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Supplemental information

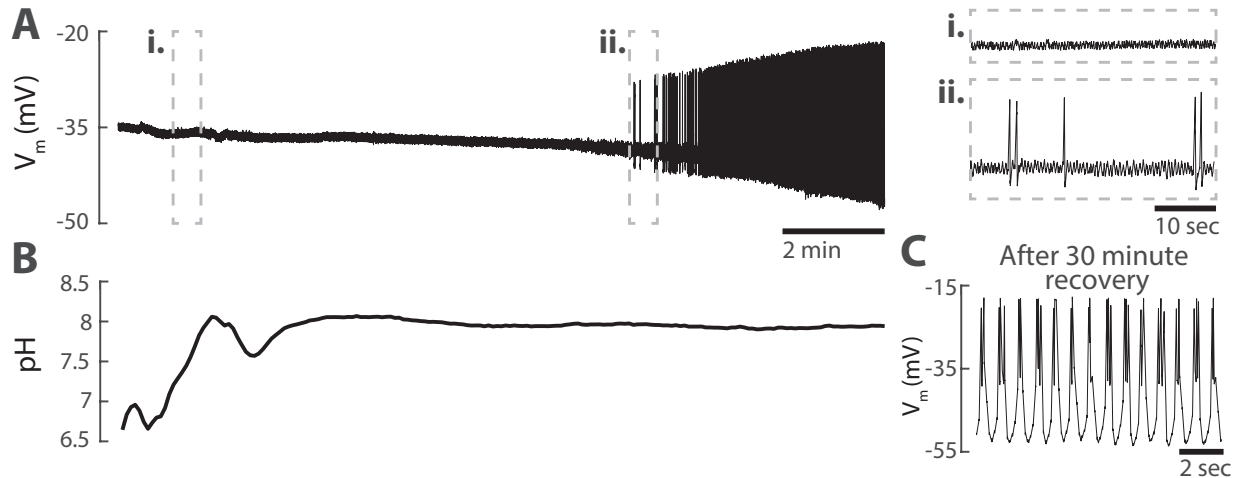
Neuronal oscillator robustness to multiple global perturbations

Jacob Ratliff, Alessio Franci, Eve Marder, and Timothy O'Leary

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Supplemental Materials



Supplemental Figure 1: Recovery of isolated oscillator in physiological pH. **A)** Intracellular recording from the PD neuron during recovery in physiological pH saline. Insets **i.** and **ii.** correspond to the same periods in left and right panels. **B)** pH recorded simultaneously with **A.** **C)** Intracellular recording from the PD neuron after 30 minutes in physiological saline.

