Errors in Differential Equations

Mathematica Differential Equations

1) d[x1]/dt = 0

CellML Equations

1) d[x1]/dt = -v1

Flux equations relating to differential equations:

1) v1 → (k1*x1[t]*x2[t] – kd1*x3[t])

   → d[x1]/dt = -v1

   BUT

   In the paper – says assume no change in x1 (EGF) as it is constantly replenished by the blood (ie source term keeps at zero).

Errors in Original CellML code

Original CellML Code:

1) d[x24]/dt = v17 + v25 + v35 + v40 + v64 + v72 + v130 + v131
2) d[x26]/dt = v18 + v21 + v26 + v31 + v65 + v68 + v73 + v78
3) d[x69]/dt = v74 + v75 - v66
4) d[x82]/dt = -(v96 + v97)

Actual differential equations (verified against flux equations):

1) d[x24]/dt = -(v17 + v25 + v35 + v40 + v64 + v72 + v130 + v131)
2) d[x26]/dt = -(v18 + v21 + v26 + v31 + v65 + v68 + v73 + v78)
3) d[x69]/dt = -(v66 + v74 + v75)
4) d[x82]/dt = v96 + v97

Errors in Kinetic Parameters

Listed in the paper/used in CellML:

1) k13 = 4.28E+04
2) kd18 = 3.80E+04
3) k29 = 1.17E-02
4) k44 = 1.95E-01
5) kd45 = 3.81E+04
6) kd47 = 3.82E+04

7) k48 = 2.38E-01

8) kd49 = 5.80E-02

9) k52 = 8.91E-01

10) kd55 = 3.82E+04

11) k58 = 8.33E-02

Used in Mathematica Model:

Given constants:

- a = 6*10^23
- Vz = 1*10^-12
- KmMEK = 3*10^-7
- kd45 = 3.5 (see below)
- kd44 = 1.83*10^-2
- k48 = 2.38*10^-5 (see below)
- KmPase = 6*10^-8
- kd48 = 8*10^-1
- kd53 = 16
- kd52 = 3.3*10^-2
- KmERK = 3*10^-7

Equations:

1) k13 = 217*10^-2 = 2.17E+00

2) kd18 = 13*10^-1 = 1.30E+00

3) k29 = 7*10^5 / a / Vz

   = 1.17E-06

4) k44 = (kd45 + kd44) / a / Vz / KmMEK

   = 1.95E-05

5) kd45 = 35*10^-1 = 3.50E+00

6) kd47 = 29*10^-1 = 2.90E+00

7) k48 = 143*10^5 / a / Vz

   = 2.38E-05

8) kd49 = k48 * a * Vz * KmPase – kd48

   = 5.68E-02

9) k52 = (kd53 + kd52) / a / Vz / KmERK

   = 8.91E-05

10) kd55 = 57*10^-1 = 5.70E+00

11) k58 = 5*10^6 / a / Vz

   = 8.33E-06

Errors in Given Equations

Original Equations:

1) v9: [(EGF-EGFR*)2-GAP] → [(EGF-EGFRi*)2-GAP]
   → v9 = k6*c(23)*1   -   kd6*c(18)
   c(23) = (EGF-EGFR*)2-GAP-Grb2
   c(18) = (EGF-EGFRi*)2-GAP-Grb2

Correct Solution:

1) c(15) = (EGF-EGFR*)2-GAP

   c(17) = (EGF-EGFRi*)2-GAP

   → v9 = k6*c(15)*1 – kd6*c(17)

Required Changes:

1) v9 =   k6*c(23)*1 - kd6*c(18) → v9 = k6*c(15)*1 – kd6*c(17)

   → d[x15]/dt = v8 – (v9 + v16 + v22 + v32 + v34 + v37 + v39 + v102)

   → d[x17]/dt = v14 + v102 – (v9 + v63 + v69 + v79 + v80 + v81 + v82 + v132)

   → d[x18]/dt = ~~v9~~ + v63 – (v5 + v64 + v133)

   → d[x23]/dt = v16 – (v4 + ~~v9~~ + v17)