Find steady states for non-ratiometric and ratiometric situations

Ra: Active receptor

Ri: Inactive receptor

Total receptor R = Ra+Ri

In a linear gradient, where x goes from 0 to 5 microns:

Ra = R*(f0 + m*x) -- where f0<0.5

Ri =R*(1 - f0 - m*x)

m = (1-2*f0)/5 -- since 5 microns is width of the cell

Ga: Active G protein

Gi : inactive G protein

Gi = G - Ga

Activation: Gi to Ga at kp*Ra*Gi

Inactivation: Ga to Gi at km*Ga (non-ratiometric) OR kr*Ri*Ga (ratiometric)

```
clear all
syms R_a R_i R f_0 m x G_a G_i G k_p k_m k_r GaNR GaR beta


NRSS = k_p*R_a*G_i == k_m*G_a;
RSS = k_p*R_a*G_i == k_r*R_i*G_a;

G_i = G - G_a;
m=(1-2*f_0)/5;
R_a = R*(f_0 + m*x);
R_i=R*(1 - f_0 - m*x);

%solve steady state for non-ratiometric case
NRSS = k_p*R_a*G_i == k_m*G_a;
GaNR = solve(NRSS,G_a);
GaNR = subs(GaNR,k_m, 0.5*R*k_r);
GaNR = subs(GaNR,k_p,k_r/beta)
```

GaNR =

$$\frac{G\,R\,k_r\,\left(f_0 - x\,\left(\frac{2\,f_0}{5} - \frac{1}{5}\right)\right)}{\beta\,\left(\frac{R\,k_r}{2} + \frac{R\,k_r\,\left(f_0 - x\,\left(\frac{2\,f_0}{5} - \frac{1}{5}\right)\right)}{\beta}\right)}$$

```
%disp(latex(GaNR))
```

```
%solve steady state for ratiometric case
RSS = k_p*R_a*G_i == k_r*R_i*G_a;
GaR = solve(RSS,G_a);
GaR = subs(GaR,k_p,k_r/beta)
```

GaR =

$$\frac{G\,R\,k_r\,\left(f_0-x\,\left(\frac{2\,f_0}{5}-\frac{1}{5}\right)\right)}{\beta\,\left(R\,k_r\,\left(x\,\left(\frac{2\,f_0}{5}-\frac{1}{5}\right)-f_0+1\right)+\frac{R\,k_r\,\left(f_0-x\,\left(\frac{2\,f_0}{5}-\frac{1}{5}\right)\right)}{\beta}\right)}$$

```
%disp(latex(GaR))

%Find difference between signal at x=5 and x=0
GaNR5 = subs(GaNR,x,5);
GaNR0 = subs(GaNR,x,0);
deltaGaNR = GaNR5 - GaNR0
```

deltaGaNR =

$$-\frac{G\,R\,k_r\,\left(f_0-1\right)}{\beta\,\left(\frac{R\,k_r}{2}-\frac{R\,k_r\,\left(f_0-1\right)}{\beta}\right)}-\frac{G\,R\,f_0\,k_r}{\beta\,\left(\frac{R\,k_r}{2}+\frac{R\,f_0\,k_r}{\beta}\right)}$$

```
%disp(latex(deltaGaNR))

GaR5 = subs(GaR,x,5);
GaR0 = subs(GaR,x,0);
deltaGaR = GaR5 - GaR0
```

deltaGaR =

$$\frac{G\,R\,f_0\,k_r}{\beta\,\left(R\,k_r\,\left(f_0-1\right)-\frac{R\,f_0\,k_r}{\beta}\right)}-\frac{G\,R\,k_r\,\left(f_0-1\right)}{\beta\,\left(R\,f_0\,k_r-\frac{R\,k_r\,\left(f_0-1\right)}{\beta}\right)}$$

```
%disp(latex(deltaGaR))

%Find ratio of the differences

%express everything in terms of kr
SR = deltaGaR/deltaGaNR
```

