Biological Modeling of Neural Networks (PAL

Week 3 - Reducing detail: Two-dimensional neuron models

Wulfram Gerstner EPFL, Lausanne, Switzerland

Reading for week 3: NEURONAL DYNAMICS - Ch. 4.1- 4.3

Cambridge Univ. Press

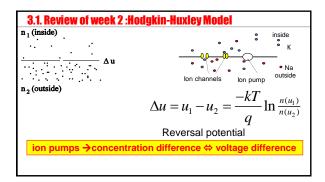
3.1 From Hodgkin-Huxley to 2D

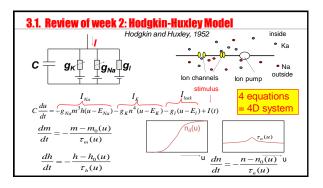
- Overview: From 4 to 2 dimensions
 MathDetour 1: Exploiting similarities
 MathDetour 2: Separation of time scales
- 3.2 Phase Plane Analysis
- Role of nullclines 3.3 Analysis of a 2D Neuron Model

 - constant input vs pulse input MathDetour 3: Stability of fixed points

| 3.1. Review of week 2 :Hodgkin-Huxley Model |
|--|
| cortical neuron T · d/du = Hodgkin-Huxley mode Compartmental model |
| |

| 3.1 Review of week 2: Hodgkin-Huxley Model | | | | | |
|--|--|--|--|--|--|
| Week 2: Cell membrane contains | Dendrites (week x:video): Active processes? | | | | |
| - ion channels - ion pumpsa -70mV | assumption: passive dendrite point neuron spike generation | | | | |
| lons/proteins | potential | | | | |

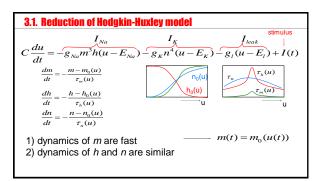




| | 1 |
|---|---|
| Week 3 – 3.1. Overview and aims | |
| Can we understand the dynamics of the HH model? | |
| → Reduce from 4 to 2 equations | |
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| | |
| Week 3 – Quiz 3.1. | |
| A - A biophysical point neuron model with 3 ion channels, leach with activation and inactivation, | |
| has a total number of equations equal to [] 3 or [] 4 or | |
| [] 6 or | |
| | |
| Uideo Week 3.1-3.5 (82 minutes total) | |
| http://lcn.epfl.ch/~gerstner/NeuronalDynamics-MOOC1.html | |
| , a | |
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| Week 3 – 3.1. Overview and aims | |
| Toward a | |
| two-dimensional neuron model | |
| -Reduction of Hodgkin-Huxley to 2 dimension -step 1: separation of time scales | |
| -step 2: exploit similarities/correlations | |

| 3.1. Reduction of Hodgkin-Huxley model | | | | | |
|---|---|--|--|--|--|
| $C\frac{du}{dt} = \overbrace{-g_{Na}m^3h(u - E_{Na})}^{I_{Na}}$ | | | | | |
| $\frac{dm}{dt} = -\frac{m - m_0(u)}{\tau_m(u)}$ $\frac{dh}{dt} = -\frac{h - h_0(u)}{\tau_h(u)}$ | $m_0(u)$ $n_0(u)$ $\tau_n(u)$ $\tau_m(u)$ | | | | |
| $\frac{dn}{dt} = -\frac{n - n_0(u)}{\tau_n(u)}$ 1) dynamics of <i>m</i> are fast | | | | | |
| | | | | | |

| Reduction of dimensionality: Separation of time scales | | | |
|--|---|--|--|
| $\tau_1 \frac{dx}{dt} = -x + c(t)$ | Two coupled differential equations $\tau_i \frac{dx}{dt} = -x + h(y)$ | | |
| Exercise 1 (week 3) (later today!) | $\tau_2 \frac{dy}{dt} = f(y) + g(x)$ Separation of time scales $\tau_1 \ll \tau_2 \rightarrow x = h(y)$ | | |
| | Reduced 1-dimensional system $\tau_2 \frac{dy}{dt} = f(y) + g(h(y))$ | | |



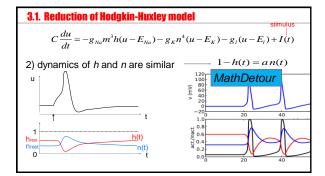
3.1. Reduction of Hodgkin-Huxley model

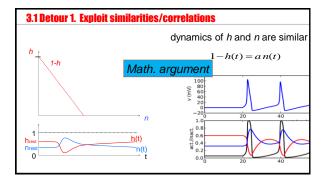
Reduction of Hodgkin-Huxley Model to 2 Dimension

-step 1: separation of time scales

-step 2: exploit similarities/correlations

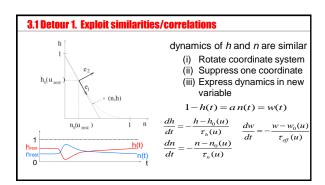
Now!





