Biological Modeling of Neural Networks

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Week 4

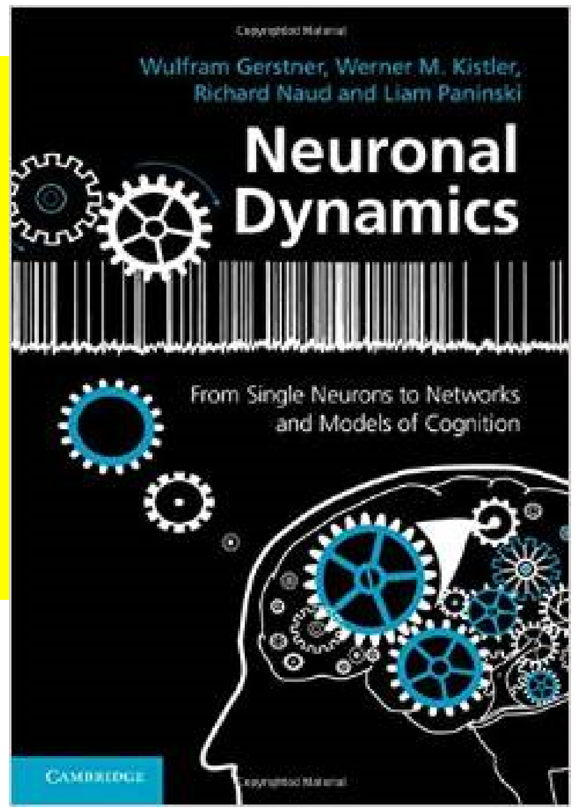
Reducing detail:

Analysis of 2D models

Wulfram Gerstner

EPFL, Lausanne, Switzerland

Reading for week 4:
NEURONAL DYNAMICS
- Ch. 4.4 – 4.7



Cambridge Univ. Press

√ 3.1 From Hodgkin-Huxley to 2D

√ 3.2 Phase Plane Analysis

√ 3.3 Analysis of a 2D Neuron Model

4.1 Type I and II Neuron Models
- limit cycles

4.2 Pulse input
- where is the firing threshold?
- separation of time scales

4.3. Further reduction to 1 dim
- nonlinear integrate-and-fire (again)

Week 4 – Review from week 3

-**Reduction of Hodgkin-Huxley to 2 dimension**

-step 1: separation of time scales

-step 2: exploit similarities/correlations

Week 4 – Review from week 3

$$C\frac{du}{dt} = \underbrace{-g_{Na}[m(t)]^3 h(t)(u(t)-E_{Na})}_{I_{Na}} \underbrace{-g_K[n(t)]^4(u(t)-E_K)}_{I_K} \underbrace{-g_l(u(t)-E_l)}_{I_{leak}} + I(t)$$

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

1) dynamics of *m* are fast $\longrightarrow$ $m(t) = m_0(u(t))$

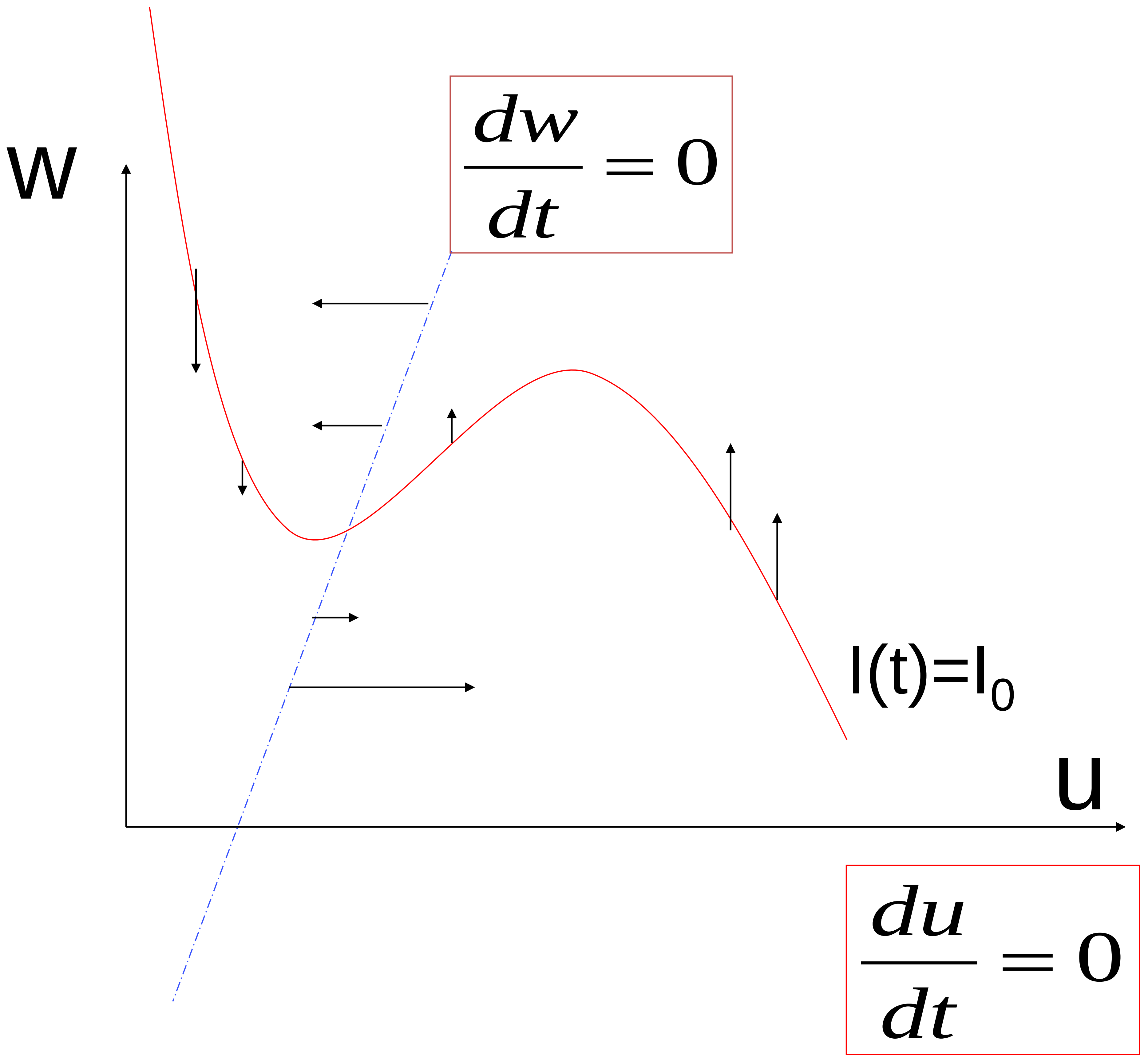
2) dynamics of *h* and *n* are similar $\longrightarrow$ $\underbrace{1-h(t)}_{w(t)} = \underbrace{a\, n(t)}_{w(t)}$

