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Supplemental information

Neuronal oscillator robustness to multiple global perturbations

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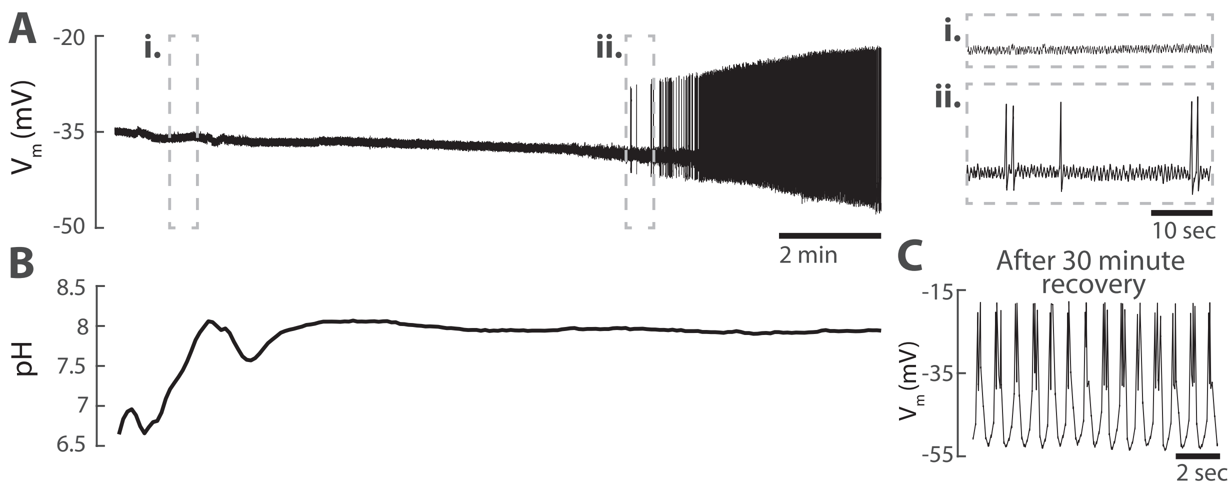
Supplemental Materials



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=-
   0.5:0.001:1.0,
19.      dIapp=-0.5:0.001:0.5
20.
```

```
    #βfmin=-2.:0.01:2., βfmax=-2.:0.01:2.,
    #βsmin=-2.:0.01:2., βsmax=-2.:0.01:2.,

    βfmin=βf-0.2;
    βfmax=βf+0.2;
    βsmin=βs-0.1;
    βsmax=βs+0.1;


    βfvec=range(βfmin,βfmax,length=10001);

    p1=plot(βfvec,lambdaTC.(γ,xTCm.(γ,βfvec)),label="TC variety",lw=2)
    p1=plot!(βfvec,lambdaTC.(γ,xTCp.(γ,βfvec)),label="TC variety",lw=2)
    p1=plot!(βfvec,lambdaHY.(βfvec,γ,xHY.(γ)),label="HY variety",lw=2)
    p1=plot!(βfvec,lambdaHYf.(βfvec,γ,xHYf.(γ)),label="fast HY variety", lw=2, legend=false,
        ylims=(βsmin,βsmax),grid=false)
        #xticks = βfmin:(βfmax+0.0001-βfmin)/20:βfmax+0.0001, xtickfont = font(5),
        #yticks = βsmin:(βsmax+0.0001-βsmin)/40:βsmax+0.0001,
        #ytickfont = font(5),dpi=150)
    p1=scatter!([βf],[βs],xlabel=L"\beta_f",ylabel=L"\beta_s")

    xvec=range(-1.5,1.5,length=250)

    p2=plot(xvec,-Ifast.(xvec,βf,βs,γ),lc=:black,label=L"I_{fast}")
    p2=plot!(xvec,-Islow.(xvec,βf,βs,γ),ylims=(-0.2,0.2),grid=false,lc=:gray,label=L"I_{slow}",
    legend=false,xlabel=L"V",)

