

Sodium Glucose Symporter

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Note: This example is discussed in detail by (Gawthrop and Pan, 2020) available [here](#).

Note: this is the SGLT.ipynb notebook. The PDF version "Sodium Glucose Symporter" is available [here](#).

1 Introduction

The Sodium-Glucose Transport Protein 1 (SGLT1) (also known as the Na⁺-glucose symporter (Keener and Sneyd, 2009, § 2.4.2)) was studied experimentally by Parent et al. (1992a) and explained by a biophysical model (Parent et al., 1992b); further experiments and modelling were conducted by Chen et al. (1995). Eskandari et al. (2005) examined the kinetics of the reverse mode using similar experiments and analysis to Parent et al. (1992a,b) but with reverse transport and currents.

This note looks at a bond graph based model of SGLT1 based on the model of Eskandari et al. (2005).

The model of Figure 6B of Eskandari et al. (2005) is based on the six-state biomolecular cycle of Figure 2 of Parent et al. (1992b). When operating normally, sugar is transported from the outside to the inside of the membrane driven against a possibly adverse gradient by the concentration gradient of Na⁺.

A similar situation is analysed in §~1.1 of the book by Hill (1989) and the corresponding bond graph of the biomolecular cycle is described by Gawthrop and Crampin (2017).

```
In [1]: ## Some useful imports
import BondGraphTools as bgt
import numpy as np
import sympy as sp
import matplotlib.pyplot as plt

## Stoichiometric analysis
import stoich as st

## SVG
import svgBondGraph as sbg

## Display (eg disp.SVG(), disp.
import IPython.display as disp

quiet = True

## Data file
import json

## Save the figure
SaveFig = False
```

```
In /home/peterg/.local/lib/python3.6/site-packages/matplotlib/mpl-data/stylelib/_classic_test.mp
The text.latex.unicode rcparam was deprecated in Matplotlib 3.0 and will be removed in 3.2.
In /home/peterg/.local/lib/python3.6/site-packages/matplotlib/mpl-data/stylelib/_classic_test.mp
The savefig.frameon rcparam was deprecated in Matplotlib 3.1 and will be removed in 3.3.
```

In /home/peterg/.local/lib/python3.6/site-packages/matplotlib/mpl-data/stylelib/_classic_test.mp
The pgf.debug rcparam was deprecated in Matplotlib 3.0 and will be removed in 3.2.
In /home/peterg/.local/lib/python3.6/site-packages/matplotlib/mpl-data/stylelib/_classic_test.mp
The verbose.level rcparam was deprecated in Matplotlib 3.1 and will be removed in 3.3.
In /home/peterg/.local/lib/python3.6/site-packages/matplotlib/mpl-data/stylelib/_classic_test.mp
The verbose.fileo rcparam was deprecated in Matplotlib 3.1 and will be removed in 3.3.

```
In [2]: ## Load data from Eskandari et. al. Fig 3A
        ## Digitised using https://apps.automeris.io/wpd/
```

```
def loadData():

    with open('SGLT_data.json') as f:
        Dict = json.load(f)

    List = Dict['datasetColl'][0]['data']

    X = []
    Y = []
    for item in List:
        xy = item['value']
        X.append(xy[0])
        Y.append(xy[1])

    return X,Y

print(loadData())
```

```
([-149.08132530120483, -128.50492880613362, -108.26396495071195, -88.92935377875138, -68.9204545
```