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

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

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

Week 4 – review from week 3



2-dimensional equation

stimulus

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

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

Enables graphical analysis!

-Pulse input

→ AP firing (or not)

- Constant input

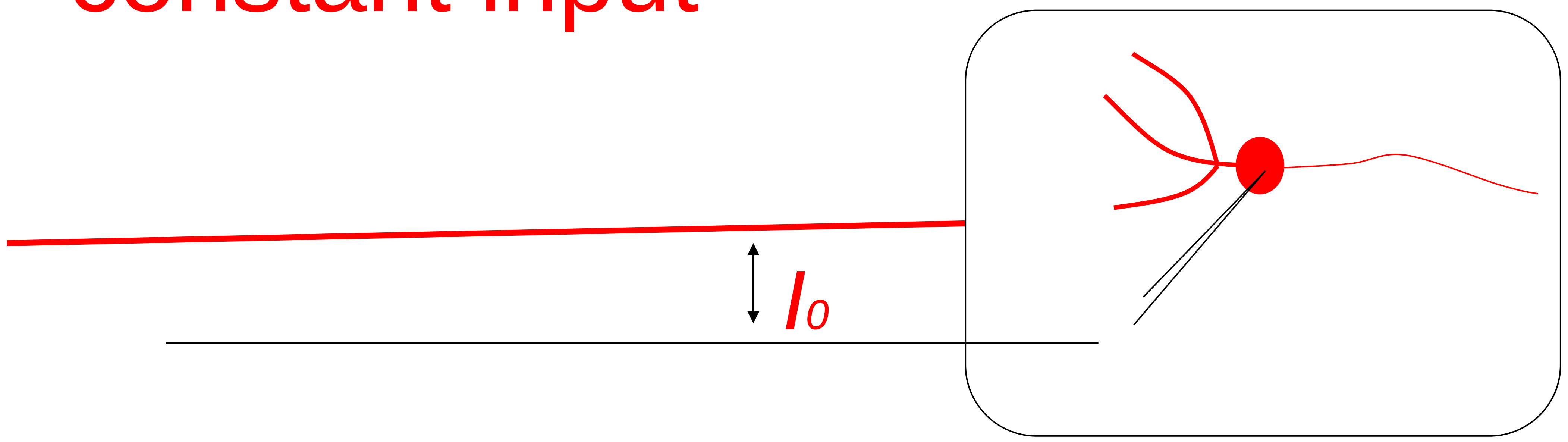
→ repetitive firing (or not)

→ limit cycle (or not)

