**Biological Modeling of Neural Networks**

**Week 3 – Reducing detail:**
Two-dimensional neuron models

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

Cambridge Univ. Press

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### 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

- Rate 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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### 3.1. Review of week 2: Hodgkin-Huxley Model

- Cortical neuron
- Hodgkin-Huxley model
- Compartmental models

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**3.1 Review of week 2: Hodgkin-Huxley Model**

**Week 2:**
- Cell membrane contains
  - ion channels
  - ion pumps

**Dendrites (week x: video):**
- Active processes?
  - assumption: passive dendrite
  - point neuron
  - spike generation

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**Ions/proteins**

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3.1. Review of week 2: Hodgkin-Huxley Model

\[ \Delta u = u_1 - u_2 = \frac{-kT}{q} \ln \frac{n(u_1)}{n(u_2)} \]

Reversal potential

Ion pumps \( \rightarrow \) concentration difference \( \leftrightarrow \) voltage difference

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3.1. Review of week 2: Hodgkin-Huxley Model

Hodgkin and Huxley, 1952

\[ C \frac{du}{dt} = I_{Na} - I_{K} - I_{leak} \]

\[ \frac{dm}{dt} = \frac{m - m_n(u)}{\tau_m(u)} \]

\[ \frac{dh}{dt} = \frac{h - h_n(u)}{\tau_h(u)} \]

4 equations \( \rightarrow \) 4D system

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Week 3 – 3.1. Overview and aims

Can we understand the dynamics of the HH model?
- mathematical principle of Action Potential generation?
- constant input current vs pulse input?
- Types of neuron model (type I and II)? (next week)
- threshold behavior? (next week)

\( \rightarrow \) Reduce from 4 to 2 equations

<table>
<thead>
<tr>
<th>Type I models</th>
<th>Type II models</th>
</tr>
</thead>
<tbody>
<tr>
<td>( I ) curve</td>
<td>( f ) curve</td>
</tr>
</tbody>
</table>
Can we understand the dynamics of the HH model?

→ Reduce from 4 to 2 equations.

A biophysical point neuron model with 3 ion channels, each with activation and inactivation, has a total number of equations equal to

- 3 or
- 4 or
- 6 or
- 7 or
- 8 or more

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

\[
\frac{du}{dt} = \frac{I_{Na}}{C_m} - \frac{I_K}{C_m} - g_C m^4 h(u - E_K) - g_L (u - E_L) + I(t)
\]

\[
\frac{dm}{dt} = \frac{m - m_0(u)}{\tau_m(u)}
\]

\[
\frac{dh}{dt} = \frac{h - h_0(u)}{\tau_h(u)}
\]

\[
\frac{dn}{dt} = \frac{n - n_0(u)}{\tau_n(u)}
\]

1) dynamics of \( m \) are fast  
\[ m(t) = m_0(u(t)) \]

2) dynamics of \( h \) and \( n \) are similar

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**Reduction of dimensionality:** Separation of time scales

Two coupled differential equations

\[
\begin{align*}
\tau_1 \frac{dx}{dt} &= -x + c(t) \\
\tau_2 \frac{dy}{dt} &= f(y) + g(x)
\end{align*}
\]

**Exercise 1 (week 3)**  
(later today!)

Separation of time scales

\( \tau_1 \ll \tau_2 \Rightarrow x = h(y) \)

Reduced 1-dimensional system

\[
\tau_1 \frac{dy}{dt} = f(y) + g(h(y))
\]

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In the context of the Hodgkin-Huxley model, the dynamics of the membrane potential \( u \) can be described by the following set of equations:

\[
\frac{du}{dt} = \frac{I_{Na}}{C_m} - \frac{I_K}{C_m} - g_C m^4 h(u - E_K) - g_L (u - E_L) + I(t)
\]

where:

- \( I_{Na} \) is the sodium current
- \( I_K \) is the potassium current
- \( g_C \) and \( E_K \) are the conductance and equilibrium potential of the potassium channels
- \( g_L \) and \( E_L \) are the conductance and equilibrium potential of the leakage current
- \( I(t) \) is the stimulus

The dynamics of the gating variables \( m, h, \) and \( n \) are given by:

\[
\begin{align*}
\frac{dm}{dt} &= \frac{m - m_0(u)}{\tau_m(u)} \\
\frac{dh}{dt} &= \frac{h - h_0(u)}{\tau_h(u)} \\
\frac{dn}{dt} &= \frac{n - n_0(u)}{\tau_n(u)}
\end{align*}
\]

with \( m_0(u), h_0(u), \) and \( n_0(u) \) being the steady-state values and \( \tau_m, \tau_h, \) and \( \tau_n \) being time constants.

