

Program used for elementary model calculations of translocation probe distribution

Programming environment is IGOR-Pro Version 4 (Wavemetrics Inc., Lake Oswego, OR)

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#pragma rtGlobals=1           // Use modern global access method.

// to calculate time course of PH-EGFP, call function PH() on the command line
// to calculate time course of C1-EGFP, call function C1() on the command line
// to calculate long time distribution exponential time courses, call function BigTau() on the command line

Function PH()

// model of nuclear diffusion of PH-mRFP for confocal paper
// waves (arrays) for time dependent probe molar concentrations
Make /o/n=400 CMemW, CCytW, CNucW, CLipFreeW, TimeW
Variable Vcell, Vnuc, Vcyt, Anuc          // volumes and areas (liters and um2)
Variable Mem, Cyt, Nuc                  // probe amounts (moles/cell)
Variable kon, koff                     // rate constants (M-1 s-1 and s-1)
Variable Ccyt, Cnuc                   // probe concentrations (Molar)
Variable LipO, LipFree                // Occupied and free lipid (moles/cell)
Variable Pnuc                         // Nuclear permeability (um s-1), Flux
Variable Flux, dBound                 // Flux into nucleus (mol dt-1/cell), binding
mol dt-1/cell
Variable Rnuc, Rcell                 // radii of nucleus and cell (um)
Variable i = 0, t = -1000, dt        // index, time and time-step (s)
Variable MakeLipid, kRemoveLipid, LipidMetab // synth (mole s-1/cell), rate const, dLipid (mol dt-1/cell)
Variable LipidPerSec                  // fraction of lipid produced per second
Variable j                            //counter for point storage

CMemW = NaN
CCytW = NaN
CNucW = NaN
CLipFreeW = NaN
TimeW = NaN

dt = 0.025
Rnuc = 4.4                           //radii in um
Rcell = 6
Pnuc = 0.0032
kon = 0.4e6                          //rate constants for PH/PIP2 binding
koff = 0.5

Ccyt = 0.77e-6                      //starting probe concentrations
Cnuc = 0.1e-6                        //not same in nuc and cyt because PIP2 sucks up cyt

Vcell = 1e-15 * 4 * 0.333 * pi * Rcell^3      //volumes in liters
Vnuc = 1e-15 * 4 * 0.333 * pi * Rnuc^3
Vcyt = Vcell-Vnuc
//print "Vnuc ",Vnuc, "  Vcell ",VCell, "  Vcyt ",Vcyt, "  FracCyt ",Vcyt/Vcell
//Vnuc  3.56461e-13   Vcell  9.03874e-13   Vcyt  5.47413e-13   FracCyt  0.60563
Anuc = 4 * pi * Rnuc^2

LipFree = 5.0e-6 * Vcell             //PIP2 parameters (conc. & synth. and destruct. rates)
LipidPerSec = 0.0085
MakeLipid = LipFree * LipidPerSec
kRemoveLipid = LipidPerSec

Nuc = Cnuc * Vnuc                  //probe moles per cell
Cyt = Ccyt * Vcyt
Mem = 0
CMemW[i] = Mem/Vcyt
CCytW [i] = Cyt/Vcyt
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CNucW[i] = Nuc/Vnuc
CLipFreeW[i] = LipFree/Vcell

Do // big loop of integration in time
    if (t >= 69) // turn on and off the lipid production-destruction at stim times
        kRemoveLipid = 50*LipidPerSec
        if (t > 249)
            kRemoveLipid = LipidPerSec
        endif
    endif
    if (t >= 719)
        kRemoveLipid = 50*LipidPerSec
        if (t >= 879)
            kRemoveLipid = LipidPerSec
        endif
    endif
    if (t >= 0)
        i += 1
    endif
    Do //smaller internal integration loop per plotted time
        j += 1
        t += dt //calculate flux and binding and update concentrations
        Flux = Pnuc * Anuc * (Ccyt - Cnuc) * 1.0e-15 * dt
        dBound = (Ccyt * LipFree * kon - Mem * koff) * dt
        LipidMetab = (MakeLipid - LipFree*kRemoveLipid) * dt //integrate
        Mem += dBound
        Cyt += -Flux -dBound
        Nuc += Flux
        LipFree += LipidMetab - dBound