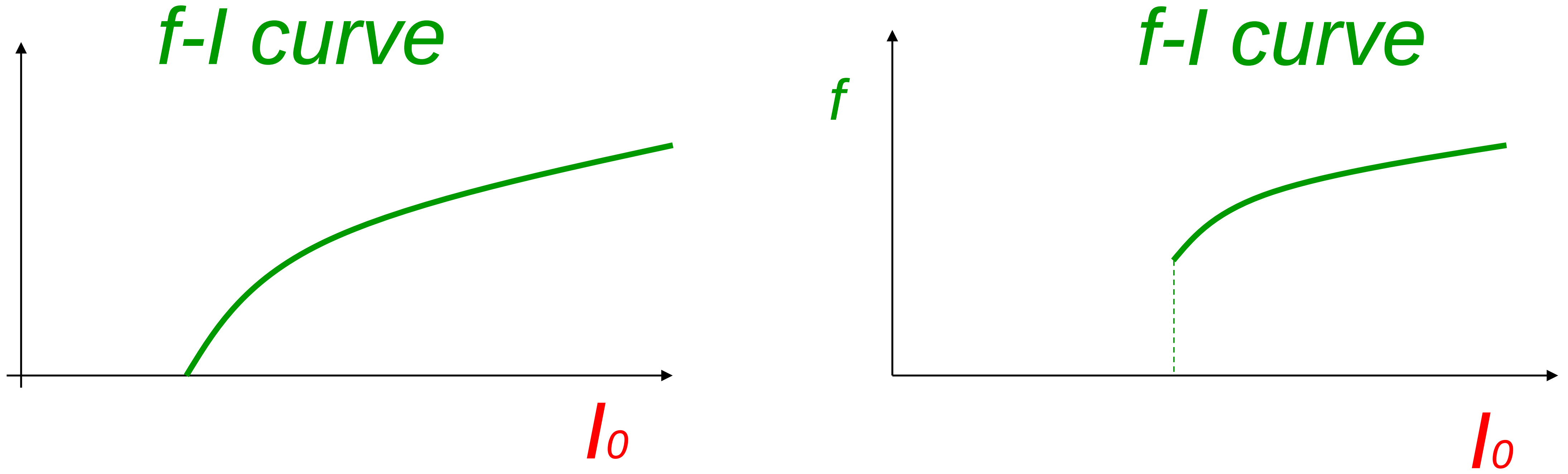
Week 4 – Reducing Detail – 2D models

ramp input/
constant input

neuron

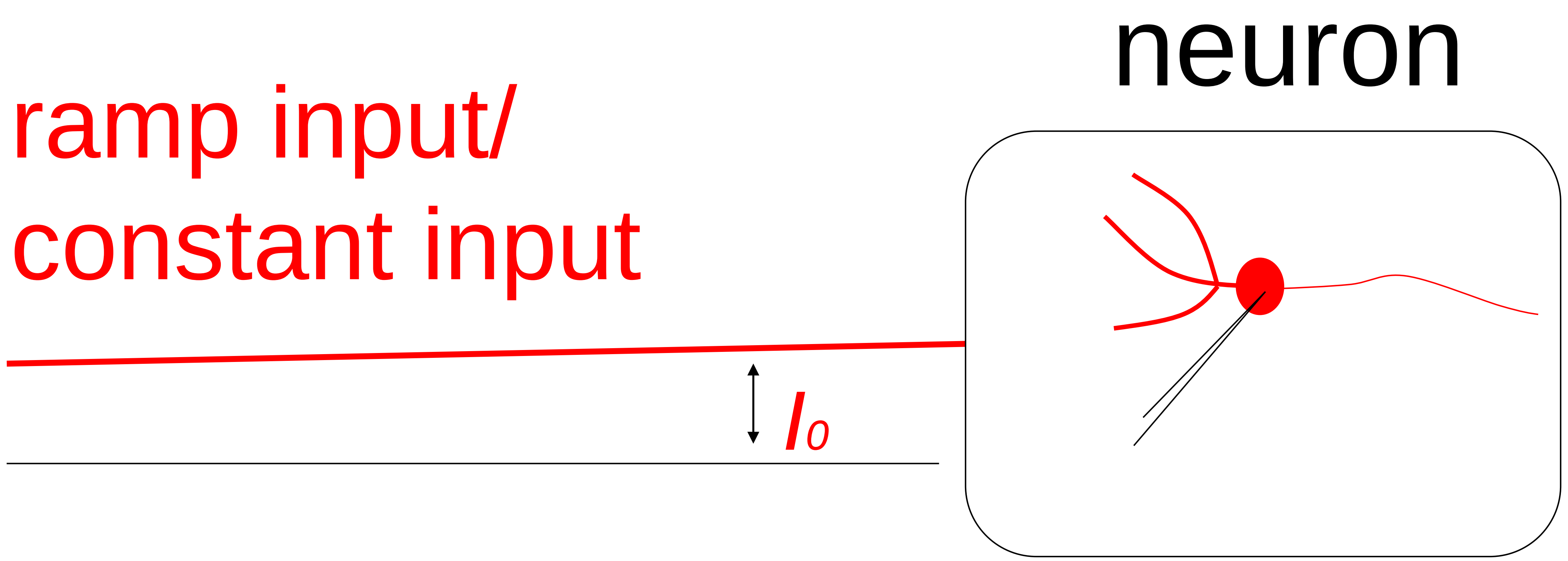


Type I and type II

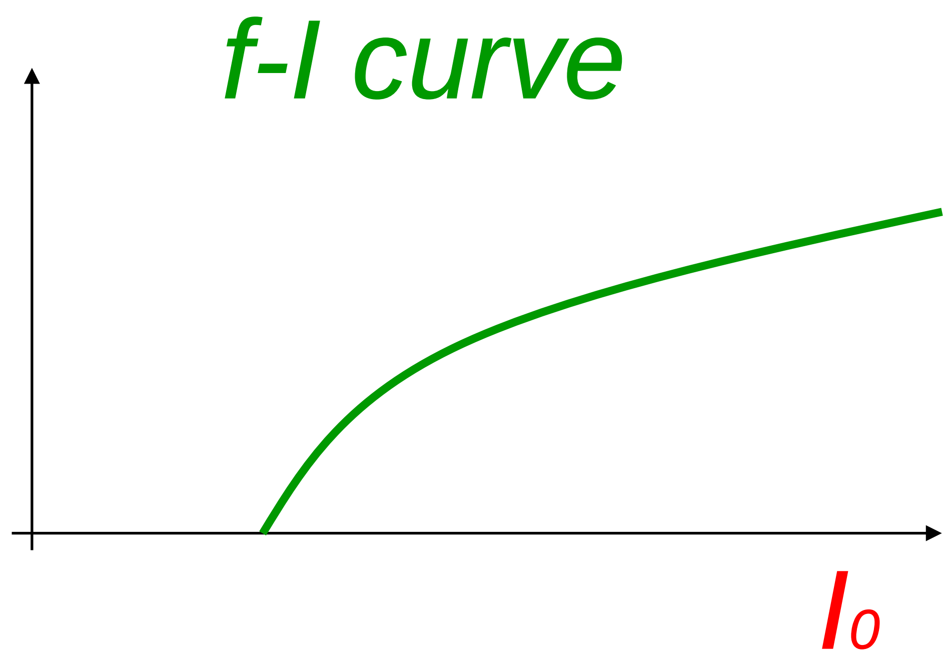


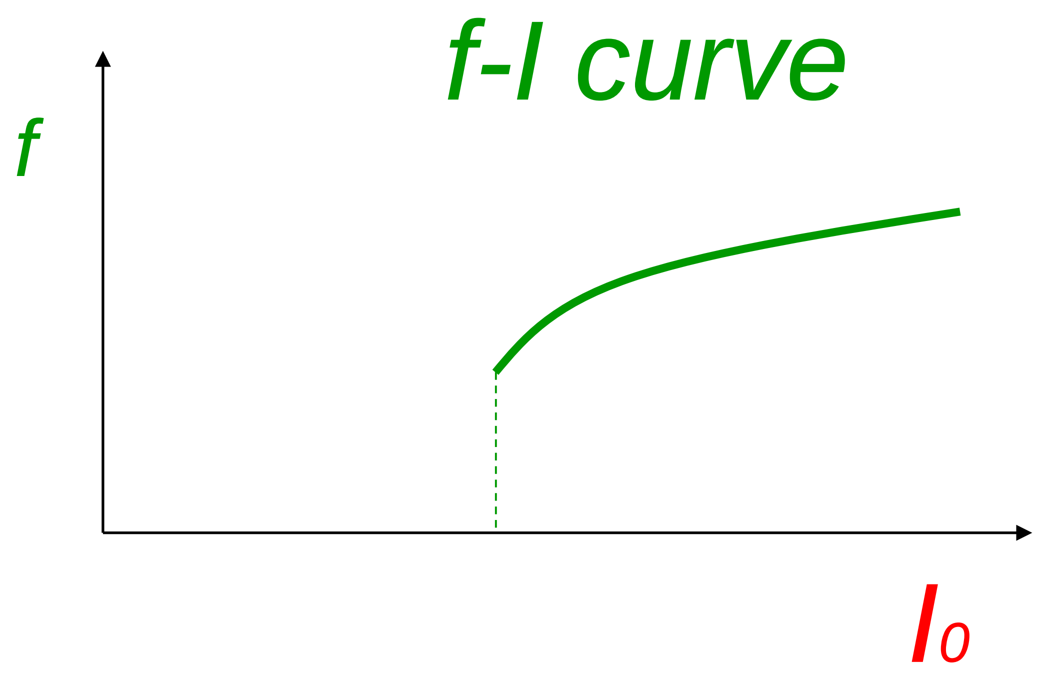
- 3.1 From Hodgkin-Huxley to 2D
- 3.2 Phase Plane Analysis
- 3.3 Analysis of a 2D Neuron Model
- **4.1 Type I and II Neuron Models**
  - limit cycles
  - where is the firing threshold?
  - separation of time scales
- 4.2. Further Reduction to 1D