3.1 Detour 1. Exploit similarities/correlations dynamics of h and n are similar $1-h(t)=a\,n(t)$ at rest $\frac{dh}{dt}=-\frac{h-h_0(u)}{\tau_k(u)}$ these h(t) $\frac{dh}{dt}=n-n_0(u)$

 $\tau_n(u)$



| 3.1. Reduction of Hodgkin-Huxley model |
|--|
| $C\frac{du}{dt} = -g_{Na}[m(t)]^{3}h(t)(u(t) - E_{Na}) - g_{K}[n(t)]^{4}(u(t) - E_{K}) - g_{I}(u(t) - E_{I}) + I(t)$ |
| $C\frac{du}{dt} = -g_{Na} m_0(u)^3 (1 - w)(u - E_{Na}) - g_K \left[\frac{w}{a}\right]^4 (u - E_K) - g_I(u - E_I) + I(t)$ |
| 1) dynamics of m are fast $ m(t) = m_0(u(t)) $ |
| 2) dynamics of h and n are similar $ \frac{1-h(t)}{2} = an(t)$ |
| w(t) $w(t)$ |
| $\frac{dh}{dt} = -\frac{h - h_0(u)}{\tau_h(u)} \qquad dw = w - w_0(u)$ |
| $\frac{dt}{dt} = \frac{\tau_n(u)}{\tau_n(u)} \qquad \frac{dw}{dt} = -\frac{w - w_0(u)}{\tau_{eff}(u)}$ |

| R | 11 | R | led | luct | inn | ωf | Ho | lak | in-l | Hiry | ev | mod | le |
|---|----|---|-----|------|-----|----|----|-----|------|------|----|-----|----|

$$C\frac{du}{dt} = -g_{Na} m_0(u)^3 (1-w)(u-E_{Na}) - g_K (\frac{w}{a})^4 (u-E_K) - g_I(u-E_I) + I(t)$$

$$\frac{dw}{dt} = -\frac{w-w_0(u)}{\tau_{eff}}(u)$$

$$\tau \frac{du}{dt} = F(u(t), w(t)) + RI(t)$$

$$\tau_w \frac{dw}{dt} = G(u(t), w(t))$$

3.1. Reduction to 2 dimensions

2-dimensional equation

$$C\frac{du}{dt} = f(u(t), w(t)) + I(t)$$
$$\frac{dw}{dt} = g(u(t), w(t))$$

Enables graphical analysis! ———— Phase plane analysis

- -Discussion of threshold
- Constant input current vs pulse input
- -Type I and II
- Repetitive firing

Week 3 – Quiz 3.2-similar dynamics

Exploiting similarities:

A sufficient condition to replace two gating variables r,s by a single gating variable w is

- [] Both r and s have the same time constant (as a function of u)
- [] Both r and s have the same activation function
- [] Both r and s have the same time constant (as a function of u)

AND the same activation function

- [] Both r and s have the same time constant (as a function of u)
- AND activation functions that are identical after some additive rescaling
- [] Both r and s have the same time constant (as a function of u)
- AND activation functions that are identical after some multiplicative rescaling

Biological Modeling of Neural Networks



Week 3 - Reducing detail:

Two-dimensional neuron models

√ 3.1 From Hodgkin-Huxley to 2D

- Overview: From 4 to 2 dimensions
- MathDetour 1: Exploiting similarities
 MathDetour 2: Separation of time scales