**MathDetour**

1) dynamics of \( m \) are fast  
\[ m(t) = m_0(u(t)) \]

2) dynamics of \( h \) and \( n \) are similar
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

\[ \frac{du}{dt} = C \left( -g_{Na}m^3h(u-E_{Na}) - g_{K}n^4(u-E_{K}) - g_{L}(u-E_{L}) + I(t) \right) \]

2) dynamics of \( h \) and \( n \) are similar

MathDetour

3.1 Detour 1. Exploit similarities/correlations

dynamics of \( h \) and \( n \) are similar

Math. argument
3.1 Detour 1. Exploit similarities/correlations

Dynamics of $h$ and $n$ are similar

1. $1 - h(t) = a n(t)$

at rest

\[
\begin{align*}
\frac{dh}{dt} &= \frac{h - h_i(a)}{\tau_h(a)} \\
\frac{dn}{dt} &= \frac{n - n_i(a)}{\tau_n(a)}
\end{align*}
\]

3.1. Reduction of Hodgkin-Huxley model

\[
\begin{align*}
C \frac{dm}{dt} &= -g_m m(t)(m(t) - E_m) - g_k m(t)(u(t) - E_k) \quad 1) \text{dynamics of } m \text{ are fast} \\
C \frac{dh}{dt} &= -g_h [m(t)]^3 h(t)(n(t) - E_h) - g_k [m(t)]^3 (u(t) - E_k) - g_{\text{leak}} (u(t) - E_{\text{leak}}) + I(t) \\
C \frac{dn}{dt} &= -g_n m(t)(1-u(t)(a-E_m)) - g_k [m(t)]^3 u(t)(a-E_k) - g_{\text{leak}} (u(t) - E_{\text{leak}}) + I(t) \\
\end{align*}
\]

2) dynamics of $h$ and $n$ are similar

\[
\begin{align*}
1 - h(t) &= a n(t) \\
\frac{dh}{dt} &= \frac{h - h_i(a)}{\tau_h(a)} \\
\frac{dn}{dt} &= \frac{n - n_i(a)}{\tau_n(a)} \\
\frac{dw}{dt} &= \frac{w - w_i(a)}{\tau_{\text{eff}}(a)}
\end{align*}
\]
3.1. Reduction of Hodgkin-Huxley model

\[
\begin{align*}
\frac{du}{dt} &= C_{Na} I_{Na} - g_{Na} m_{h}(u)(1-w)(u-E_{K}) - g_{K} h(u)(u-E_{K}) \left(1 - g_{Na}(u - E_{Na}) + I(t) \right) \\
\frac{dw}{dt} &= \frac{w - w_0(u)}{\tau_{off}(u)} \\
\frac{\tau}{dt} &= F(u(t), w(t)) + R I(t) \\
\tau_{w} \frac{dw}{dt} &= G(u(t), w(t))
\end{align*}
\]

3.1. Reduction to 2 dimensions

2-dimensional equation

\[
\begin{align*}
C \frac{du}{dt} &= f(u(t), w(t)) + I(t) \\
\frac{dw}{dt} &= g(u(t), w(t))
\end{align*}
\]

Enables graphical analysis!  
Phase plane analysis

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

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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
NOW Exercise 1.1-1.4: separation of time scales

\[
\begin{align*}
C \frac{dv}{dt} & = -g_{Na}m^3h(v - E_{Na}) - g_{K}n^4(v - E_{K}) - g_{L}(v - E_{L}) + I(t) \\
\frac{dm}{dt} & = \frac{m - m_a(u)}{\tau_m(u)} \\
\frac{dn}{dt} & = \frac{n - n_a(u)}{\tau_n(u)} \\
\frac{dh}{dt} & = \frac{h - h_a(u)}{\tau_h(u)}
\end{align*}
\]

Exercises:
1.1-1.4 now!
1.5 homework

Exerc. 10h15-10h30
Next lecture:
10h30

A: calculate \( x(t) \)
- what if \( \tau \) is small?