Week 4 – 4.1. Type I and II Neuron Models



Type I and type II models





4.1 Nullclines change for constant stimulus

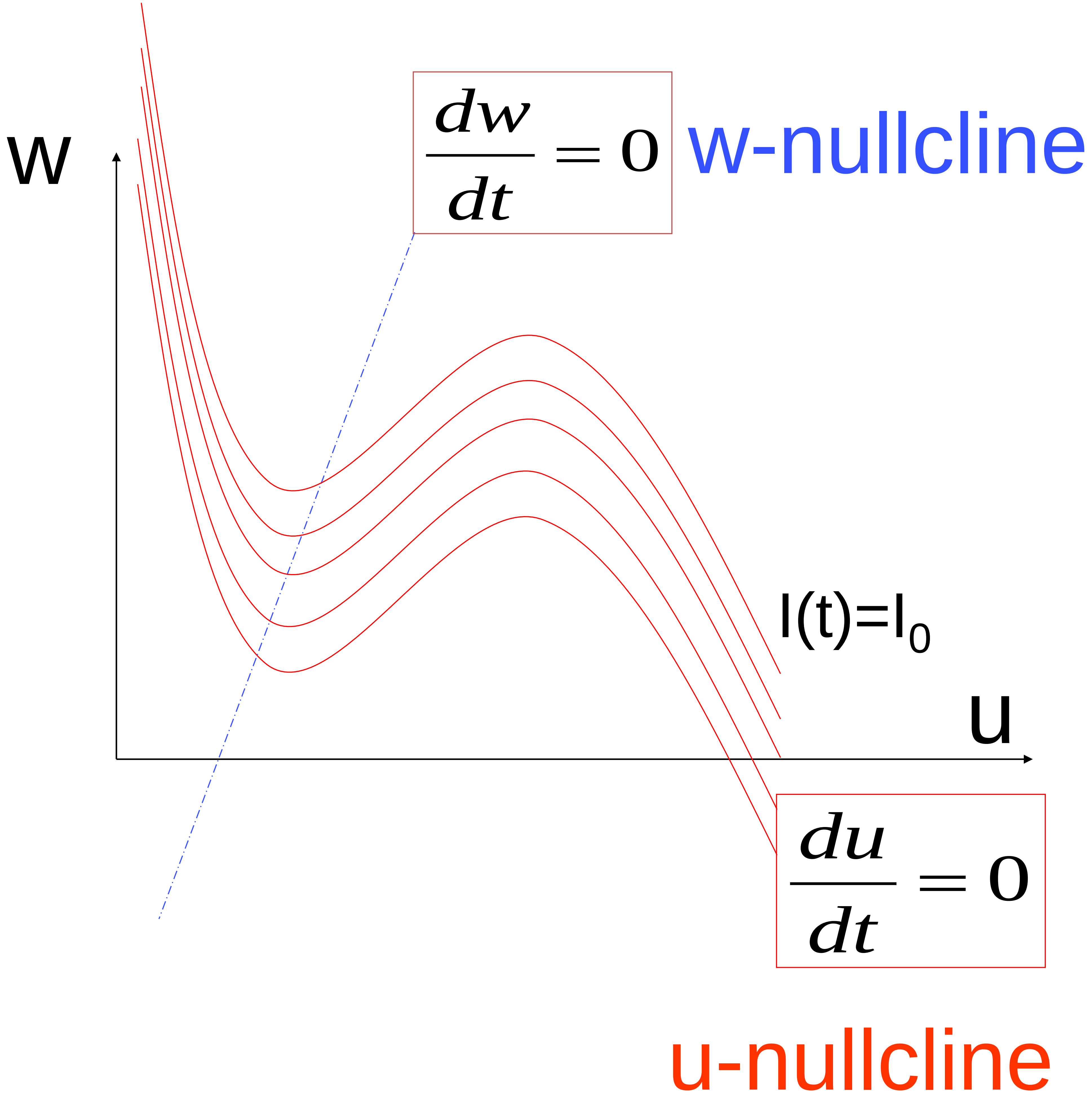
stimulus

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

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

apply constant stimulus I_0

Blackboard $\varepsilon = \frac{\tau}{\tau_w}$



4.1. Separation of time scales

stimulus