Code for generating Figures 6 and 7

```
1. # MirroredFHN_interactive_tempH.jl
2.
3. using Plots, DifferentialEquations, Interact, Blink, LaTeXStrings
4.
5. # Run lines 1-85 to open an interactive window where you can
6. # play around with parameters and simulate the resulting behavior
7.
8. include("MirroredFHN_function.jl")
9.
10. x0=zeros(3)
11.
12. T=20000.
13. tspan=(0,T)
14.
15. ε=0.01
16. εz=0.0001
17.
18. ui = @manipulate for γ=-1.99:0.01:1.0, βf=-0.5:0.001:1.0, βs=-
19.     0.5:0.001:1.0,
20.     dIapp=-0.5:0.001:0.5
```

```

21.     #βfmin=-2.:0.01:2., βfmax=-2.:0.01:2.,
22.     #βsmin=-2.:0.01:2., βsmax=-2.:0.01:2.,
23.
24.     βfmin=βf-0.2;
25.     βfmax=βf+0.2;
26.     βsmin=βs-0.1;
27.     βsmax=βs+0.1;
28.
29.
30.     βfvec=range(βfmin,βfmax,length=10001);
31.
32.     p1=plot(βfvec,lambdaTC.(γ,xTCm.(γ,βfvec)),label="TC variety",lw=2)
33.     p1=plot!(βfvec,lambdaTC.(γ,xTCp.(γ,βfvec)),label="TC
    variety",lw=2)
34.     p1=plot!(βfvec,lambdaHY.(βfvec,γ,xHY.(γ)),label="HY variety",lw=2)
35.     p1=plot!(βfvec,lambdaHYf.(βfvec,γ,xHYf.(γ)),label="fast HY
    variety",lw=2,legend=false,
36.     ylims=(βsmin,βsmax),grid=false)
37.     #xticks = βfmin:(βfmax+0.0001-βfmin)/20:βfmax+0.0001,
    xtickfont = font(5),
38.     #yticks = βsmin:(βsmax+0.0001-βsmin)/40:βsmax+0.0001,
39.     #ytickfont = font(5),dpi=150)
40.     p1=scatter!([βf],[βs],xlabel=L"\beta_f",ylabel=L"\beta_s")
41.
42.     xvec=range(-1.5,1.5,length=250)
43.
44.     p2=plot(xvec,-Ifast.(xvec,βf,βs,γ),lc=:black,label=L"I_{fast}")
45.     p2=plot!(xvec,-Islow.(xvec,βf,βs,γ),ylims=(-
    0.2,0.2),grid=false,lc=:gray,label=L"I_{slow}",
46.     legend=false,xlabel=L"V",)
47.
48.     ITC=I_TC(βf,γ)
49.     if isnan(ITC)
50.         ITC=0.0
51.     end
52.
53.     Iapp=ITC+dIapp
54.
55.     p=(βf,γ,βs,Iapp,ε,εz)
56.
57.     prob = ODEProblem(MirroredFHN_ODE!,x0,tspan,p)
58.
59.     sol = solve(prob,BS3(),reltol=1e-3,abstol=1e-6);
60.
61.     tt=minimum(findall(t->t>T/2,sol.t))
62.     p3=plot(sol.t[tt:length(sol.t)],sol[1,tt:length(sol.t)],
63.     legend=false,grid=false,ylims=(-1.33,1.0))
64.
65.     xnullcline(x,y) = -x^3 + βf*x - 1/2*γ*x^2 - γ*βs*x - (y+βs)^2 -
    1/2*γ*y^2
66.     ynullcline(x,y) = -y + x
67.
68.     xvec=range(-1.1,1.0,length=250)
69.     yvec=range(-1.1,0.35,length=250)
70.
71.     p4=contour(xvec,yvec,xnullcline,levels=[-ITC],lc=:red)
72.     p4=contour!(xvec,yvec,ynullcline,levels=[0],colorbar=false)

```

```

73.
74.     l = @layout [
75.         [a{0.5w} b{0.5w}
76.         c{1.0w,0.75h}] d{0.5w}
77.     ]
78.
79.     vbox(
80.         plot(p1,p2,p3,p4,layout=l,size=(1400,500))
81.     )
82.
83. end
84.
85. w = Window()
86. body!(w, ui)
87.
88.
89.
90. ## Static Drawing - In this part you can generate the static
91. # figures used to produce Figures 6 and 7
92. # uncomment the various parts of the code to define parameters
93. # as in figure 6 and being able to generate all the behaviors
94. # in that figure
95.
96. include("MirroredFHN_function.jl")
97.
98.  $\gamma = -0.1$ 
99.
100.  $\beta_{fmin} = -0.1$ 
101.  $\beta_{fmax} = 0.5$ 
102.  $\beta_{smin} = 0.1$ 
103.  $\beta_{smax} = 0.5$ 
104.
105. ## perturbation paths
106. # Starting point (A)
107. #  $\beta_f = 0.3$ 
108. #  $\beta_s = 0.15$ 
109. #  $ITC = I\_TC(\beta_f, \gamma)$ 
110. # if isnan(ITC)
111. #      $ITC = 0.0$ 
112. # end
113. #  $I_{app} = ITC - 0.4$ 
114.
115. # Interm ph (B)
116. #  $\beta_f = 0.25$ 
117. #  $\beta_s = 0.285$ 
118. #  $ITC = I\_TC(\beta_f, \gamma)$ 
119. # if isnan(ITC)
120. #      $ITC = 0.0$ 
121. # end
122. #  $I_{app} = ITC - 0.25$ 
123.
124. # Interm ph 3 (C)
125. #  $\beta_f = -0.05$ 
126. #  $\beta_s = 0.35$ 
127. #  $ITC = I\_TC(\beta_f, \gamma)$ 
128. # if isnan(ITC)
129. #      $ITC = 0.0$ 

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130. # end
131. # Iapp=ITC-0.0
132.
133.
134. # Interm Temp 2 (D)
135. #  $\beta_f=0.05$ 
136. #  $\beta_s=0.145$ 
137. #  $ITC=I\_TC(\beta_f, \gamma)$ 
138. # if isnan(ITC)
139. #     ITC=0.0
140. # end
141. # Iapp=ITC-0.3975
142.
143. # Final temp (E)
144.  $\beta_f=-0.033$ 
145.  $\beta_s=0.11$ 
146.  $ITC=I\_TC(\beta_f, \gamma)$ 
147. if isnan(ITC)
148.     ITC=0.0
149. end
150. Iapp=ITC-0.366
151.
152. D=0.001
153. T=40000.
154. tspan=(0, T)
155.
156. p1, p2, p3, p4, p5=plot_pchart( $\gamma, \beta_{fmin}, \beta_{fmax}, \beta_{smin}, \beta_{smax}, \beta_f, \beta_s, Iapp, D, T, tspan$ )
157. #p1: parameter chart
158. #p2: IV curves
159. #p3: solution over time
160. #p4: phase plane
161. #p5: composite figure
162. plot(p3)