SR =

$$-\frac{\frac{G\,R\,f_0\,k_r}{\beta\,\left(R\,k_r\,(f_0-1)-\frac{R\,f_0\,k_r}{\beta}\right)}-\frac{\sigma_2}{\beta\,(R\,f_0\,k_r-\sigma_1)}}{\frac{\sigma_2}{\beta\,\left(\frac{R\,k_r}{2}-\sigma_1\right)}+\frac{G\,R\,f_0\,k_r}{\beta\,\left(\frac{R\,k_r}{2}+\frac{R\,f_0\,k_r}{\beta}\right)}}$$

where

$$\sigma_1=\frac{R\,k_r\,(f_0-1)}{\beta}$$

$$\sigma_2=G\,R\,k_r\,(f_0-1)$$

```
%disp(latex(SR))
%SR = subs(SR,k_m, 0.5*R*k_r);
%SR = subs(SR,k_p,k_r/beta);

%SR = subs(SR,f0,0.3);
%SR = subs(SR,a,4);

SR = simplify(SR)
```

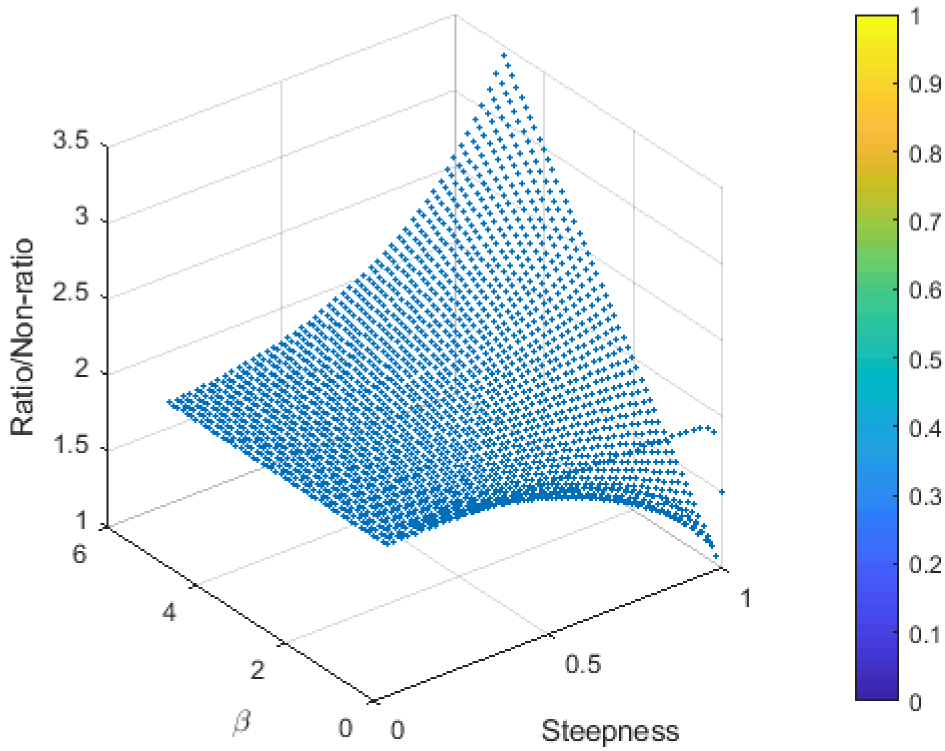
SR =

$$\frac{\beta^2+2\,\beta-4\,{f_0}^2+4\,f_0}{2\,\left(-\beta^2\,{f_0}^2+\beta^2\,f_0+2\,\beta\,{f_0}^2-2\,\beta\,f_0+\beta-{f_0}^2+f_0\right)}$$

```
%disp(latex(SR))
```