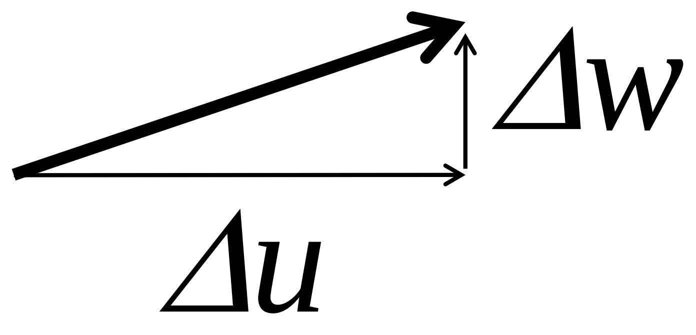
$$\tau \frac{du}{dt} = F(u,w) + RI(t)$$

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

Separation of time scales

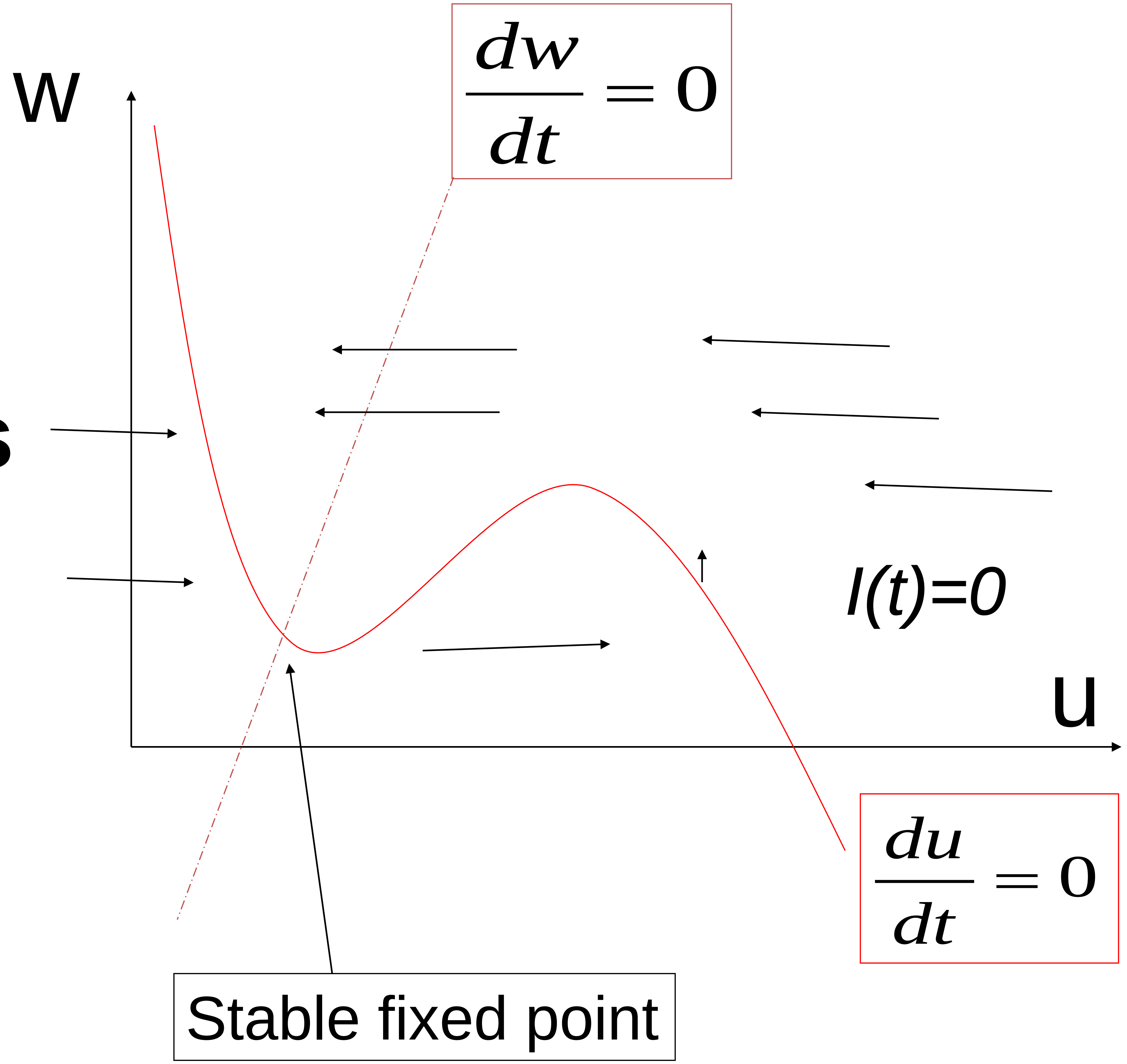
$$\tau_w >> \tau_u$$

blackboard

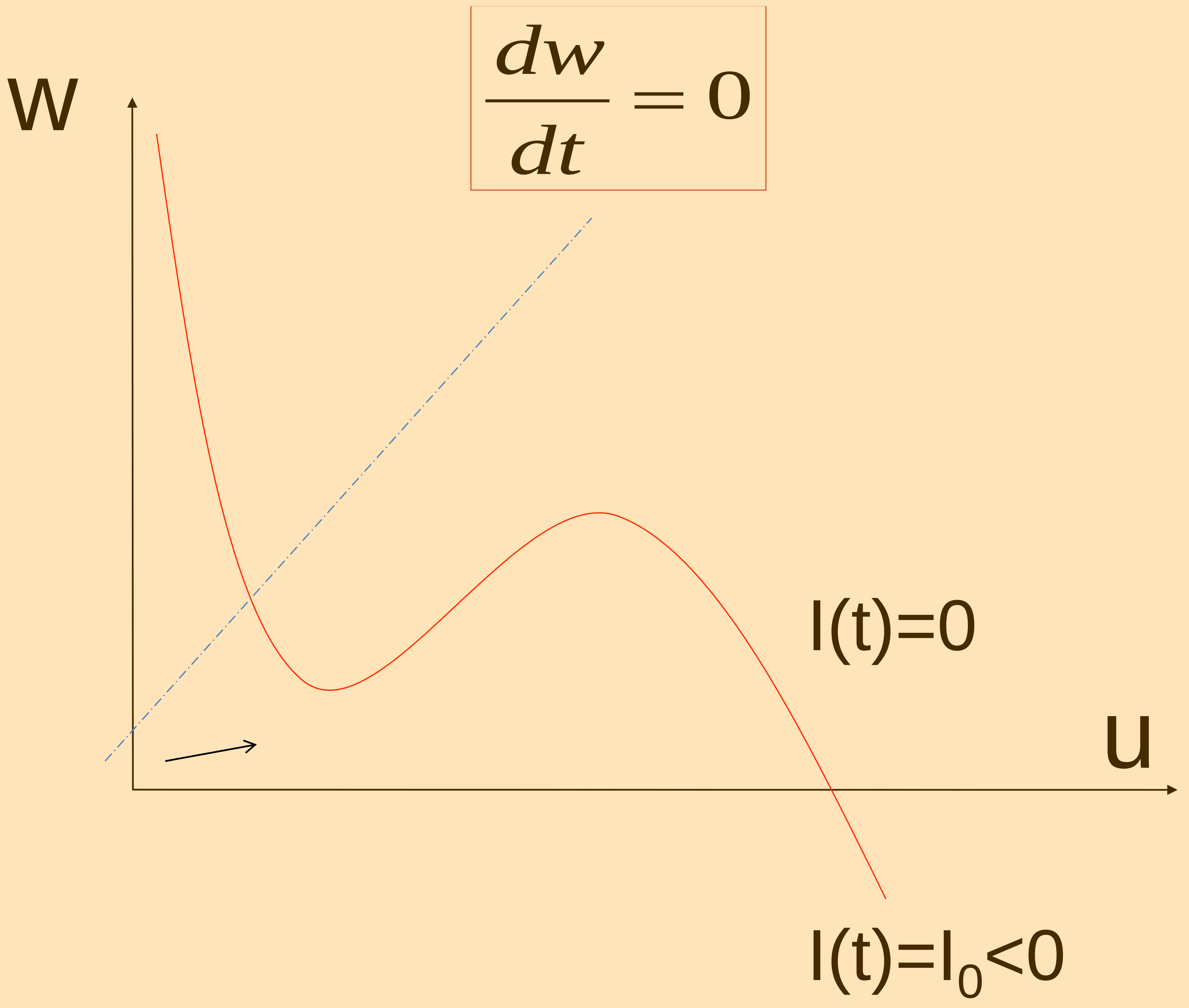


$$\tau_w >> \tau_u \longrightarrow \Delta w << \Delta u$$

Unless close to nullcline



Week 4 - Exercise inhibitory rebound NOW!