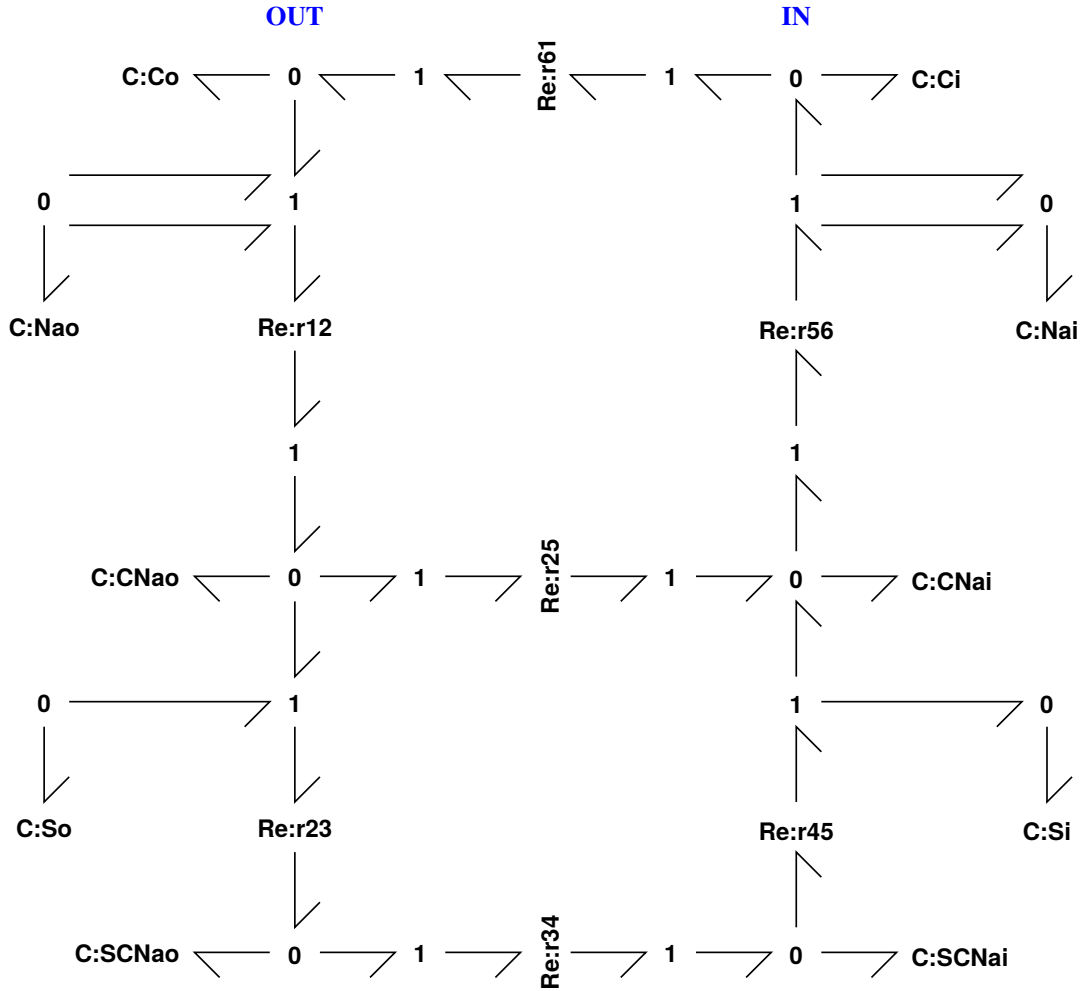
2 Sodium-Glucose Symporter - zero membrane potential.

This non-electrogenic version is used to compute species and reaction parameters from the published model values.

2.1 Bond graph

```
In [3]: ## Sodium-Glucose transporter - no E
        sbg.model('SGLT_abg.svg')
        import SGLT_abg
        disp.SVG('SGLT_abg.svg')
```

```
Out[3]:
```



2.2 Stoichiometry

```
In [4]: ## Stoichiometry
s0 = st.stoich(SGLT_abg.model(),quiet=quiet)
chemostats = ['Nai','Nao','Si','So']
sc0 = st.statify(s0,chemostats=chemostats)
#print(s['species'])
#disp.Latex(st.sprint(s0,'K'))
#print(st.sprints(s))
```