B: calculate \( m(t) \)
if \( \tau \) is small!
- reduce to 1 eq.

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Two-dimensional neuron models

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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
- Rate 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
\[
\begin{align*}
\frac{dx}{dt} & = -x + c(t) \\
\tau_1 \frac{dy}{dt} & = f(y) + g(x)
\end{align*}
\]

Draw graph, blackboard

Ex. 1-A
- step
\[
\begin{align*}
\tau_1 \frac{dx}{dt} & = -x + c(t) \\
\tau_2 \frac{dy}{dt} & = f(y) + g(c(t))
\end{align*}
\]

Separation of time scales
\( \tau_1 \ll \tau_2 \)

Reduced 1-dimensional system
Discussion Exercise 1 – MathDetour 3.1 Separation of time scales

Two coupled differential equations

\[ \tau_1 \frac{dx}{dt} = -x + c(t) \]
\[ \tau_2 \frac{dc}{dt} = -c + f(x) \]

Draw graph, blackboard

\[ \tau_1 \ll \tau_2 \]

'slow drive'

\[ x \]
\[ c \]
\[ I \]

Exercise 1 (week 3)

even more general

Discuss Exercise 1 – MathDetour 3.1: Separation of time scales

Two coupled differential equations

\[ \tau_1 \frac{dx}{dt} = -x + b(x) \]
\[ \tau_2 \frac{dy}{dt} = f(y) + g(x) \]

Separation of time scales

\[ \tau_1 \ll \tau_2 \rightarrow x = h(y) \]

Reduced 1-dimensional system

\[ \tau_1 \frac{dy}{dt} = f(y) + g(h(y)) \]

Discuss exercise 1 – Reduction of Hodgkin-Huxley model

\[ C \frac{du}{dt} = -g_{Na} m^3 h(u-E_{Na}) - g_K n^4 (u-E_K) - g_L (u-E_L) + I(t) \]

\[ \frac{dm}{dt} = \frac{m_n(t)}{\tau_m(t)} \]
\[ \frac{dh}{dt} = \frac{b_n(t)}{\tau_h(t)} \]
\[ \frac{dn}{dt} = \frac{n_n(t)}{\tau_n(t)} \]
\[ \frac{du}{dt} = \frac{m(t)}{\tau_m(t)} \]

dynamics of \( m \) is fast

\[ m(t) = m_0(u(t)) \]

Fast compared to what?
Neuronal Dynamics – Quiz 3.3.

**A. Separation of time scales**

We start with two equations:

\[ \frac{dx}{dt} = -x + \gamma + I(t) \]

\[ \frac{dy}{dt} = -y + x^2 + A \]

If \( \gamma \ll \tau \), then the system can be reduced to

\[ \frac{dy}{dt} = -y + \gamma + I(t) \]

If \( \gamma \gg \tau \), then the system can be reduced to

\[ \frac{dx}{dt} = -x + \gamma + I(t) \]

None of the above is correct.

Pay attention to \( I(t) \): We assume that \( I(t) \) is slow compared to both time constants.

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3.2. Reduced Hodgkin-Huxley model

\[ C \frac{du}{dt} = -g_{Na,}(u) (1-w)(u-E_{Na}) - g_{K,}(u) (u-E_{K}) - g_{leak,}(u)(u-E_{leak}) + I(t) \]

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

\[ \frac{ds}{dt} = F(u, w) + RI(t) \]

\[ \frac{dw}{dt} = G(u, w) \]
3.2. Phase Plane Analysis/nullclines

2-dimensional equation
\[ \tau \frac{du}{dt} = F(u, w) + R(t) \]
\[ \tau \frac{dw}{dt} = G(u, w) \]

First step:
- **u-nullcline**: all points with \( \frac{du}{dt} = 0 \)
- **w-nullcline**: all points with \( \frac{dw}{dt} = 0 \)

Enables graphical analysis!
- Discussion of threshold
- Type I and II

3.2. FitzHugh-Nagumo Model

\[ \frac{du}{dt} = F(u, w) + R(t) = u - \frac{1}{3} u^3 - w + R(t) \]
\[ \tau \frac{dw}{dt} = G(u, w) = \beta u + b w - w \]