        CCyt = Cyt/Vcyt
        CNuc = Nuc/Vnuc
    while (j < 5/dt) //end of smaller loop
        j = 0
    // store results in Waves (arrays)
    CMemW[i] = Mem/Vcyt
    CCytW[i] = CCyt
    CNucW[i] = CNuc
    CLipFreeW[i] = LipFree/Vcell
    TimeW[i] = t

    if (i == 15)
        print "flux, dbound, cyt, nuc, free lip, mem"
        print flux, dbound, cyt, nuc, lipfree, mem
    endif

While (t < 1200) //end of big loop

//Display CLipFreeW,CNucW,CCytW,CMemW vs TimeW
//Edit CLipFreeW,CNucW,CCytW,CMemW,TimeW

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End function

Function C10

// model of nuclear diffusion of C1-EGFP for confocal paper

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Variable Ccyt, Cnuc // probe concentrations (Molar)
Variable LipO, LipFree // Occupied and free lipid (moles)
Variable Pnuc // Nuclear permeability (uM s-1), Flux
Variable Flux, dBound // Flux into nucleus (mol dt-1), binding mol dt-1
Variable Rnuc, Rcell // radii of nucleus and cell (um)
Variable i = 0, t = -1000, dt // index, time and time-step (s)
Variable MakeLipid, kRemoveLipid, LipidMetab // synth (mole s-1), rate const, dLipid (mol dt-1)
Variable LipidPerSec, MakeLipid0 // fraction of lipid produced per second
Variable j //counter for point storage

CcMemW = NaN
CcCytW = NaN
CcNucW = NaN
CcLipFreeW = NaN
cTimeW = NaN

dt = 0.025
Rnuc = 4.4
Rcell = 6
Pnuc = 0.005
kon = 0.1e6
koff = 0.3

Ccyt = 0.5e-6
Cnuc = 0.5e-6

Vcell = 1e-15 * 4 * 0.333 * pi * Rcell^3
Vnuc = 1e-15 * 4 * 0.333 * pi * Rnuc^3
Vcyt = Vcell-Vnuc
Anuc = 4 * pi * Rnuc^2

LipFree = 5.0e-6 * Vcell/25
LipidPerSec = 0.022
MakeLipid = LipFree * LipidPerSec
MakeLipid0 = MakeLipid
kRemoveLipid = LipidPerSec

Nuc = Cnuc * Vnuc
Cyt = Ccyt * Vcyt
Mem = 0
CcMemW[i] = Mem/Vcyt
CcCytW [i] = Cyt/Vcyt
CcNucW[i] = Nuc/Vnuc
CcLipFreeW[i] = LipFree/Vcell

Do // big loop of integration in time
  if (t>= 59) // turn on and off the lipid production.destruction
    MakeLipid = Makelipid0 * (14 + 140 * exp(-(t-60)/5))
    if (t>+ 239)
      MakeLipid = Makelipid0
    endif
  endif
  if (t>= 829)
    MakeLipid = Makelipid0 * (14 + 140 * exp(-(t-830)/5))
    if (t >= 1009)
      MakeLipid = Makelipid0
    endif
  endif
  if (t>=0)
    i += 1
  endif
Do //smaller internal integration loop per plotted time
  j += 1

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t += dt

Flux = Pnuc * Anuc * (Ccyt - Cnuc) * 1.0e-15 * dt
dBound = (Ccyt * LipFree * kon - Mem * koff) * dt
LipidMetab = (MakeLipid - LipFree*kRemoveLipid ) * dt
//integrate
Mem += dBound
Cyt += -Flux -dBound
Nuc += Flux
LipFree += LipidMetab - dBound

CCyt = Cyt/Vcyt
CNuc = Nuc/Vnuc
while (j < 5/dt)
j = 0
// store results
CcMemW[i] = Mem/Vcyt
CcCytW[i] = CCyt
CcNucW[i] = CNuc
CcLipFreeW[i] = LipFree/Vcell
cTimeW[i] = t

if (i==15)
    print "flux,      dbound,      cyt,      nuc,      free lip,      mem"
    print flux,dbound, cyt, nuc, lipfree, mem
endif

While (t<1350)

//Display CcLipFreeW,CcNucW,CcCytW,CcMemW vs cTimeW
//Edit CcLipFreeW,CcNucW,CcCytW,CcMemW,cTimeW

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End function

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#pragma rtGlobals=1           // Use modern global access method.