3.2 Phase Plane Analysis - Role of nullclines

3.3 Analysis of a 2D Neuron Model

- constant input vs pulse input
- MathDetour 3: Stability of fixed points
- Wulfram Gerstner EPFL, Lausanne, Switzerland

| 3.2. Reduced | Hodgkin-Huxley | / model |
|--------------|----------------|---------|
|--------------|----------------|---------|

$$C\frac{du}{dt} = -g_{Na} \frac{I_{Na}}{m_0(u)^3 (1-w)(u-E_{Na})} - g_K (\frac{w}{a})^4 (u-E_K) - g_I (u-E_I) + I(t)$$

$$\frac{dw}{dt} = -\frac{w - w_0(u)}{\tau_w(u)}$$

stimulus

$$\tau \frac{du}{dt} = F(u, w) + RI(t)$$
$$\tau_{w} \frac{dw}{dt} = G(u, w)$$

$$\tau_w \frac{dw}{dt} = G(u, w)$$

3.2. Phase Plane Analysis/nullclines

2-dimensional equation

$$\tau \frac{du}{dt} = F(u, w) + RI(t)$$
$$\tau_{w} \frac{dw}{dt} = G(u, w)$$

$$\tau_{w} \frac{dw}{dt} = G(u, w)$$

First step:

u-nullcline:

all points with du/dt=0

w-nullcline:

all points with dw/dt=0

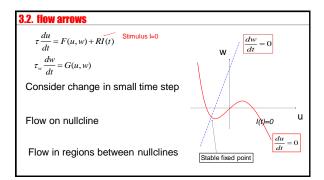
$$\tau \frac{du}{dt} = F(u, w) + RI(t)$$

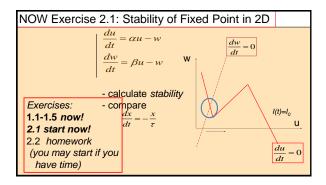
$$\tau_w \frac{dw}{dt} = G(u, w)$$

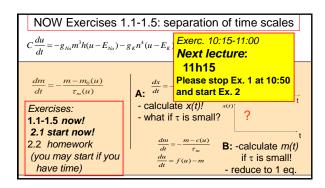
Enables graphical analysis!

- -Discussion of threshold
- -Type I and II

| 3.2. FitzHugh-Nagumo Model | | |
|--|--------------------------|--|
| $\tau \frac{du}{dt} = F(u, w) + RI(t)$ | | |
| $= u - \frac{1}{3}u^3 - w + RI(t)$ | MathAnalysis, blackboard | |
| $\tau_{w} \frac{dw}{dt} = G(u, w) = b_0 + b_1 u - w$ | | |
| u-nullcline | | |
| w-nullcline | | |





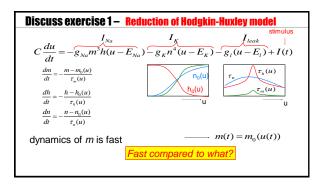


| COST POSTICIONALE PERSONAL DE LAGRANDE | 3.1 From Hodgkin-Huxley to 2D |
|---|---|
| Week 3 – Reducing detail: Two-dimensional neuron models | Overview: From 4 to 2 dimensions MathDetour 1: Exploiting similarities MathDetour 2: Separation of time scale: 2.2 MathDetour 2: Separation of time scale: 2.3 MathDetour 3: MathDetour 3 |
| | 3.2 Phase Plane Analysis - Role of nullclines 3.3 Analysis of a 2D Neuron Model |
| | constant input vs pulse input MathDetour 3: Stability of fixed points |
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| Discussion Exercise 1 – MathDetour 3.1: Separation of time scales | | | | | |
|---|---|--|--|--|--|
| Exercise 1 (week 3) | Two coupled differential equations | | | | |
| Ex. 1-A $\tau_1 \frac{dx}{dt} = -x + c(t)$ | $\tau_1 \frac{dx}{dt} = -x + c(t)$ | | | | |
| | $\tau_2 \frac{dy}{dt} = f(y) + g(x)$ | | | | |
| | Separation of time scales | | | | |
| f | $	au_1 \ll 	au_2$ | | | | |
| | Reduced 1-dimensional system | | | | |
| step Draw graph, blackboard | $\tau_2 \frac{dy}{dt} = f(y) + g(c(t))$ | | | | |

| Discussion Exercise 1 – MathDetour 3.1 Separation of time | scales |
|---|----------|
| Two coupled differential equations | |
| $\tau_1 \frac{dx}{dt} = -x + c(t)$ a=0 a=1 | x |
| $\tau_2 \frac{dc}{dt} = -c + f(x) \mathbf{a} + I(t)$ | |
| $	au_1 \ll 	au_2$ | ○ c |
| 'slow drive' | |
| Draw graph, | <u> </u> |
| blackboard | • |

