S_i + S_e\cdot D\dots\right)} \\[1em] 2\cdot D_C\cdot K\cdot C_{total}\cdot D_{CS}\cdot \dfrac{\left(-S_i + S_e\right)}{\left[\delta\cdot\left(S_i\cdot K\cdot D_C + S_i\cdot K\cdot D_{CS} + 2\cdot D_C\cdot K^2 + S_e\cdot D_C\cdot K + 2\cdot S_e\cdot D_{CS}\cdot S_i \dots\right)\right]} \end{bmatrix}$$

$$\text{flux} = 2\cdot D_{CS}\cdot C_{total}\cdot K\cdot D_C\cdot \frac{S_e - S_i}{\left(S_i\cdot K\cdot D_{CS} + S_i\cdot K\cdot D_C + 2\cdot D_C\cdot K^2 + 2\cdot S_e\cdot D_{CS}\cdot S_i + S_e\cdot D_{CS}\cdot K + S_e\cdot D_C\cdot K\right)\cdot \delta}$$

$$. = 2\cdot\frac{D_{CS}\cdot C_{total}}{\delta}\cdot K\cdot \frac{S_e - S_i}{2\cdot K^2 + (1 + \alpha)\cdot K\cdot\left(S_e + S_i\right) + 2\cdot\alpha\cdot S_e\cdot S_i} \qquad \text{where} \quad \alpha = \frac{D_{CS}}{D_C}$$

Special case: identical diffusion coefficient for CS and C. $\longrightarrow \quad \alpha = 1$

$$\text{flux} = \frac{D_{CS}\cdot C_{total}}{\delta}\cdot \frac{K\cdot\left(S_e - S_i\right)}{\left(K + S_e\right)\cdot\left(K + S_i\right)} = \text{flux}_{max}\cdot \frac{K\cdot\left(S_e - S_i\right)}{\left(K + S_e\right)\cdot\left(K + S_i\right)} \qquad \text{where} \quad \text{flux}_{max} = \frac{D_{CS}\cdot C_{total}}{\delta}$$

Special case: Very rapid rate of consumption of the substrate in the cell leads to a minimal intracellular concentration of S.

$$S_i = 0$$

$$\text{flux} = \text{flux}_{max}\cdot \frac{S_e}{K + S_e} \qquad \text{... Michaelis-Menten saturation expression}$$

4 Alternate a -- correct. The total concentration of the carrier molecules is conserved at each side -- a better interpretation of "$C_{total.e}=CS_e+C_e$" is not "conservation" but a mere definitino of what "$C_{total.e}$" is . Note that conservation of the total number of moles of carrier species is a fact; however, we cannot impose $C_{total.i}=C_{total.e}$, because that does not follow from material balance and because doing so will result in an over-specified system of equations with 6 equations and only 5 unknowns to solve for: CS_e, C_e, CS_i, C_i, flux. Indeed, the result below shows that **$C_{total.i} \neq C_{total.e}$**. (Think hard why in general the total carrier concentrations may be different between the extracellular and the intracelluar sides.)

Given

  Steady-state in- and out- fluxes.

$$\text{flux} = \frac{D_{CS}}{\delta} \cdot (CS_e - CS_i) \qquad \text{flux} = -\frac{D_C}{\delta} \cdot (C_e - C_i)$$

  Definition of dissociation constant.

$$K = \frac{C_e \cdot S_e}{CS_e} \qquad K = \frac{C_i \cdot S_i}{CS_i}$$

  Conservation of different forms.

$$C_{total.e} = CS_e + C_e \qquad C_{total.i} = CS_i + C_i$$

The above 6 equations allows us to solve for 6 variables.