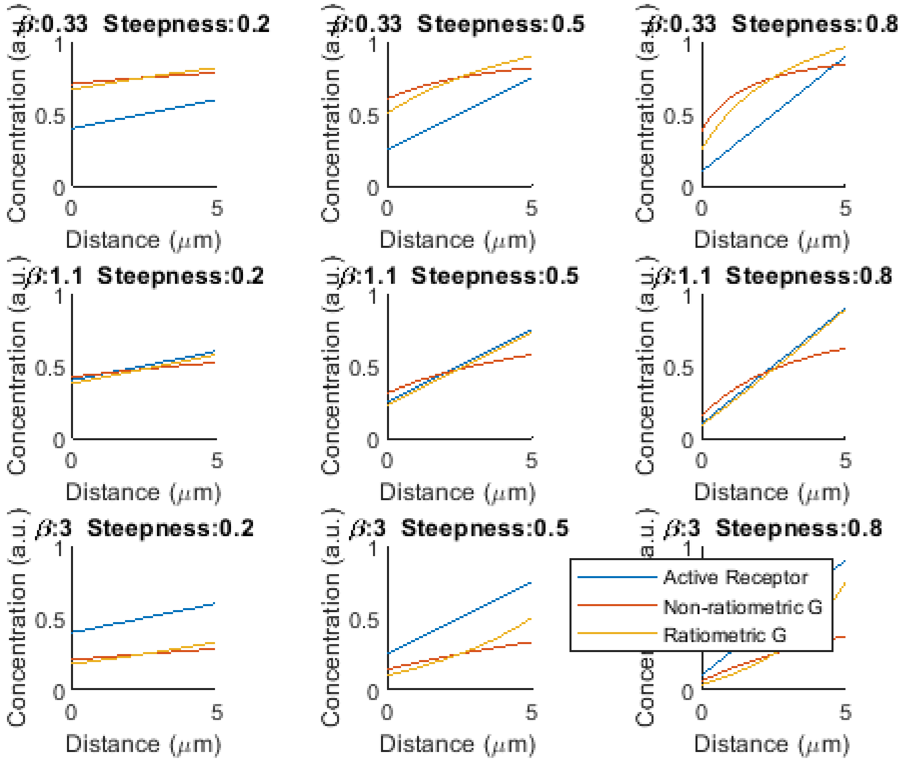
```
%convert to numerical form and plot some graphs

%see what the signal ration for rationmetric/nonratiometrix sensing looks
%like for a range of different parameters.

f_0 = [0.001:0.01:0.49]; %find a range for f_0
beta = [0.001:0.1:5]'; % find a range for a
nf = numel(f_0); %these parameters are meant to define a 2d matrix
na = numel(beta);

f_0 = repmat(f_0,[na 1]);
beta = repmat(beta,[1 nf]);

SR = (beta.^2 + 2*beta - 4*f_0.^2 + 4*f_0)./(2*(- beta.^2.*f_0.^2 + beta.^2.*f_0 + 2*be

%convert f_0 to steepness

steepness = (1-2*f_0);

scatter3(steepness(:),beta(:),SR(:),5,'filled')
colorbar
```

```
xlabel('Steepness'); ylabel('\beta'); zlabel('Ratio/Non-ratio');
  set(gcf ,'renderer' ,'painters') %do this or matlab will fucking fail to generate a v

axis square
```




```
%% plot G protein gradients
close all
betas = [0.33 1.1 3];
f_0s = [ 0.40 0.25 0.1];

plotcount = 0;

for ii = 1:3
    for jj = 1:3


        x = [0:0.2:5];
        f_0 = f_0s(jj);
        m=(1-2*f_0)/5;
        steepness = (1-2*f_0);
        R = 1; G = 1;
        R_a = R*(f_0 + m*x);
        R_i=R*(1 - f_0 - m*x);
        k_r = 1;
        beta = betas(ii);
```

```
        GaNR = (G.*R.*k_r.*(f_0 - x.*((2.*f_0)./5 - 1./5)))./(beta.*((R.*k_r)./2 + (R.*

        GaR = (G.*R.*k_r.*(f_0 - x.*((2.*f_0)./5 - 1./5)))./(beta.*(R.*k_r.*(x.*((2.*f_



        plotcount = plotcount+1;
        subplot( 3,3,plotcount)
        hold on

        title(['\beta:',num2str(beta),'  Steepness:',num2str(steepness)   ])
        plot(x,R_a)
        plot(x,GaNR)

        plot(x,GaR)
        ylim([0 1])
        xlim([0 5])

        xlabel('Distance (\mum)')
        ylabel('Concentration (a.u.)')


        axis square

    end
end


legend('Active Receptor','Non-ratiometric G','Ratiometric G')
```



β:0.33 Steepness:0.2
β:0.33 Steepness:0.5
β:0.33 Steepness:0.8
β:1.1 Steepness:0.2
β:1.1 Steepness:0.5
β:1.1 Steepness:0.8
β:3 Steepness:0.2
β:3 Steepness:0.5
β:3 Steepness:0.8
Concentration (a.u.)
Distance (μm)
Active Receptor
Non-ratiometric G
Ratiometric G