| Discuss Exercise 1 – MathDetour 3.1: Separation of time scales | | | | | |
|--|---|--|--|--|--|
| | Two coupled differential equations | | | | |
| Exercise 1 (week 3) | $\tau_1 \frac{dx}{dt} = -x + h(y)$ $\tau_2 \frac{dy}{dt} = f(y) + g(x)$ Separation of time scales | | | | |
| even more general | $\tau_1 \ll \tau_2 \rightarrow x = h(y)$ Reduced 1-dimensional system $\tau_2 \frac{dy}{dt} = f(y) + g(h(y))$ | | | | |



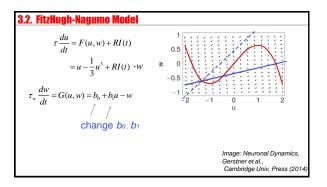
| ı | Neuronal Dynamics – Quiz | 3.3. |
|---|---|------------------------------|
| ı | A- Separation of time scales: | l |
| ı | We start with two equations | |
| I | $\tau_1 \frac{dx}{dt} = -x + y + I(t)$ | |
| I | $\tau_2 \frac{dy}{dt} = -y + x^2 + A$ | |
| I | [] If $\tau_{\rm l} \! < \! < \! \tau_{\rm 2}$ then the system can be reduded to | Doughtontion to 1/th |
| I | $\tau_2 \frac{dy}{dt} = -y + [y + I(t)]^2 + A$ | Pay attention to <i>I(t)</i> |
| I | [] If $	au_2 << 	au_1$ then the system can be reduded to | |
| I | $\tau_1 \frac{dx}{dt} = -x + x^2 + A + I(t)$ [] None of the above is correct. | |
| ı | [] None of the above is correct. | |

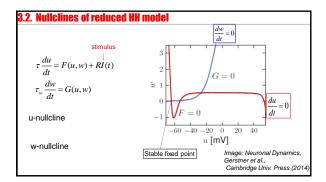
| Week 3 – Quiz 3.2-similar dynamics |
|---|
| Exploiting similarities: |
| A sufficient condition to replace two gating variables r,s by a single gating variable w is |
| Both r and s have the same time constant (as a function of u) Both r and s have the same activation function Both r and s have the same time constant (as a function of u) |
| AND the same activation function [] Both <i>r</i> and <i>s</i> have the same time constant (as a function of u) |
| AND activation functions that are identical after some additive rescaling [] Both <i>r</i> and <i>s</i> have the same time constant (as a function of u) AND activation functions that are identical after some multiplicative |
| rescaling |

Biological Modeling of Neural Networks Value 3.1 From Hodgkin-Huxley to 2D - Overview: From 4 to 2 dimensions - MathDetour 1: Exploiting similarities - MathDetour 2: Separation of time scales 3.2 Phase Plane Analysis - Role of nullclines 3.3 Analysis of a 2D Neuron Model - constant input vs pulse input - MathDetour 3: Stability of fixed points Wulfram Gerstner EPFL, Lausanne, Switzerland

| Neuronal Dynamics – 3.2. flow arrows | |
|---|--|
| $\tau \frac{du}{dt} = F(u, w) + R\widetilde{I(t)} $ Stimulus I=0 $\tau_w \frac{dw}{dt} = G(u, w)$ | $\mathbf{W} = 0$ |
| Consider change in small time step | |
| Flow on nullcline | /(t)=0 u |
| Flow in regions between nullclines | $\frac{du}{dt} = 0$ Stable fixed point |

| A. u-Nu | Ilclines | | | |
|----------|---------------------|---------------------|---------------------|---------------|
| | | ws are always verti | | Take 1 minute |
| | | ws point always ve | | |
| | | ws are always horiz | | |
| | | ws point always to | | |
| [] On th | e u-nullcline, arro | ws point always to | the right | |
| B. w-Nu | Ilclines | | | |
| [] On th | e w-nullcline, arro | ws are always vert | ical | |
| [] On th | e w-nullcline, arro | ws point always ve | ertically upward | |
| [] On th | e w-nullcline, arro | ws are always hori | zontal | |
| [] On th | e w-nullcline, arro | ws point always to | the left | |
| [] On th | e w-nullcline, arro | ws point always to | the right | |
| [] On th | e w-nullcline, arro | ws can point in an | arbitrary direction | n |