Function BigTau()
// with Pnuc = 0.0025, got tau distribution = 360 s
// with Pnuc = 0.004, got tau distribution = 225 s
// taken from model of nuclear diffusion of PH-mRFP for confocal paper

Make /o/n=400 CMemW, CCytW, CNucW, CLipFreeW, TimeW
//waves for time dependent probe molar concentrations
Variable Vcell, Vnuc, Vcyt, Anuc      // volumes and areas (liters and um2)
Variable Mem, Cyt, Nuc                // probe amounts (moles)
Variable kon, koff                   // rate constants (M-1 s-1 and s-1)
Variable Ccyt, Cnuc                  // probe concentrations (Molar)
Variable LipO, LipFree               // Occupied and free lipid (moles)
Variable Pnuc                        // Nuclear permeability (uM s-1), Flux
Variable Flux, dBound                // Flux into nucleus (mol dt-1), binding mol dt-1
Variable Rnuc, Rcell                 // radii of nucleus and cell (um)
Variable i = 0, t = -1000, dt        // index, time and time-step (s)
Variable MakeLipid, kRemoveLipid, LipidMetab // synth (mole s-1), rate const, dLipid (mol dt-1)
Variable LipidPerSec                 // fraction of lipid produced per second
Variable j                           //counter for point storage

CMemW = NaN
CCytW = NaN
CNucW = NaN
CLipFreeW = NaN
TimeW = NaN

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dt = 0.025
Rnuc = 4.4
Rcell = 6
Pnuc = 0.0025
kon = 1.0e6
koff = 4

Ccyt = 1e-6
Cnuc = 2e-7

Vcell = 1e-15 * 4 * 0.333 * pi * Rcell^3
Vnuc = 1e-15 * 4 * 0.333 * pi * Rnuc^3
Vcyt = Vcell-Vnuc
Anuc = 4 * pi * Rnuc^2

LipFree = 5.0e-6 * Vcell
LipidPerSec = 0.0085
MakeLipid = LipFree * LipidPerSec
kRemoveLipid = LipidPerSec

Nuc = Cnuc * Vnuc
Cyt = Ccyt * Vcyt
Mem = 0
CMemW[i] = Mem/Vcyt
CCytW [i] = Cyt/Vcyt
CNucW[i] = Nuc/Vnuc
CLipFreeW[i] = LipFree/Vcell

Do // big loop of integration in time
    if (t>= 69) // turn on and off the lipid production.destruction
        kRemoveLipid = 50*LipidPerSec
    //
    // if (t>+ 249)
    //     kRemoveLipid = LipidPerSec
    //
    endif
    //
    // if (t>= 719)
    //     kRemoveLipid = 50*LipidPerSec
    //     if (t >= 879)
    //         kRemoveLipid = LipidPerSec
    //
    endif
    endif
    if (t>=0)
        i += 1
    endif
Do //smaller internal integration loop per plotted time
    j += 1
    t += dt

    Flux = Pnuc * Anuc * (Ccyt - Cnuc) * 1.0e-15 * dt
    dBound = (Ccyt * LipFree * kon - Mem * koff) * dt
    LipidMetab = (MakeLipid - LipFree*kRemoveLipid) * dt
    //integrate
    Mem += dBound
    Cyt += -Flux -dBound
    Nuc += Flux
    LipFree += LipidMetab - dBound

    CCyt = Cyt/Vcyt
    CNuc = Nuc/Vnuc
    while (j < 5/dt)
        j = 0
    // store results
    CMemW[i] = Mem/Vcyt
    CCytW [i] = CCyt
    CNucW[i] = CNuc

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CLipFreeW[i] = LipFree/Vcell
TimeW[i] = t

if (i==15)
    print "flux,          dbound,          cyt,          nuc,          free lip,          mem"
    print flux,dbound, cyt, nuc, lipfree, mem
endif

While (t<1200)

//Display CLipFreeW,CNucW,CCytW,CMemW vs TimeW
//Edit CLipFreeW,CNucW,CCytW,CMemW,TimeW
```

End function