$$\text{Find}(CS_e, C_e, CS_i, C_i, \text{flux}, C_{total.i}) \rightarrow \begin{bmatrix} C_{total.e} \cdot \dfrac{S_e}{(K+S_e)} \\[2mm] K \cdot \dfrac{C_{total.e}}{(K+S_e)} \\[2mm] C_{total.e} \cdot \dfrac{(D_C \cdot K + S_e \cdot D_{CS})}{(S_e \cdot D_{CS} \cdot S_i + D_C \cdot K^2 + S_i \cdot K \cdot D_{CS} + S_e \cdot D_C \cdot K)} \cdot S_i \\[2mm] K \cdot C_{total.e} \cdot \dfrac{(D_C \cdot K + S_e \cdot D_{CS})}{(S_e \cdot D_{CS} \cdot S_i + D_C \cdot K^2 + S_i \cdot K \cdot D_{CS} + S_e \cdot D_C \cdot K)} \\[2mm] (-S_i + S_e) \cdot D_{CS} \cdot D_C \cdot K \cdot \dfrac{C_{total.e}}{\left[(K+S_e) \cdot \left[\delta \cdot (D_C \cdot K + D_{CS} \cdot S_i)\right]\right]} \\[2mm] (D_C \cdot K + S_e \cdot D_{CS}) \cdot C_{total.e} \cdot \dfrac{(K+S_i)}{(S_e \cdot D_{CS} \cdot S_i + D_C \cdot K^2 + S_i \cdot K \cdot D_{CS} + S_e \cdot D_C \cdot K)} \end{bmatrix}$$

$$C_{total.i} = C_{total.e} \cdot \frac{(D_C \cdot K + D_{CS} \cdot S_e) \cdot (K + S_i)}{(D_C \cdot K + D_{CS} \cdot S_i) \cdot (K + S_e)} \qquad \text{... in general, } C_{total.i} \neq C_{total.e} \text{ if } D_C \neq D_{CS}$$

$$C_{total.i} = C_{total.e} \qquad \text{if } D_C = D_{CS}.$$

4 Alternate b -- ok. *Assume* the total concentration of the carrier molecules is conserved at each side, and they are equal on both sides "$C_{total}=CS_e+C_e=CS_i+C_i$". As mentioned in section "Alternative a" above, we will later examine when this assumption holds. Because keeping all the equations will result in an over-specified system of equations with 6 equations and only 5 unknowns to solve for, we take away one of the flux equations.

Given
  Steady-state in- and out- fluxes.

$$flux = \frac{D_{CS}}{\delta} \cdot \left(CS_e - CS_i\right)$$

  Definition of dissociation constant.

$$K = \frac{C_e \cdot S_e}{CS_e} \qquad K = \frac{C_i \cdot S_i}{CS_i}$$

  Conservation of different forms.

$$C_{total} = CS_e + C_e \qquad C_{total} = CS_i + C_i$$

The above 6 equations allows us to solve for 6 variables.

$$Find\left(CS_e, C_e, CS_i, C_i, flux\right) \rightarrow \begin{bmatrix} S_e \cdot \dfrac{C_{total}}{\left(K + S_e\right)} \\[2em] C_{total} \cdot \dfrac{K}{\left(K + S_e\right)} \\[2em] S_i \cdot \dfrac{C_{total}}{\left(K + S_i\right)} \\[2em] C_{total} \cdot \dfrac{K}{\left(K + S_i\right)} \\[2em] D_{CS} \cdot C_{total} \cdot K \cdot \dfrac{\left(-S_i + S_e\right)}{\left[\delta \cdot \left(K^2 + K \cdot S_i + S_e \cdot K + S_e \cdot S_i\right)\right]} \end{bmatrix}$$

This alternative yields the following expression for flux, which is **eqn (4.2) of Shuler**

$$flux = \frac{D_{CS}}{\delta} \cdot \left(CS_e - CS_i\right) = \frac{D_{CS}}{\delta} \cdot C_{total} \cdot \left(\frac{S_e}{K + S_e} - \frac{S_i}{K + S_i}\right) = J_{max} \cdot \left(\frac{S_e}{K + S_e} - \frac{S_i}{K + S_i}\right)$$

  where $J_{max} = \dfrac{D_{CS}}{\delta} \cdot C_{total}$

Check: Let's see when the reverse flux equals to the forward flux. Basically how the diffusivities of CS and C (i.e., D_{CS} & D_C) need to be related.