3.2. Phase Plane Analysis

2-dimensional equation stimulus
$$\tau \frac{du}{dt} = F(u, w) + RI(t)$$

$$\tau_w \frac{dw}{dt} = G(u, w)$$

Enables graphical analysis! — → Application to neuron models Important role of

- nullclines
- flow arrows

| Week 3 – part 3: Anal | ysis of a 2D neuron model |
|-----------------------------------|--|
| ECCL PATTERINGS HORAL OLASANNE | 3.1 From Hodgkin-Huxley to 2D |
| | 3.2 Phase Plane Analysis - Role of nullcline |
| | 3.3 Analysis of a 2D Neuron Model |
| | - pulse input |
| | - constant input |
| | -MathDetour 3: Stability of fixed points |
| | |
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3.3. Analysis of a 2D neuron model

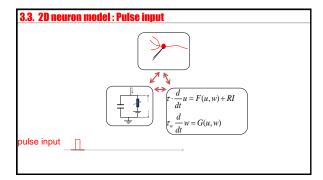
2-dimensional equation

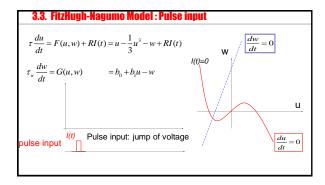
$$\tau \frac{du}{dt} = F(u, w) + RI(t)$$
$$\tau_{w} \frac{dw}{dt} = G(u, w)$$

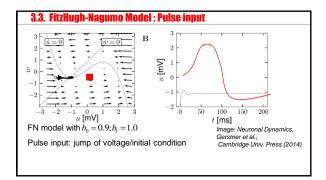
2 important input scenarios

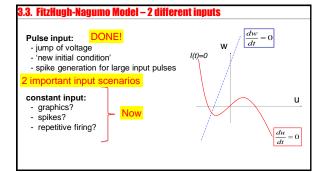
- Pulse input
- Constant input

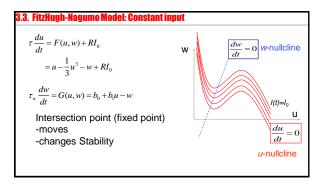
Enables graphical analysis!

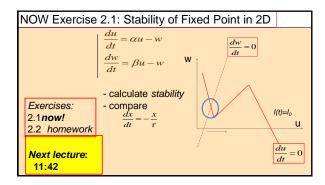






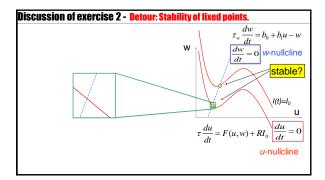


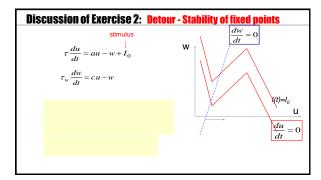


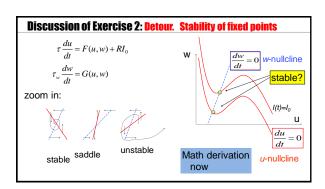


| Week 3 – part 3: Ana | alysis of a 2D neuron model |
|-------------------------------------|---|
| COUL PREVENINGS FORM TO LOSSONES | √3.1 From Hodgkin-Huxley to 2D |
| | 3.2 Phase Plane Analysis - Role of nullcline 3.3 Analysis of a 2D Neuron Model - pulse input - constant input |
| | -MathDetour 3: Stability of fixed points |
| | |
| | |

| Discussion of exercise 2 | Detour. | Stability of fixed points |
|--------------------------|---------|--|
| | | 2-dimensional equation |
| | | $\tau \frac{du}{dt} = F(u, w) + RI_0$ |
| | | $\tau_{w} \frac{dw}{dt} = G(u, w)$ |
| | | How to determine stability of fixed point? |