Start at 9:25
Next lecture at 9:40

Now exercises

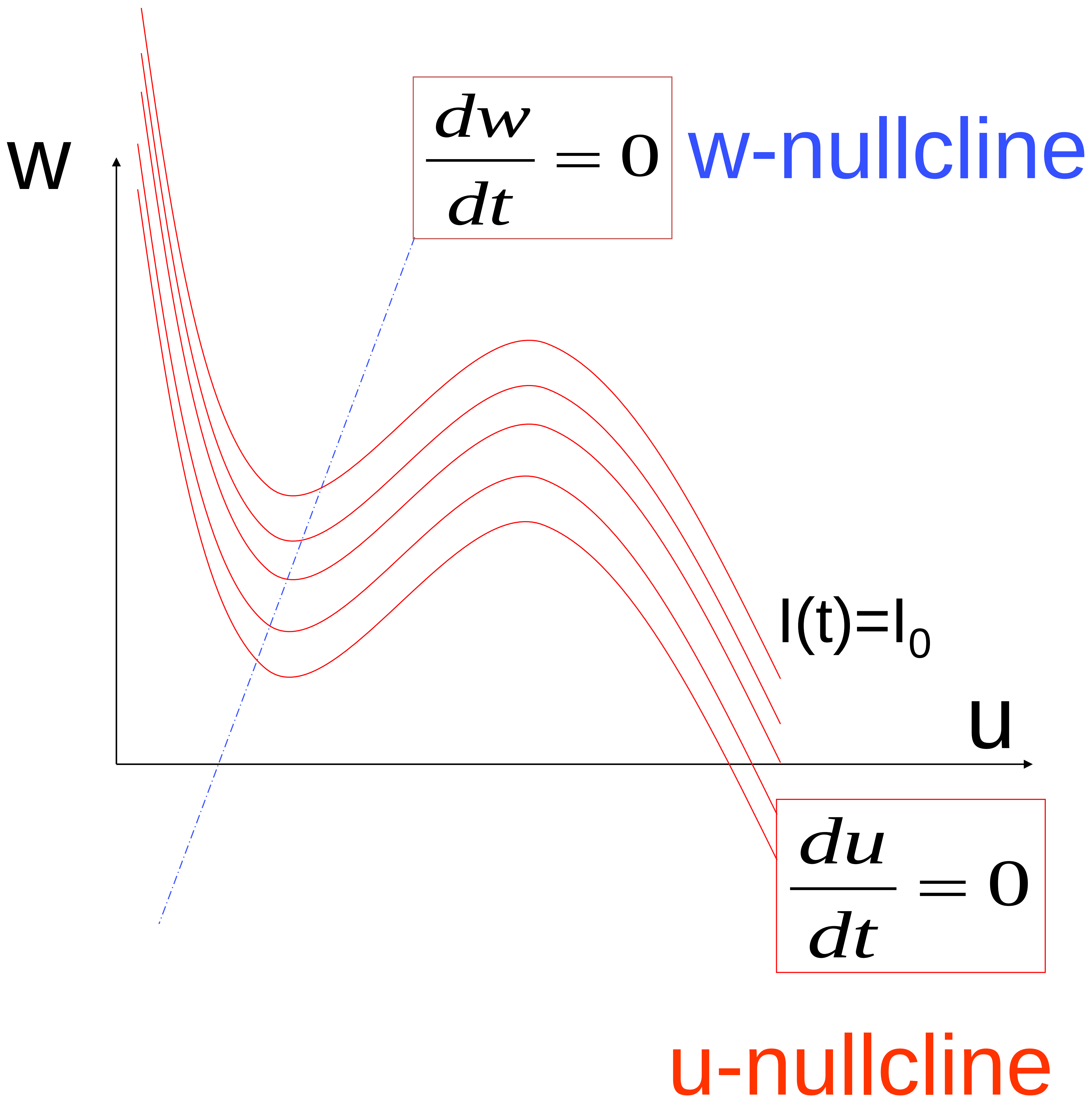
4.1 Nullclines change for constant stimulus