reverse $flux = -\dfrac{D_C}{\delta} \cdot \left(C_e - C_i\right) = \dfrac{D_C}{\delta} \cdot C_{total} \cdot K \cdot \left(\dfrac{1}{S_i + K} - \dfrac{1}{S_e + K}\right)$

For the forward and reverse flux to be equal, we require:

$$\frac{D_{CS}}{\delta} \cdot C_{total} \cdot \left(\frac{S_e}{K + S_e} - \frac{S_i}{K + S_i}\right) = \frac{D_C}{\delta} \cdot C_{total} \cdot K \cdot \left(\frac{1}{S_i + K} - \frac{1}{S_e + K}\right) \qquad \longrightarrow \qquad D_C = D_{CS}$$

Thus, the total carrier concentrations are idential on both sides when diffusivities are equal: $D_C = C_{CS}$. Conversely, the total carrier concentrations are different on two sides when diffusivities are unequal.

4 Alternate b -- repeat of above. Instead of a*ssuming* the total concentration of the carrier molecules are equal on both sides "$C_{total}=CS_e+C_e=CS_i+C_i$", we state they *are* (not an assumption).

We solve a system of 6 equations and 6 unknowns, by adding D_{CS} as an unknown.

Given

Steady-state in- and out- fluxes.

$$flux = \frac{D_{CS}}{\delta} \cdot \left(CS_e - CS_i\right) \quad flux = -\frac{D_C}{\delta} \cdot \left(C_e - C_i\right)$$

Definition of dissociation constant.

$$K = \frac{C_e \cdot S_e}{CS_e} \qquad K = \frac{C_i \cdot S_i}{CS_i}$$

Conservation of different forms.

$$C_{total} = CS_e + C_e \qquad C_{total} = CS_i + C_i$$

The above 6 equations allows us to solve for 6 variables.

$$Find\left(CS_e, C_e, CS_i, C_i, flux, D_{CS}\right) \rightarrow \begin{bmatrix} S_e \cdot \dfrac{C_{total}}{\left(K + S_e\right)} \\[2ex] C_{total} \cdot \dfrac{K}{\left(K + S_e\right)} \\[2ex] S_i \cdot \dfrac{C_{total}}{\left(K + S_i\right)} \\[2ex] C_{total} \cdot \dfrac{K}{\left(K + S_i\right)} \\[2ex] D_C \cdot C_{total} \cdot K \cdot \dfrac{\left(-S_i + S_e\right)}{\left[\delta \cdot \left(K^2 + K \cdot S_i + S_e \cdot K + S_e \cdot S_i\right)\right]} \\[2ex] D_C \end{bmatrix}$$

As expected, the results are identical to the last section, including the requirement: $D_{CS} = D_C$

Graph to show general behavior.　　$K := 1$　　$flux_{max} := 1$　　$S_i := 1$

$$flux(S_e) := flux_{max} \cdot \frac{K \cdot (S_e - S_i)}{(K + S_e) \cdot (K + S_i)}$$

$S_e := 0, 0.1 .. 10$

Facilitated Transport

Substrate Flux Into Cells

$\overline{flux(S_e)}$

$\overline{0}$

S_e

Extracelluar Substrate Conc.
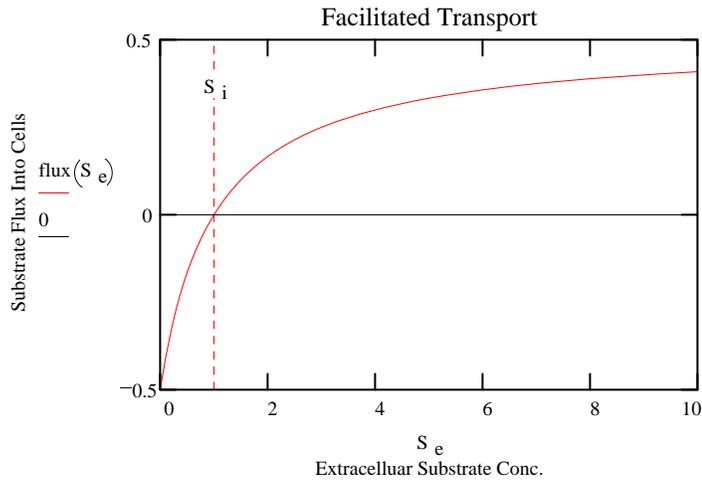
Flux as a function of the driving force, which is the difference in the extracellular and intracellular substrate concentrations: S_e-S_i.