2.3 Convert parameters

The model of [Eskandari et al. \(2005\)](#) is based on rate constants. The following code converts this into the parameters required for the bond graph model.

```
In [5]: def Keq2K(K_eq,N,K,tol=1e-6):
        ## Compute BG C parameters K_c from equilibrium constants K_eq.
```

```

## NB K_eq must be thermodynamically consistent.

logK_eq = np.log(K_eq)
#print(K_eq)
#print(logK_eq)

if len(K) is not 0:
    ##First check that Keq is thermodynamically consistent.
    check = np.linalg.norm(K.T*logK_eq)/np.linalg.norm(logK_eq)
    print(check)

## Transformation of mu to affinities
NN = -N.T

## Pseudo inverse
pNN = np.linalg.pinv(NN)

## BG C constants
K_c = np.exp(pNN@logK_eq)

return K_c

```

In [6]: *## Set non-unit parameters using data from EskWriLoo05*

```

def setPar(s,tol=1e-6):

    ## Extract stoichiometry
    N = s['N']
    Nf = s['Nf']
    Nr = s['Nr']
    K = s['K']

    n_V = s['n_V']

    ## Rate constants from Fig 6.
    kf = {}
    kr = {}

    ## Rate constants from Fig 6.
    kf['r12'] = 8e4;
    kr['r12'] = 500;

    kf['r23'] = 1e5;
    kr['r23'] = 20;

    kf['r34'] = 50;
    kr['r34'] = 50;

```

```

kf['r45'] = 800;
kr['r45'] = 12190;

kf['r56'] = 10;
kr['r56'] = 4500;

kf['r61'] = 3;
kr['r61'] = 350;

kf['r25'] = 0.3;
kr['r25'] = 9.1e-4;

## Equilibrium constants.
K_eq = np.zeros(n_V)
k_f = np.zeros(n_V)
k_r = np.zeros(n_V)
for i, reac in enumerate(s['reaction']):
    K_eq[i] = kf[reac]/kr[reac]
    k_f[i] = kf[reac]
    k_r[i] = kr[reac]

## Compute Ce constants from equilibrium constants
K_c = Keq2K(K_eq,N,K)

#     print(K_eq)
#     print(s['n_X'], K_c.shape)

# Forward rates induced by Cs
k_f0 = np.exp(Nf.T@np.log(K_c))

## Rate constants kappa (Amps)
kappa = (k_f/k_f0)*st.F()

## Sanity check
k_r0 = np.exp(Nr.T@np.log(K_c))
kappa_r = (k_r/k_r0)*st.F()
check = np.linalg.norm(kappa-kappa_r)

if check>tol:
    print(f'Error in kappa: {check:.2}')

## Parameters
parameter = {}

## Ce constants
for i,spec in enumerate(s['species']):
    print(f'K_{spec} = {K_c[i]:.4}')

```

```

        parameter['K_'+spec] = K_c[i]

    ## Re constants
    for i, reac in enumerate(s['reaction']):
        print(f'{reac} K_eq = {K_eq[i]:.4f}; kappa = {kappa[i]:.4f}')
        parameter['kappa_'+reac] = kappa[i]

    return parameter

par = setPar(s0)
#print(par)

Error in kappa: 1.2e-05
K_CNai = 0.149
K_CNao = 49.12
K_Ci = 0.3457
K_Co = 40.33
K_Nai = 13.93
K_Nao = 13.96
K_SCNai = 0.099
K_SCNao = 0.099
K_Si = 10.12
K_So = 10.08
r12 K_eq = 160.0000; kappa = 982183.7246
r23 K_eq = 5000.0000; kappa = 19492291.8173
r25 K_eq = 329.6703; kappa = 589.3102
r34 K_eq = 1.0000; kappa = 48730729.5432
r45 K_eq = 0.0656; kappa = 779691672.6910
r56 K_eq = 0.0022; kappa = 6475936.6454
r61 K_eq = 0.0086; kappa = 837303.6199