**MathAnalysis, blackboard**

3.2. flow arrows

Consider change in small time step

Flow on nullcline

Flow in regions between nullclines
3.1 From Hodgkin-Huxley to 2D
- Overview: From 4 to 2 dimensions
- MathDetour 1: Exploiting similarities
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3.2 Phase Plane Analysis
- Rate of nullclines

3.3 Analysis of a 2D Neuron Model
- Constant input vs pulse input
- MathDetour 3: Stability of fixed points

Neuronal Dynamics – 3.2. flow arrows
\[ \frac{du}{dt} = F(u, w) + RI(t) \]
\[ \tau_w \frac{dv}{dt} = G(u, w) \]

Consider change in small time step:
Flow on nullcline
Flow in regions between nullclines

Week 3 – Quiz 3.4

A. u-Nullclines
- On the u-nullcline, arrows are always vertical
- On the u-nullcline, arrows always point vertically upward
- On the u-nullcline, arrows are always horizontal
- On the u-nullcline, arrows point always to the left
- On the u-nullcline, arrows point always to the right

Take 1 minute

B. w-Nullclines
- On the w-nullcline, arrows are always vertical
- On the w-nullcline, arrows point always vertically upward
- On the w-nullcline, arrows are always horizontal
- On the w-nullcline, arrows point always to the left
- On the w-nullcline, arrows can point in an arbitrary direction
3.2. FitzHugh-Nagumo Model

\[
\tau \frac{du}{dt} = F(u, w) + RI(t)
\]
\[
= u - \frac{1}{3} u^3 + RI(t) \cdot w
\]
\[
\tau w \frac{dw}{dt} = G(u, w) = h_u + b u - w
\]

change \( b_r, b_l \)

Image: Neuronal Dynamics, Gerstner et al., Cambridge Univ. Press (2014)

3.2. Nullclines of reduced HH model

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

u-nullcline

w-nullcline

Stable fixed point

Image: Neuronal Dynamics, Gerstner et al., Cambridge Univ. Press (2014)

3.2. Phase Plane Analysis

2-dimensional equation

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

Enables graphical analysis!

Important role of
- nullclines
- flow arrows

Application to neuron models

Image: Neuronal Dynamics, Gerstner et al., Cambridge Univ. Press (2014)
3.3. Analysis of a 2D neuron model

2-dimensional equation

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

2 important input scenarios:
- Pulse input
- Constant input

Enables graphical analysis!

3.3. 2D neuron model: Pulse input

\[ \frac{du}{dt} = F(u, w) + RI(t) \]
\[ \frac{dw}{dt} = G(u, w) \]
3.3. FitzHugh-Nagumo Model: Pulse Input

\[ \tau \frac{du}{dt} = F(u, w) + R(t) = u - \frac{1}{3} u^3 - w + R(t) \]

\[ \tau \frac{dw}{dt} = G(u, w) = b_1 + b_2 u - w \]

Pulse input: jump of voltage

Pulse input: jump of voltage/initial condition

FN model with \( b_1 = 0.9, b_2 = 1.0 \)

Image: Neuronal Dynamics, Gerstner et al., Cambridge Univ. Press (2014)

3.3. FitzHugh-Nagumo Model – 2 different inputs

Pulse input: jump of voltage
- new initial condition
- spike generation for large input pulses

2 important input scenarios

constant input:
- graphics?
- spikes?
- repetitive firing?

Now
3.3. FitzHugh-Nagumo Model: Constant input

\[ \tau \frac{du}{dt} = F(u, w) + RI \]
\[ = u - \frac{1}{3} u^3 - w + RI \]
\[ \tau \frac{dw}{dt} = G(u, w) = b_u + b_u w - w \]

Intersection point (fixed point)
- moves
- changes Stability

NOW Exercise 2.1: Stability of Fixed Point in 2D

\[ \frac{du}{dt} = \alpha u - w \]
\[ \frac{dw}{dt} = \beta u - w \]

Exercises:
2.1 start now!
2.2 homework (you may start if you have time)

Exercise: later

Week 3 – part 3: Analysis of a 2D neuron model
- From Hodgkin-Huxley to 2D
- Phase Plane Analysis
  - Rate of nullcline
- 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

\[ \begin{align*}
\tau \frac{du}{dt} &= F(u, w) + RI
\end{align*} \]

\[ \begin{align*}
\tau \frac{dw}{dt} &= G(u, w)
\end{align*} \]

How to determine stability of fixed point?