```

```

1. # MirroredFHN_function.jl
2.
3. function MirroredFHN_ODE!(du, u, p, t)
4.
5.      $\beta_f = p[1]$ 
6.      $\gamma = p[2]$ 
7.      $\beta_s = p[3]$ 
8.     Iapp = p[4]
9.      $\varepsilon = p[5]$ 
10.     $\varepsilon z = p[6]$ 
11.
12.    x = @view u[1]
13.    y = @view u[2]
14.    z = @view u[3]
15.
16.    dx = @view du[1]
17.    dy = @view du[2]
18.    dz = @view du[3]
19.
20.    @. dx =  $-x^3 + \beta_f*x - 1/2*\gamma*x^2 - \gamma*\beta_s*x - (y+\beta_s)^2 - 1/2*\gamma*y^2 -$ 
    z + Iapp

```

```

21.     @. dy = ε*(-y+x)
22.     @. dz = εz*(-z+x)
23.
24. end
25.
26. function MirroredFHN_σ(du,u,p,t)
27.     D=p[7]
28.     du[1]=0.0
29.     du[2]=D
30.     du[3]=0.0
31. end
32.
33. ## IV curves
34.
35. Ifast(x,βf,βs,γ) = -x^3 + βf*x - 1/2*γ*x^2 - γ*βs*x
36. Islow(x,βf,βs,γ) = -x^3 + βf*x - 1/2*γ*x^2 - γ*βs*x - (x+βs)^2 -
1/2*γ*x^2
37. Iuslow(x,βf,βs,γ) = -x^3 + βf*x - 1/2*γ*x^2 - γ*βs*x - (x+βs)^2 -
1/2*γ*x^2 - x
38.
39. ## Transition varieties
40.
41. function xTCm(gamma,beta)
42.     if gamma^4 + 48*beta>0
43.         f=( gamma^2 - (gamma^4 + 48*beta)^(1/2) )/( 12 )
44.     else
45.         f=NaN
46.     end
47.     return f
48. end
49.
50. function xTCp(gamma,beta)
51.     if gamma^4 + 48*beta>0
52.         f=( gamma^2 + (gamma^4 + 48*beta)^(1/2) )/( 12 )
53.     else
54.         f=NaN
55.     end
56.     return f
57. end
58.
59. lambdaTC(gamma,x)=- (x*(2+gamma))/2
60.
61. xHY(gamma)=- (1+gamma)/3
62. lambdaHY(beta,gamma,x)=(beta-3*x^2-x*(2+2*gamma))/(2+gamma)
63.
64. xHYf(gamma)=-gamma/6
65. lambdaHYf(beta,gamma,x)=(beta-gamma*x-3*x^2)/gamma
66.
67. I_TC(beta,gamma)=- (-xTCm(gamma,beta)^3+beta*xTCm(gamma,beta)-
68.     (xTCm(gamma,beta)+lambdaTC(gamma,xTCm(gamma,beta)))^2-
gamma*xTCm(gamma,beta)*(xTCm(gamma,beta)+lambdaTC(gamma,xTCm(gamma,beta)
)))
69. I_Hy(beta,gamma)=- (-xHY(gamma)^3+beta*xHY(gamma)-
(xHY(gamma)+lambdaHY(beta,gamma,xHY(gamma)))^2)
70.
71. ## Plotting
72.