Discussion of Exercise 2 Detour. Stability of fixed points

 $y = w - w_0$

Discussion of Exercise 2 - Detour. Stability of fixed points

$$\tau\frac{du}{dt} = F(u,w) + RI_0 \qquad \text{Fixed point at } (u_0,w_0)$$
 At fixed point
$$\tau_w\frac{dw}{dt} = G(u,w) \qquad 0 = F(u_0,w_0) + RI_0$$
 zoom in:
$$x = u - u_0 \qquad 0 = G(u_0,w_0)$$

$$\tau\frac{dx}{dt} = F_u x + F_w y \qquad \frac{\mathrm{d}}{\mathrm{d}t} x = \left(\begin{array}{cc} F_u & F_w \\ G_u & G_w \end{array}\right) x \ .$$

$$\tau_w\frac{dy}{dt} = G_u x + G_w y$$

Discussion of Exercise 2 Detour. Stability of fixed points

Linear matrix equation

$$\frac{\mathrm{d}}{\mathrm{d}t}\boldsymbol{x} = \left(\begin{array}{cc} F_u & F_w \\ G_u & G_w \end{array}\right) \, \boldsymbol{x} \, ,$$

Search for solution

$$x(t) = e \exp(\lambda t)$$

Two solution with Eigenvalues λ_+, λ_-

$$\lambda_{+} + \lambda_{-} = F_{u} + G_{w}$$
$$\lambda_{+} \lambda_{-} = F_{u} G_{w} - F_{w} G_{u}$$

Discussion of Exercise 2: Detour. Stability of fixed points

Linear matrix equation

$$\frac{\mathrm{d}}{\mathrm{d}t} oldsymbol{x} = \left(egin{array}{cc} F_u & F_w \ G_u & G_w \end{array}
ight) oldsymbol{x}$$

Search for solution

$$x(t) = e \exp(\lambda t)$$

Two solution with Eigenvalues $~\lambda_{_{\!\scriptscriptstyle +}},\lambda_{_{\!\scriptscriptstyle -}}$

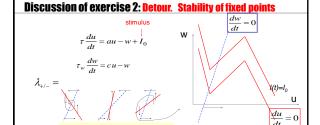
$$\lambda_{+} + \lambda_{-} = F_{u} + G_{w}$$
$$\lambda_{+} \lambda_{-} = F_{u} G_{w} - F_{w} G_{u}$$

Stability requires:



$$F_u + G_w < 0$$

and
$$F_u G_w - F_w G_u > 0$$



3.3. Neuron models and Stability of fixed points

Now Back:

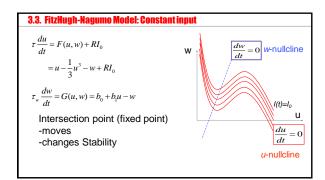
Application to our neuron model

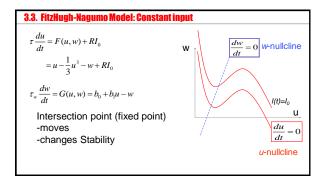
2-dimensional equation

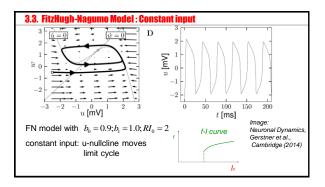
$$\tau \frac{du}{dt} = F(u, w) + RI_0$$
$$\tau_w \frac{dw}{dt} = G(u, w)$$

Stability characterized by Eigenvalues of linearized equations

$$\frac{\mathrm{d}}{\mathrm{d}t}\boldsymbol{x} = \left(\begin{array}{cc} F_u & F_w \\ G_u & G_w \end{array} \right) \, \boldsymbol{x}$$







| Neuronal Dynamics – Quiz 3.5. |
|---|
| A. Short current pulses. In a 2-dimensional neuron model, the effect of a delta |
| current pulse can be analyzed |
| [] By moving the u-nullcline vertically upward |
| [] By moving the w-nullcline vertically upward |
| [] As a potential change in the stability or number of the fixed point(s) |
| [] As a new initial condition |
| [] By following the flow of arrows in the appropriate phase plane diagram |
| B. Constant current. In a 2-dimensional neuron model, the effect of a constant current can be analyzed |
| [] By moving the u-nullcline vertically upward |
| [] By moving the w-nullcline vertically upward |
| [] As a potential change in the stability or number of the fixed point(s) |
| [] By following the flow of arrows in the appropriate phase plane diagram |
| |
| |
| |

| Computer exercise Can we understand | now d the dynamics of th | ne 2D model? | _ | | | |
|-------------------------------------|------------------------------------|----------------|---|--|--|--|
| The E | END for | today | - | | | |
| Now: computer exe | rcises | | | | | |
| ramp input/ constant input | f-I curve | type II models | _ | | | |
| | lo | lo | _ | | | |