Discussions of exercise 2 - Detour: Stability of fixed points.

Stable?

Discussion of exercise 2 - Detour: Stability of fixed points.

Stable?
**Discussion of Exercise 2: Detour. Stability of fixed points**

\[ \frac{du}{dt} = F(u, w) + RI \]
\[ \frac{dw}{dt} = G(u, w) \]

Stable saddle unstable

**Math derivation now**

**3.3. Neuron models and Stability of fixed points**

2-dimensional equation
\[ \frac{du}{dt} = F(u, w) + RI \]
\[ \frac{dw}{dt} = G(u, w) \]

Stability characterized by Eigenvalues of linearized equations
\[ \frac{d}{dt} \mathbf{x} = \begin{pmatrix} F_u & F_w \\ G_u & G_w \end{pmatrix} \mathbf{x} \]

**Now Back:**

Application to our neuron model

**3.3. FitzHugh-Nagumo Model: Constant input**

\[ \frac{du}{dt} = F(u, w) + RI \]
\[ = u - \frac{1}{3} u^3 - w + RL \]
\[ \frac{dw}{dt} = G(u, w) = h_0 + hu - w \]

Intersection point (fixed point) changes Stability
3.3. FitzHugh-Nagumo Model: Constant Input

\[ \frac{du}{dt} = F(u, w) + RI \]
\[ = u - \frac{1}{3} u^3 - w + RI \]
\[ \frac{dw}{dt} = G(u, w) = b_0 + b u - w \]

Intersection point (fixed point)
- moves
- changes Stability

\[ \text{FN model with } b_0 = 0.9, b_1 = 1.0, RI = 2 \]
constant input: u-nullcline moves limit cycle

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 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
NOW Exercise 2.1: Stability of Fixed Point in 2D

\[ \frac{du}{dt} = \alpha u - w \]
\[ \frac{dw}{dt} = \beta u - w \]

Exercises:
- calculate stability
- compare

\[ \frac{dx}{dt} = \frac{1}{\tau} \]

\[ \frac{du}{dt} = 0 \]
\[ \frac{dw}{dt} = 0 \]

\[ I(t) = I_0 \]

Type I and type II models

Computer exercise now
Can we understand the dynamics of the 2D model?

The END for today

Now: computer exercises

Type I and type II models

Discussion of Exercise 2 Detour. Stability of fixed points

\[ \frac{du}{dt} = F(u, w) + RI_b \]
\[ \frac{dw}{dt} = G(u, w) \]

Fixed point at \((u_0, w_0)\)

At fixed point
\[ 0 = F(u_0, w_0) + RI_b \]
\[ 0 = G(u_0, w_0) \]

zoom in:
\[ x = u - u_0 \]
\[ y = w - w_0 \]
**Discussion of Exercise 2 - Detour: Stability of fixed points**

- **Fixed point at** \((u_0, w_0)\)
  - \(\frac{du}{dt} = F(u, w) + RI_u\)
  - \(\frac{dw}{dt} = G(u, w)\)

**Zoom in:**
- \(x = u - u_0\)
- \(y = w - w_0\)

\[
\begin{align*}
\frac{dx}{dt} &= F_x + F_y y \\
\frac{dy}{dt} &= G_x + G_y y
\end{align*}
\]

\[
d\frac{dx}{dt} = \begin{pmatrix} F_x & F_y \\ G_x & G_y \end{pmatrix} x.
\]

**Stability requires:**
- \(\lambda_{-} < 0\) and \(\lambda_{+} < 0\)

**Two solution with Eigenvalues** \(\lambda_{-}, \lambda_{+}\)
- \(\lambda_{+} + \lambda_{-} = F_x + G_y\)
- \(\lambda_{+} \lambda_{-} = F_x G_y - F_y G_x\)

**Search for solution**
- \(x(t) = e^{\exp(\lambda t)}\)
Discussion of exercise 2: Detour. Stability of fixed points

\[ \frac{dI}{dt} = I_0 \]

\[ \frac{dw}{dt} = \tau w \]

\[ \frac{du}{dt} = \tau (w - u) \]

\[ \lambda_{-} = \text{unstable} \]

\[ \lambda_{+} = \text{stable} \]

\[ \lambda_{s} = \text{saddle} \]