```

3 Electrogenic Sodium-Glucose Symporter

3.1 Bond graph

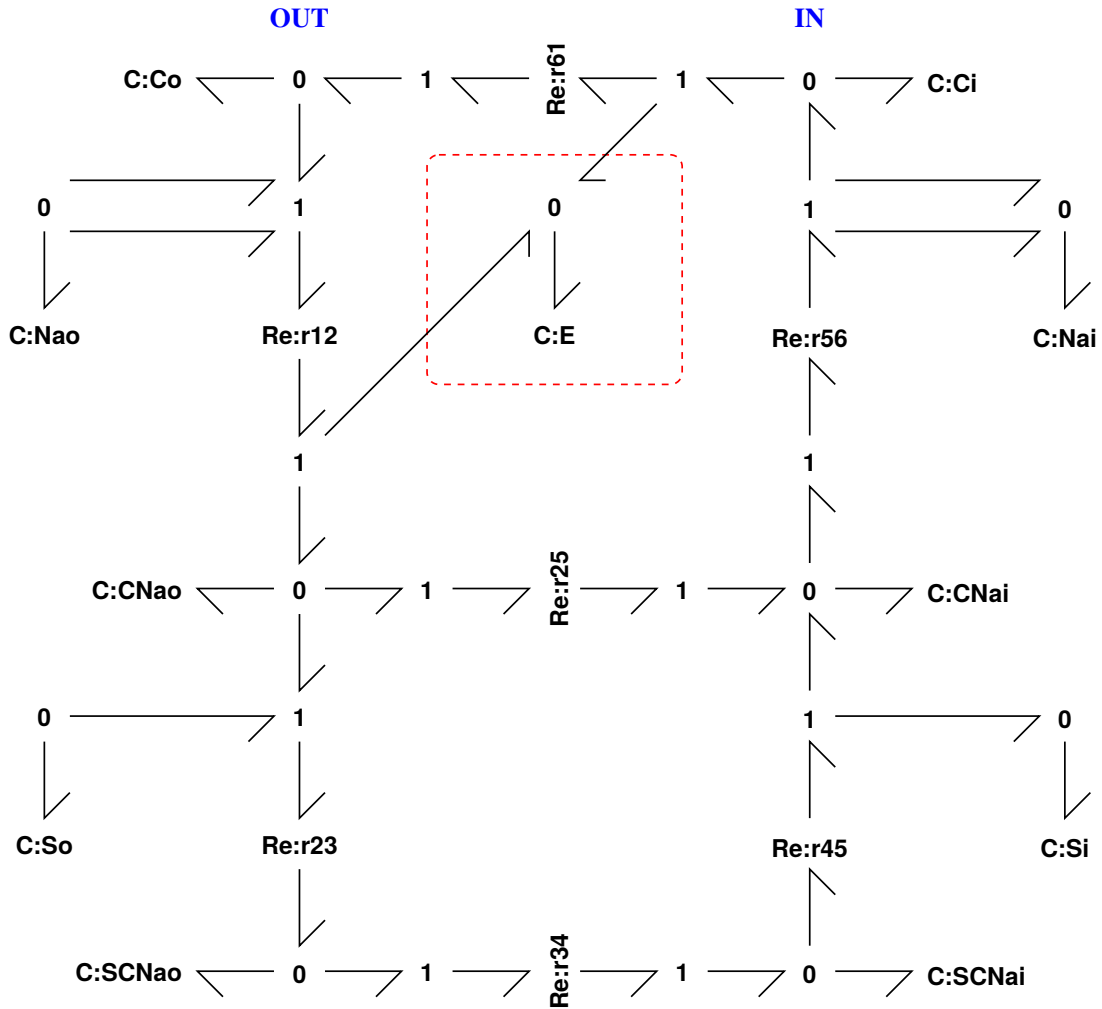
The component C:E is added to express the effect of the charged Na^+ ion crossing the membrane.

```

In [7]: ## Sodium-Glucose transporter - electrogenic
        sbg.model('ESGLT_abg.svg')
        import ESGLT_abg
        disp.SVG('ESGLT_abg.svg')

```

Out [7]:



3.2 Stoichiometry

In [8]: `## Stoichiometry`

```
s = st.stoich(ESGLT_abg.model(),linear=['E'], quiet=quiet)
chemostats = ['Nai','Nao','Si','So','E']
sc = st.statify(s,chemostats=chemostats)
```

```
disp.Latex(st.sprint(sc,'K'))
```