    ITC=I_TC(βf,γ)
    if isnan(ITC)
        ITC=0.0
    end

    Iapp=ITC+dIapp

    p=(βf,γ,βs,Iapp,ε,εz)

    prob = ODEProblem(MirroredFHN_ODE!,x0,tspan,p)

    sol = solve(prob,BS3(),reltol=1e-3,abstol=1e-6);

    tt=minimum(findall(t->t>T/2,sol.t))
    p3=plot(sol.t[tt:length(sol.t)],sol[1,tt:length(sol.t)],
    legend=false,grid=false,ylims=(-1.33,1.0))

    xnullcline(x,y)= -x^3 + βf*x - 1/2*γ*x^2 - γ*βs*x - (y+βs)^2 - 1/2*γ*y^2
    ynullcline(x,y)= -y + x

    xvec=range(-1.1,1.0,length=250)
    yvec=range(-1.1,0.35,length=250)

    p4=contour(xvec,yvec,xnullcline,levels=[-ITC],lc=:red)
    p4=contour!(xvec,yvec,ynullcline,levels=[0],colorbar=false)
```

```julia

    l = @layout [
        [a{0.5w} b{0.5w}
        c{1.0w,0.75h}] d{0.5w}
    ]

    vbox(
    plot(p1,p2,p3,p4,layout=l,size=(1400,500))
    )

end

w = Window()
body!(w, ui)



## Static Drawing - In this part you can generate the static
# figures used to produce Figures 6 and 7
# uncomment the various parts of the code to define parameters
# as in figure 6 and being able to generate all the behaviors
# in that figure

include("MirroredFHN_function.jl")

γ=-0.1

βfmin=-0.1
βfmax=0.5
βsmin=0.1
βsmax=0.5

## perturbation paths
# Starting point (A)
# βf=0.3
# βs=0.15
# ITC=I_TC(βf,γ)
# if isnan(ITC)
#     ITC=0.0
# end
# Iapp=ITC-0.4

# Interm ph (B)
# βf=0.25
# βs=0.285
# ITC=I_TC(βf,γ)
# if isnan(ITC)
#     ITC=0.0
# end
# Iapp=ITC-0.25

# Interm ph 3 (C)
# βf=-0.05
# βs=0.35
# ITC=I_TC(βf,γ)
# if isnan(ITC)
#     ITC=0.0
```

```
# end
# Iapp=ITC-0.0


# Interm Temp 2 (D)
# βf=0.05
# βs=0.145
# ITC=I_TC(βf,γ)
# if isnan(ITC)
#     ITC=0.0
# end
# Iapp=ITC-0.3975

# Final temp (E)
βf=-0.033
βs=0.11
ITC=I_TC(βf,γ)
if isnan(ITC)
    ITC=0.0
end
Iapp=ITC-0.366

D=0.001
T=40000.
tspan=(0,T)

p1,p2,p3,p4,p5=plot_pchart(γ,βfmin,βfmax,βsmin,βsmax,βf,βs,Iapp,D,T,tspan)
#p1: parameter chart
#p2: IV curves
#p3: solution over time
#p4: phase plane
#p5: composite figure
plot(p3)
```

```
# MirroredFHN_function.jl

function MirroredFHN_ODE!(du,u,p,t)

    βf = p[1]
    γ = p[2]
    βs = p[3]
    Iapp = p[4]
    ε = p[5]
    εz = p[6]

    x = @view u[1]
    y = @view u[2]
    z = @view u[3]

    dx = @view du[1]
    dy = @view du[2]
    dz = @view du[3]

    @. dx = -x^3 + βf*x - 1/2*γ*x^2 - γ*βs*x - (y+βs)^2 - 1/2*γ*y^2 - z + Iapp
```

```
    @. dy = ε*(-y+x)
    @. dz = εz*(-z+x)

end

function MirroredFHN_σ(du,u,p,t)
    D=p[7]
    du[1]=0.0
    du[2]=D
    du[3]=0.0
end

## IV curves

Ifast(x,βf,βs,γ) = -x^3 + βf*x - 1/2*γ*x^2 - γ*βs*x
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
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

