Supplement to “A modeling approach for compounds affecting body composition”

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Part I, Model

PK

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One-compartment model with zero order absorption (duration τ), and first-
order elimination
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PD

```
Tday = mod(t,24) [mod = modulus after division]
EIveh = p1*exp(-p2*tday)
IC = 1-Imax*Cp^n/(Cp^n+IC50^n)
dEIcum_dt = EIveh*IC
```

Part II, Example 1, Model

```
Initial conditions
BW(0) from body mass data
FM(0)=-12.2182+0.8115*BW(0)
FFM(0)=BW(0)-FM(0)

Input: EI(t)

Ordinary differential equations
q1=0.13
q2=0.020
q3=0.090
rho_FM=9.4
rho_FFM=1.8
gamma_FM=0.03
gamma_FFM=0.15
pi_FM=0.18
pi_FFM=0.23
beta=0.4
K=2.1
EIstand=12
deltaEI=EI(t)-EIstand
alpha=q1+q2*exp(q3*FM(t))
aa=alpha/(alpha*rho_FFM+rho_FM)
bb=1/(alpha*rho_FFM+rho_FM)
cc=K+beta*deltaEI+(gamma_FFM+lambda)*FFM+(gamma_FM+lambda)*FM
EE=(cc+pi_FM*bb*EI(t)+pi_FFM*aa*EI(t))/(1+pi_FM*bb+pi_FFM*aa)
dFFM_dt=aa*(EI-EE)
dFM_dt=bb*(EI-EE)
```

Part II, Example 2, Model

```
Initial conditions
BW(0) from body mass data
FM(0) from empirical model Eq. 12 and parameters for male C57BL/6 males in
Table 3 originally derived by Guo and Hall (2009)
FFM(0)=BW(0)-FM(0)
```

```
Input: EI(t)

Ordinary differential equations
q1=0.1
q2=1.89*0.0001
q3=0.45
rho_FM=9.4
rho_FFM=1.8
gamma_FM=0.03
gamma_FFM=0.15
pi_FM=0.18
pi_FFM=0.23
beta=0.4
K=2.1
EIstand=12
deltaEI=EI(t)-EIstand
alpha=q1+q2*exp(q3*FM(t))
aa=alpha/(alpha*rho_FFM+rho_FM)
bb=1/(alpha*rho_FFM+rho_FM)
cc=K+beta*deltaEI+(gamma_FFM+lambda)*FFM+(gamma_FM+lambda)*FM
EE=(cc+pi_FM*bb*EI(t)+pi_FFM*aa*EI(t))/(1+pi_FM*bb+pi_FFM*aa)
dFFM_dt=aa*(EI-EE)
dFM_dt=bb*(EI-EE)
```

Part II, body composition data

```
Fat mass
Rows: mice 1...18
Colums: measurements 1...4

    5.5374   17.2378   21.3537   25.5052
    3.2144   14.6289   19.2030   22.0234
    3.9501   21.9377   21.9259   26.2724
    3.1063   13.5993   15.2549   22.8631
    4.2548   19.3233   25.1137   27.4747
    3.8380   19.0632   23.9580   28.1507
    5.7365   16.6330   17.9642   20.6989
    2.8266   11.0160    8.1311   14.1187
    2.6576   12.9568   20.4541   27.4199
    2.8197    8.4021   16.6000   20.7940
    3.2387   18.5219   20.2929   22.9641
    4.0045   19.1271   22.6930   27.9677
    2.6400    9.8410   12.1806   17.6729
    4.3284   18.8176   22.3394   25.5730
    3.5687   16.7689   22.0099   25.2277
    5.6907   20.1485   24.1920   26.5608
    5.0414   21.2942   26.8575   31.2468
    3.4365   18.2780   19.9177   25.3994


Fat-free (lean) mass
Rows: mice 1...18
Colums: measurements 1...4

   15.6626   18.8623   18.1463   20.1948
   16.3856   18.3711   17.8970   21.1766
   15.8499   13.7623   18.8741   20.8276
   16.3937   17.8007   21.3451   20.1369
   16.9452   21.6767   21.9863   24.3253
   16.1620   19.9368   21.0420   23.5493
```

14.3635	15.0670	17.3358	18.9011
14.9734	18.9840	18.6689	19.4813
16.6424	19.4432	18.1459	20.8801
16.4803	18.7979	18.6000	18.8060
16.4613	18.6781	20.1071	20.6359
16.3955	18.4729	19.9070	21.8323
15.8600	16.9590	18.1194	17.4272
16.3716	19.1824	20.2606	21.6270
17.1313	19.1311	20.0901	21.1723
15.4093	19.4515	20.6080	23.6392
16.8586	19.4058	21.0425	20.7532
17.7635	18.7220	20.1823	22.2006

Part III, model

PK

One-compartment model with linear absorption Michaelis-Menten elimination

PD

```
Initial conditions
BW(0) from body mass data
FM(0)=-12.2182+0.8115*BW(0)
FFM(0)=BW(0)-FM(0)

Input: EI(t)

Ordinary differential equations
q1=0.13
q2=0.020
q3=0.090
rho_FM=9.4
rho_FFM=1.8
gamma_FM=0.03
gamma_FFM=0.15
pi_FM=0.18
pi_FFM=0.23
beta=0.4
K=2.1
EIstand=10
DELTABM=(BW0-BWendTreatment)/BW0;
te=t-TreatmentEnd
if t>=TreatmentEnd
    V2=r5*DELTABM^r6*te*exp(-r4*te);
else
    V2=0
end
V1=r3*t*exp(-r4*t)
EI=r1-V1+V2
Imax=1
drugeffect=1-Imax*C^hill/(C^hill+IC50^hill)
EI=EI*drugeffect
deltaEI=EI(t)-EIstand
alpha=q1+q2*exp(q3*FM(t))
aa=alpha/(alpha*rho_FFM+rho_FM)
bb=1/(alpha*rho_FFM+rho_FM)
cc=K+beta*deltaEI+(gamma_FFM+lambda)*FFM+(gamma_FM+lambda)*FM
EE=(cc+pi_FM*bb*EI(t)+pi_FFM*aa*EI(t))/(1+pi_FM*bb+pi_FFM*aa)
dFFM_dt=aa*(EI-EE)
dFM_dt=bb*(EI-EE)
```