$$flux = flux_{max} \cdot \frac{K \cdot (S_e - S_i)}{K^2 + S_i \cdot (2 \cdot K + S_i) + (K + S_i) \cdot (S_e - S_i)}$$

Facilitated Transport

Substrate Flux Into Cells

$\overline{flux(S_e)}$

$\overline{0}$

$\frac{K^2 + S_i \cdot (2 \cdot K + S_i)}{K + S_i}$

$flux_{max} \cdot \frac{K}{K + S_i}$

$\frac{flux_{max}}{2} \cdot \frac{K}{K + S_i}$

$S_e - S_i$

Driving Force (Conc Difference)
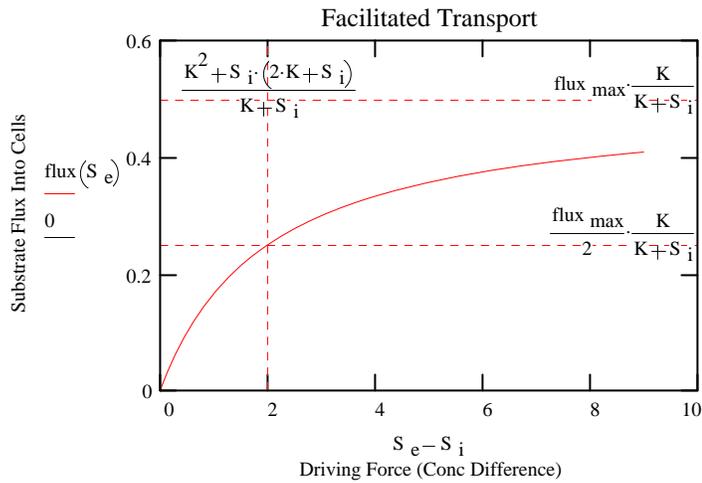
Active Transport -- when the equilibrium values are different at the outer and inner membrane. Note that when diffusivities D_{CS} & D_C are different ($D_{CS} \neq D_C$), active transport is also possible -- basically we need different/asymetric transport and/or kinetic properties..

assume S_e, S_i

Given

  Steady-state in- and out- fluxes. $\text{flux} = \dfrac{D_{CS}}{\delta} \cdot \left(CS_e - CS_i \right)$ $\text{flux} = -\dfrac{D_C}{\delta} \cdot \left(C_e - C_i \right)$

  Definition of dissociation constant. $K_e = \dfrac{C_e \cdot S_e}{CS_e}$ $K_i = \dfrac{C_i \cdot S_i}{CS_i}$

  Conservation of different forms. $C_{total} = \dfrac{1}{2} \cdot \left(CS_e + CS_i + C_e + C_i \right)$

The above 5 equations allows us to solve for 5 variables.