```

```

73. function plot_pchart( $\gamma$ ,  $\beta$ fmin,  $\beta$ fmax,  $\beta$ smin,  $\beta$ smax,  $\beta$ f,  $\beta$ s, Iapp, D, T, tspan)
74.
75.      $\beta$ fvec=range( $\beta$ fmin,  $\beta$ fmax, length=1000);
76.
77.     p1=plot( $\beta$ fvec, lambdaTC. ( $\gamma$ , xTCm. ( $\gamma$ ,  $\beta$ fvec)), label="TC variety", lw=2)
78.     p1=plot!( $\beta$ fvec, lambdaTC. ( $\gamma$ , xTCp. ( $\gamma$ ,  $\beta$ fvec)), label="TC
    variety", lw=2)
79.     p1=plot!( $\beta$ fvec, lambdaHY. ( $\beta$ fvec,  $\gamma$ , xHY. ( $\gamma$ )), label="HY variety", lw=2)
80.     p1=plot!( $\beta$ fvec, lambdaHYf. ( $\beta$ fvec,  $\gamma$ , xHYf. ( $\gamma$ )), label="fast HY
    variety", lw=2, legend=false,
81.     ylims=( $\beta$ smin,  $\beta$ smax), grid=false)
82.     #xticks =  $\beta$ fmin:( $\beta$ fmax+0.0001- $\beta$ fmin)/20: $\beta$ fmax+0.0001,
    xtickfont = font(5),
83.     #yticks =  $\beta$ smin:( $\beta$ smax+0.0001- $\beta$ smin)/40: $\beta$ smax+0.0001,
84.     #ytickfont = font(5), dpi=150)
85.     p1=scatter!([ $\beta$ f], [ $\beta$ s], xlabel=L"\beta_f", ylabel=L"\beta_s")
86.
87.     xvec=range(-1.5, 1.5, length=250)
88.
89.     p2=plot(xvec, -Ifast. (xvec,  $\beta$ f,  $\beta$ s,  $\gamma$ ), lc=:black, label=L"I_{fast}")
90.     p2=plot!(xvec, -Islow. (xvec,  $\beta$ f,  $\beta$ s,  $\gamma$ ), ylims=(-
    0.2, 0.2), grid=false, lc=:gray, label=L"I_{slow}",
91.     legend=false, xlabel=L"\gamma",)
92.
93.     p=( $\beta$ f,  $\gamma$ ,  $\beta$ s, Iapp,  $\epsilon$ ,  $\epsilon$ z, D)
94.
95.     #prob = ODEProblem(MirroredFHN_ODE!, x0, tspan, p)
96.     #sol = solve(prob, BS3(), reltol=1e-3, abstol=1e-6);
97.     x0=zeros(3)
98.     prob = SDEProblem(MirroredFHN_ODE!, MirroredFHN_ $\sigma$ , x0, tspan, p)
99.     sol = solve(prob, saveat=10);
100.
101.     #tt=minimum(findall(t->t>T/2, sol.t))
102.     p3=plot(sol.t[1:length(sol.t)], sol[1, 1:length(sol.t)],
103.     legend=false, grid=false, ylims=(-1.1, 1.0), xlims=(20000, 40000))
104.
105.     xnullcline(x, y) = -x^3 +  $\beta$ f*x - 1/2* $\gamma$ *x^2 -  $\gamma$ * $\beta$ s*x - (y+ $\beta$ s)^2 -
    1/2* $\gamma$ *y^2
106.     ynullcline(x, y) = -y + x
107.
108.     xvec=range(-1.0, 1.0, length=250)
109.     yvec=range(-1.1, 0.35, length=250)
110.
111.     p4=contour(xvec, yvec, xnullcline, levels=[-ITC+0*0.004], lc=:red)
112.     p4=contour!(xvec, yvec, ynullcline, levels=[0], colorbar=false)
113.
114.     l = @layout [
115.         [a{0.5w} b{0.5w}
116.         c{1.0w, 0.75h}] d{0.5w}
117.     ]
118.
119.     p5=plot(p1, p2, p3, p4, layout=l, size=(1400, 500))
120.
121.     return p1, p2, p3, p4, p5
122.
123. end

```