## Transition varieties

function xTCm(gamma,beta)
    if gamma^4 + 48*beta>0
        f=( gamma^2 - (gamma^4 + 48*beta)^(1/2) )/( 12 )
    else
        f=NaN
    end
    return f
end

function xTCp(gamma,beta)
    if gamma^4 + 48*beta>0
        f=( gamma^2 + (gamma^4 + 48*beta)^(1/2) )/( 12 )
    else
        f=NaN
    end
    return f
end

lambdaTC(gamma,x)=-(x*(2+gamma))/2

xHY(gamma)=-(1+gamma)/3
lambdaHY(beta,gamma,x)=(beta-3*x^2-x*(2+2*gamma))/(2+gamma)

xHYf(gamma)=-gamma/6
lambdaHYf(beta,gamma,x)=(beta-gamma*x-3*x^2)/gamma

I_TC(beta,gamma)=-(-xTCm(gamma,beta)^3+beta*xTCm(gamma,beta)-
    (xTCm(gamma,beta)+lambdaTC(gamma,xTCm(gamma,beta)))^2-gamma*xTCm(gamma,beta)*(xTCm(gamma,beta)+lambdaTC(gamma,xTCm(gamma,beta))))
I_Hy(beta,gamma)=-(-xHY(gamma)^3+beta*xHY(gamma)-(xHY(gamma)+lambdaHY(beta,gamma,xHY(gamma)))^2)

## Plotting

```

```
function plot_pchart(γ,βfmin,βfmax,βsmin,βsmax,βf,βs,Iapp,D,T,tspan)

    βfvec=range(βfmin,βfmax,length=1000);

    p1=plot(βfvec,lambdaTC.(γ,xTCm.(γ,βfvec)),label="TC variety",lw=2)
    p1=plot!(βfvec,lambdaTC.(γ,xTCp.(γ,βfvec)),label="TC variety",lw=2)
    p1=plot!(βfvec,lambdaHY.(βfvec,γ,xHY.(γ)),label="HY variety",lw=2)
    p1=plot!(βfvec,lambdaHYf.(βfvec,γ,xHYf.(γ)),label="fast HY variety", lw=2, legend=false,
        ylims=(βsmin,βsmax),grid=false)
        #xticks = βfmin:(βfmax+0.0001-βfmin)/20:βfmax+0.0001, xtickfont = font(5),
        #yticks = βsmin:(βsmax+0.0001-βsmin)/40:βsmax+0.0001,
        #ytickfont = font(5),dpi=150)
    p1=scatter!([βf],[βs],xlabel=L"\beta_f",ylabel=L"\beta_s")

    xvec=range(-1.5,1.5,length=250)

    p2=plot(xvec,-Ifast.(xvec,βf,βs,γ),lc=:black,label=L"I_{fast}")
    p2=plot!(xvec,-Islow.(xvec,βf,βs,γ),ylims=(-0.2,0.2),grid=false,lc=:gray,label=L"I_{slow}",
    legend=false,xlabel=L"V",)

    p=(βf,γ,βs,Iapp,ε,εz,D)

    #prob = ODEProblem(MirroredFHN_ODE!,x0,tspan,p)
    #sol = solve(prob,BS3(),reltol=1e-3,abstol=1e-6);
    x0=zeros(3)
    prob = SDEProblem(MirroredFHN_ODE!,MirroredFHN_σ,x0,tspan,p)
    sol = solve(prob,saveat=10);

    #tt=minimum(findall(t->t>T/2,sol.t))
    p3=plot(sol.t[1:length(sol.t)],sol[1,1:length(sol.t)],
    legend=false,grid=false,ylims=(-1.1,1.0),xlims=(20000,40000))

    xnullcline(x,y)= -x^3 + βf*x - 1/2*γ*x^2 - γ*βs*x - (y+βs)^2 - 1/2*γ*y^2
    ynullcline(x,y)= -y + x

    xvec=range(-1.0,1.0,length=250)
    yvec=range(-1.1,0.35,length=250)

    p4=contour(xvec,yvec,xnullcline,levels=[-ITC+0*0.004],lc=:red)
    p4=contour!(xvec,yvec,ynullcline,levels=[0],colorbar=false)

    l = @layout [
        [a{0.5w} b{0.5w}
        c{1.0w,0.75h}] d{0.5w}
    ]

    p5=plot(p1,p2,p3,p4,layout=l,size=(1400,500))

    return p1,p2,p3,p4,p5

end
```