$\text{Find}\left(CS_e, C_e, CS_i, C_i, \text{flux} \right) \rightarrow$

$$2 \cdot C_{total} \cdot \left(D_C \cdot K_i + D_{CS} \right) \cdot \dfrac{S_e}{\left(D_C \cdot K_e + 2 \cdot D_C \cdot K_e \cdot K_i + D_C \cdot K_i \cdot S_e + D_{CS} \cdot K_e + 2 \cdot S_e \cdot D_{CS} \right.}$$

$$2 \cdot K_e \cdot C_{total} \cdot \dfrac{\left(D_C \cdot K_i + D_{CS} \right)}{\left(D_C \cdot K_e + 2 \cdot D_C \cdot K_e \cdot K_i + D_C \cdot K_i \cdot S_e + D_{CS} \cdot K_e + 2 \cdot S_e \cdot D_{CS} + D_{CS} \right.}$$

$$2 \cdot \left(D_C \cdot K_e + S_e \cdot D_{CS} \right) \cdot \dfrac{C_{total}}{\left(D_C \cdot K_e + 2 \cdot D_C \cdot K_e \cdot K_i + D_C \cdot K_i \cdot S_e + D_{CS} \cdot K_e + 2 \cdot S_e \cdot D_{CS} + \right.}$$

$$2 \cdot K_i \cdot \left(D_C \cdot K_e + S_e \cdot D_{CS} \right) \cdot \dfrac{C_{total}}{\left(D_C \cdot K_e + 2 \cdot D_C \cdot K_e \cdot K_i + D_C \cdot K_i \cdot S_e + D_{CS} \cdot K_e + 2 \cdot S_e \cdot D_{CS} \right.}$$

$$2 \cdot D_C \cdot C_{total} \cdot D_{CS} \cdot \dfrac{\left(-K_e + K_i \cdot S_e \right)}{\left[\left(D_C \cdot K_e + 2 \cdot D_C \cdot K_e \cdot K_i + D_C \cdot K_i \cdot S_e + D_{CS} \cdot K_e + 2 \cdot S_e \cdot D_{CS} + D_C \right. \right.}$$

$$\text{flux} = \dfrac{2 \cdot D_{CS} \cdot C_{total}}{\delta} \cdot D_C \cdot \dfrac{K_i \cdot S_e - K_e \cdot S_i}{D_{CS} \cdot S_i \cdot K_e + 2 \cdot S_e \cdot D_{CS} \cdot S_i + D_{CS} \cdot K_i \cdot S_e + D_C \cdot K_e \cdot S_i + 2 \cdot D_C \cdot K_e \cdot K_i + D_C \cdot K_i \cdot S_e}$$

$$= \dfrac{2 \cdot D_{CS} \cdot C_{total}}{\delta} \cdot \dfrac{K_i \cdot S_e - K_e \cdot S_i}{2 \cdot K_e \cdot K_i + (1 + \alpha) \cdot \left(K_e \cdot S_i + K_i \cdot S_e \right) + 2 \cdot \alpha \cdot S_e \cdot S_i} \qquad \text{where} \quad \alpha = \dfrac{D_{CS}}{D_C}$$

Special case: identical diffusion coefficient for CS and C. $\longrightarrow$ $\alpha = 1$

$$\text{flux} = \dfrac{D_{CS} \cdot C_{total}}{\delta} \cdot \dfrac{K_i \cdot S_e - K_e \cdot S_i}{\left(K_e + S_e \right) \cdot \left(K_i + S_i \right)} = \text{flux}_{max} \cdot \dfrac{K_i \cdot S_e - K_e \cdot S_i}{\left(K_e + S_e \right) \cdot \left(K_i + S_i \right)} \qquad \text{where} \quad \text{flux}_{max} = \dfrac{D_{CS} \cdot C_{total}}{\delta}$$

Special case: Very rapid rate of consumption of the substrate in the cell leads to a minimal intracellular concentration of S.

  $S_i = 0$

  $\text{flux} = \text{flux}_{max} \cdot \dfrac{S_e}{K_e + S_e}$ ... Michaelis-Menten saturation expression

Special case: symmetric membrane (i.e., same properties at both the inner and outer cell membrane.

$$K_e = K_i = K$$

$$\text{flux} = \text{flux}_{max} \cdot \frac{K \cdot \left(S_e - S_i\right)}{\left(K + S_e\right) \cdot \left(K + S_i\right)}$$

For the flux to be positive, we must have $S_e > S_i$

Thus, with a symmetrical membrane it is not possible to achieve a positive flux into the cell against the concentration gradient.