K:

```
[[ 0  1]
 [ 1  0]
 [-1  1]
 [ 1  0]
 [ 1  0]
 [ 0  1]
```

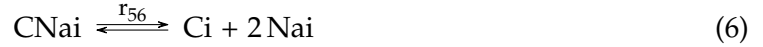
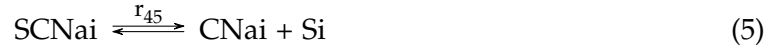

[0 1]]

Out [8]: <IPython.core.display.Latex object>

3.3 Reactions and flows

```
In [9]: ## Reactions
        disp.Latex(st.sprintrl(s,chemformula=True,all=True))
```

Out [9]:



```
In [10]: ## Flows
         disp.Latex(st.sprintvl(s))
```

Out [10]:

$$v_{r12} = \kappa_{r12} \left(-K_{\text{CNao}} x_{\text{CNao}} e^{\frac{K_{\text{E}} x_{\text{E}}}{V_{\text{N}}}} + K_{\text{Co}} K_{\text{NaO}}^2 x_{\text{Co}} x_{\text{NaO}}^2 \right) \quad (8)$$

$$v_{r23} = \kappa_{r23} (K_{\text{CNao}} K_{\text{So}} x_{\text{CNao}} x_{\text{So}} - K_{\text{SCNao}} x_{\text{SCNao}}) \quad (9)$$

$$v_{r25} = \kappa_{r25} (-K_{\text{CNai}} x_{\text{CNai}} + K_{\text{CNao}} x_{\text{CNao}}) \quad (10)$$

$$v_{r34} = \kappa_{r34} (-K_{\text{SCNai}} x_{\text{SCNai}} + K_{\text{SCNao}} x_{\text{SCNao}}) \quad (11)$$

$$v_{r45} = \kappa_{r45} (-K_{\text{CNai}} K_{\text{Si}} x_{\text{CNai}} x_{\text{Si}} + K_{\text{SCNai}} x_{\text{SCNai}}) \quad (12)$$

$$v_{r56} = \kappa_{r56} (K_{\text{CNai}} x_{\text{CNai}} - K_{\text{Ci}} K_{\text{Nai}}^2 x_{\text{Ci}} x_{\text{Nai}}^2) \quad (13)$$

$$v_{r61} = \kappa_{r61} \left(K_{\text{Ci}} x_{\text{Ci}} e^{-\frac{K_{\text{E}} x_{\text{E}}}{V_{\text{N}}}} - K_{\text{Co}} x_{\text{Co}} \right) \quad (14)$$

3.4 Sdet up initial conditions for simulation

```
In [11]: def setX(s):
         sp = s['species']
         X0 = np.zeros(s['n_X'])
         X0[sp.index('So')] = 1e-6
         X0[sp.index('Si')] = 1e-3
```

```

X0[sp.index('Nao')] = 1e-2
X0[sp.index('Nai')] = 0.5

#     X0 *= st.F()

## Normalised value
C_T = 1
others = ['Co', 'CNaO', 'SCNaO', 'Ci', 'CNai', 'SCNai']
for spec in others:
    X0[sp.index(spec)] = C_T/len(others)

#N_C = 3e6
N_C = 7.5e7
N_avo = 6.022e23
C_T_0 = N_C/N_avo

I_0_pA = 1e12*C_T_0/C_T

print(f'N_C = {N_C}; i_0 = {I_0_pA}pA')

#X0 *= st.F()

return X0, I_0_pA

#print(setX(s))

```

4 Comparison with experimental data

```

In [12]: ## Vary E
E0 = -170/1000
E1 = 50/1000
#E1 = 200/1000
X_chemo = {'E':str(E0)}

## Simulation
t = np.linspace(0,1e3,100)
parameter = setPar(s0)
X0, I_0_pA = setX(s)
dat = st.sim(s, sc=sc, t=t, parameter=parameter, X_chemo=X_chemo, X0=X0)

## Extract data
spec = s['species']
reac = s['reaction']
X_ss = dat['X'][-1, :]
print(X_ss[spec.index('E')])