Active transport, where the substrate moves against the concentration gradient, is possible for an **asymmetric membrane**. Since the denominator of the flux equation is positive, the numerator must be positive.

For $\text{flux} > 0$

$$\text{numerator} = K_i \cdot S_e - K_e \cdot S_i > 0 \qquad \frac{S_e}{S_i} > \frac{K_e}{K_i}$$

Transport against the concentration gradient means the intracellular concentration is higher than than the extracellular concentration.

For $S_e < S_i$ $1 > \dfrac{S_e}{S_i}$

Combining the last two inequality relationship yields,

$$1 > \frac{S_e}{S_i} > \frac{K_e}{K_i}$$

Thus, active transport requires the dissociation constant at the inner cell membrane to be greater than that at the outer cell membrane.

$$K_i > K_e$$

Graph to show the general behavior. $S_i := 1$

$flux_{max} := 1$ $k_{1i} := 1$ $k_{1e} := 1$ $k_{ie} := 1$ $k_{ii} := 2$ $D := 1$ $\delta := 1$

$$K_m := \frac{1}{k_{1e}} \cdot \left[k_{ie} + \frac{1}{\dfrac{\delta}{D} + \dfrac{1}{k_{ii}}} \right]$$

$$K_e := \frac{k_{ie}}{k_{1e}}$$ $$K_i := \frac{k_{ii}}{k_{1i}}$$

$$flux(S_e) := flux_{max} \cdot \frac{S_e - \dfrac{k_{1i} \cdot k_{ie}}{k_{1e} \cdot k_{ii}} \cdot S_i}{\left(S_e + K_m\right) + \dfrac{\left(\dfrac{\delta}{D} \cdot \dfrac{k_{ie}}{k_{ii}} + \dfrac{1}{k_{ii}}\right) \cdot \dfrac{k_{1i}}{k_{1e}} \cdot S_i + \dfrac{\delta}{D} \cdot \dfrac{k_{1i}}{k_{ii}} \cdot S_e \cdot S_i}{\dfrac{\delta}{D} + \dfrac{1}{k_{ii}}}}$$

$S_e := 0, 0.1 .. 2$

Active Transport

Substrate Flux Into Cells

$\dfrac{K_e}{K_i} \cdot S_i$ S_i

$flux(S_e)$

0

Facilitated -- Active -- Facilitated

S_e

Extracelluar Substrate Conc.
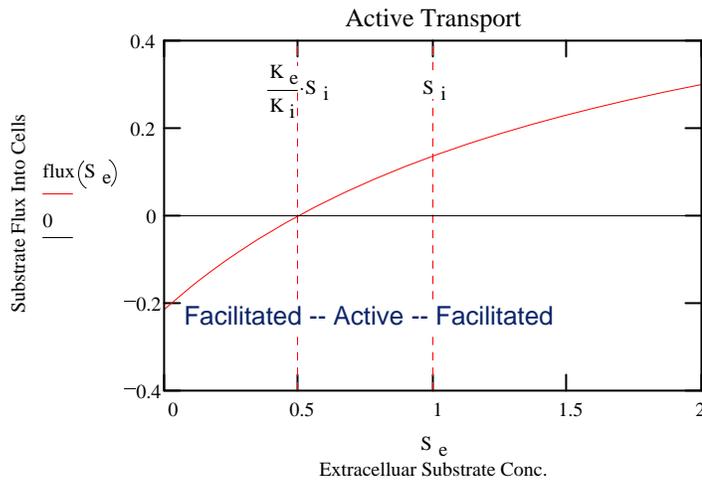
The above plot has three regions: facilitated transport along the concentration gradient (in $\longrightarrow$ out), active transport against the concentration gradient (out $\longrightarrow$ in), and facilitated transport along the concentration gradient (out $\longrightarrow$ in). Specifically, between $S_e = (K_e/K_i) \cdot S_i$ and $S_e = S_i$, substrate flux is against the concentration gradient.