```

```

x_E = f'{E0} + {(E1-E0)/max(t)}*t'
print(x_E)
X_chemo = {'E':x_E}

dat = st.sim(s,sc=sc,t=t,parameter=parameter,X0=X_ss,X_chemo=X_chemo)
f_E = dat['dX'][:,spec.index('E')]
E = dat['X'][:,spec.index('E')]

print(E[0],E[-1])

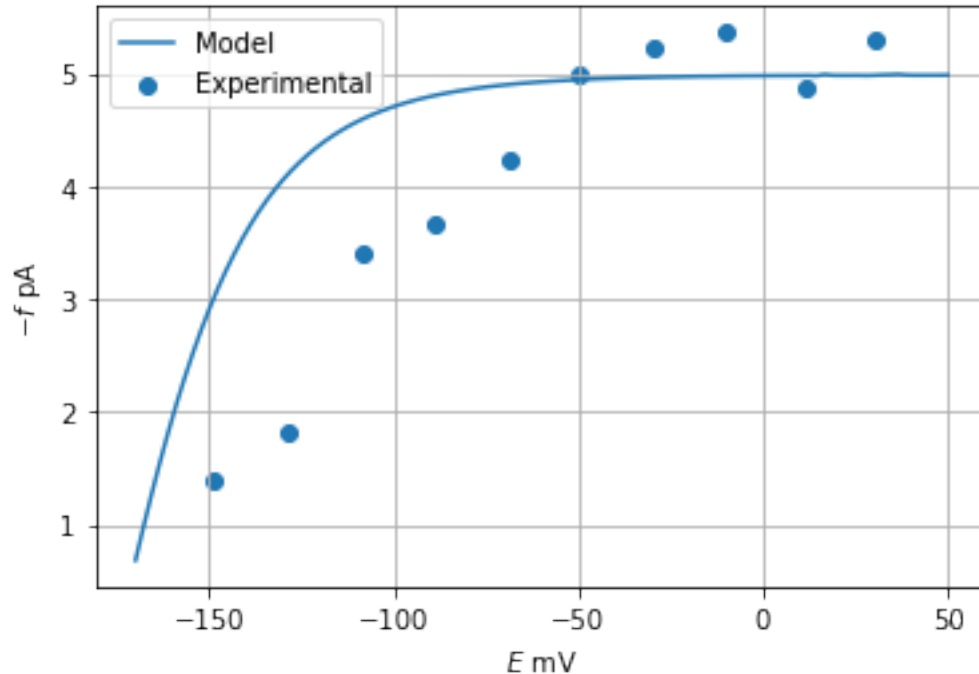
X,Y = loadData()
plt.plot(1000*E,-f_E*I_0_pA, label='Model')
plt.scatter(X,Y,label='Experimental')
plt.legend()
plt.grid()
plt.xlabel('$E$ mV')
plt.ylabel('$-f$ pA')
if SaveFig:
    plt.savefig('Figs/sglt.pdf')
plt.show()

```

```

Error in kappa: 1.2e-05
K_CNai = 0.149
K_CNao = 49.12
K_Ci = 0.3457
K_Co = 40.33
K_Nai = 13.93
K_Nao = 13.96
K_SCNai = 0.099
K_SCNao = 0.099
K_Si = 10.12
K_So = 10.08
r12 K_eq = 160.0000; kappa = 982183.7246
r23 K_eq = 5000.0000; kappa = 19492291.8173
r25 K_eq = 329.6703; kappa = 589.3102
r34 K_eq = 1.0000; kappa = 48730729.5432
r45 K_eq = 0.0656; kappa = 779691672.6910
r56 K_eq = 0.0022; kappa = 6475936.6454
r61 K_eq = 0.0086; kappa = 837303.6199
N_C = 75000000.0; i_0 = 0.00012454334108269677pA
-0.17
-0.17 + 0.00022000000000000003*t
-0.17 0.050000000000000002

```



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