stimulus

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

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

apply constant stimulus I_0



4.1. Limit cycle (example: FitzHugh Nagumo Model)

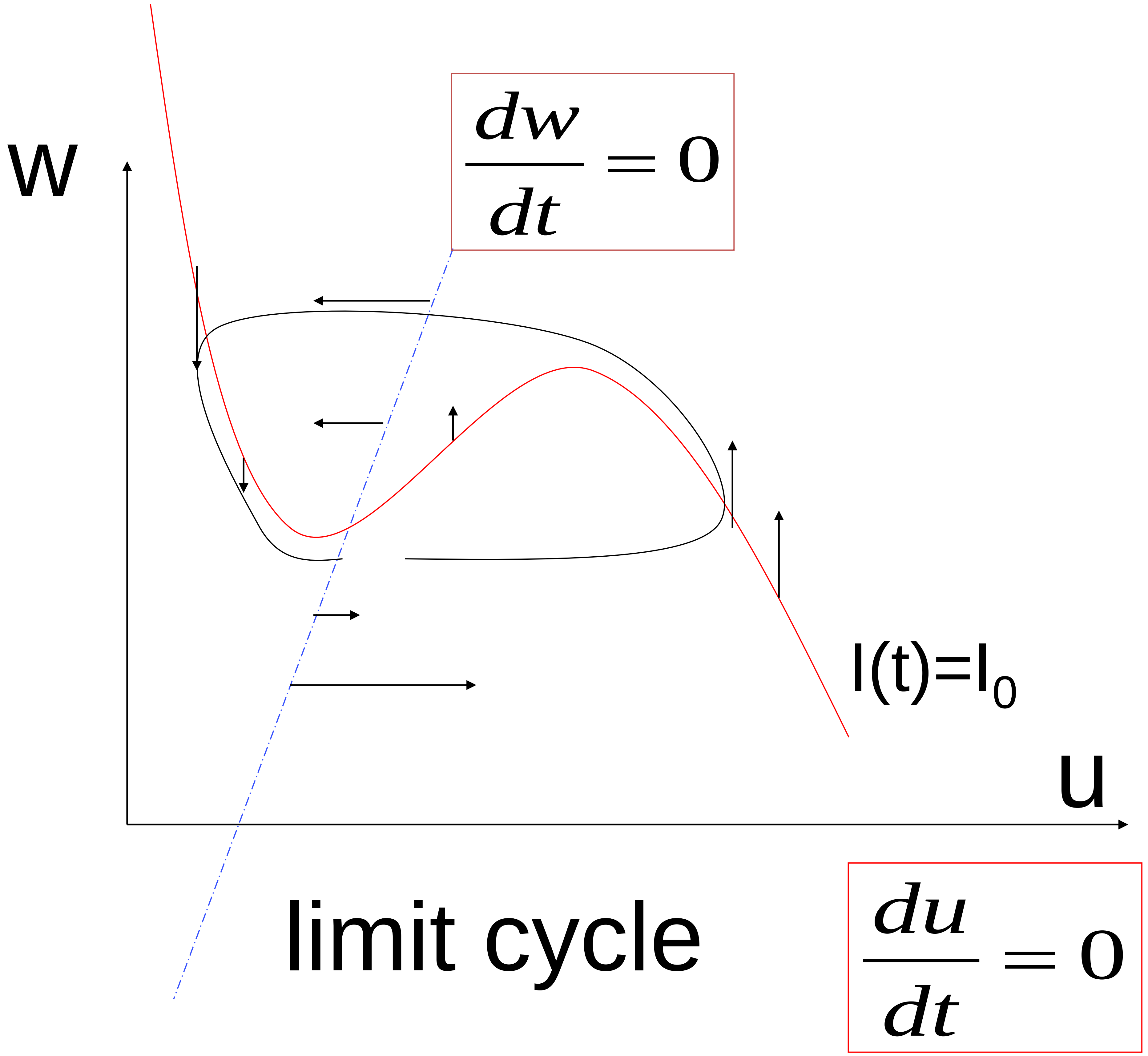
stimulus

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

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

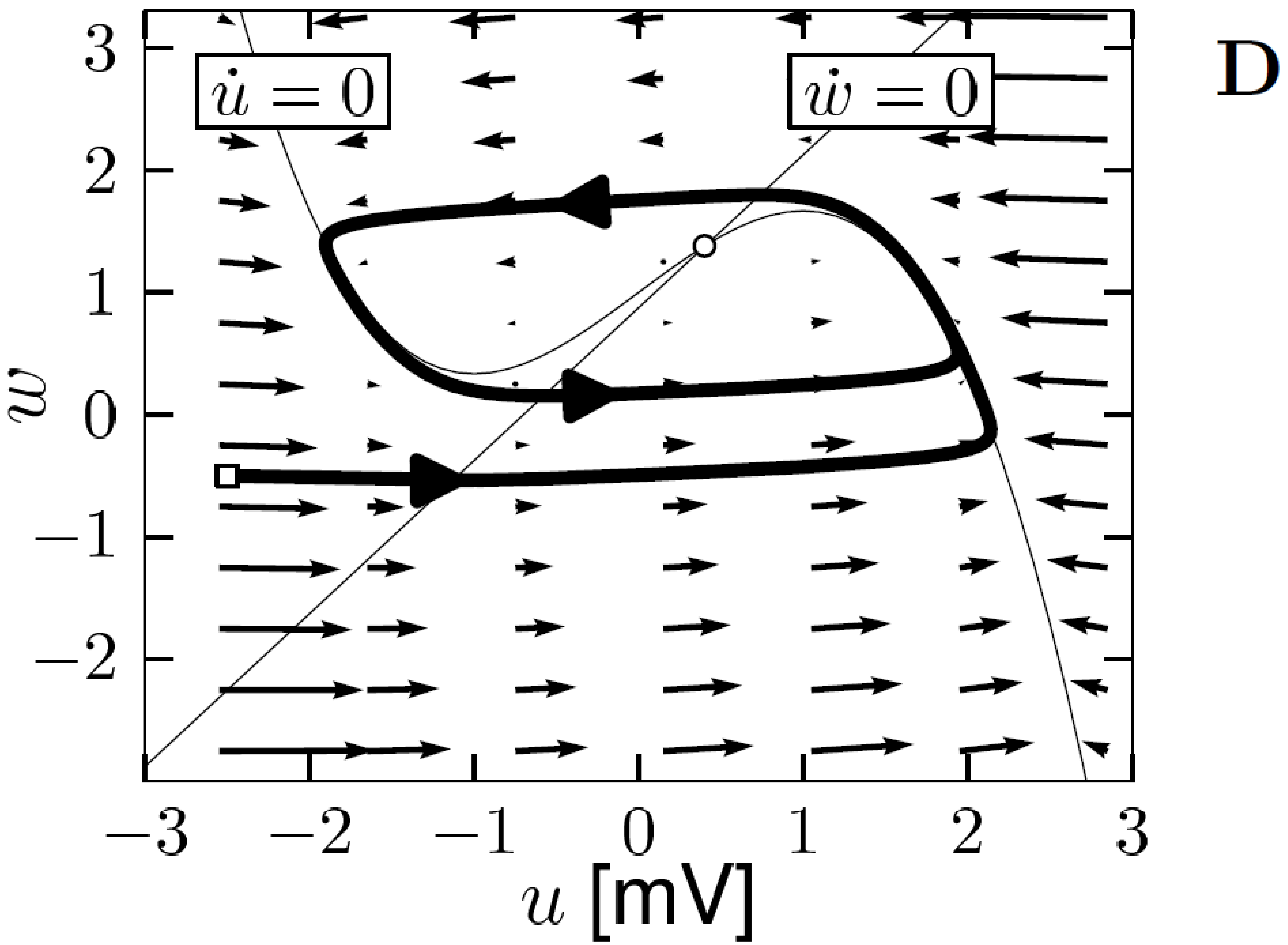
-unstable fixed point
-closed boundary
with arrows pointing inside

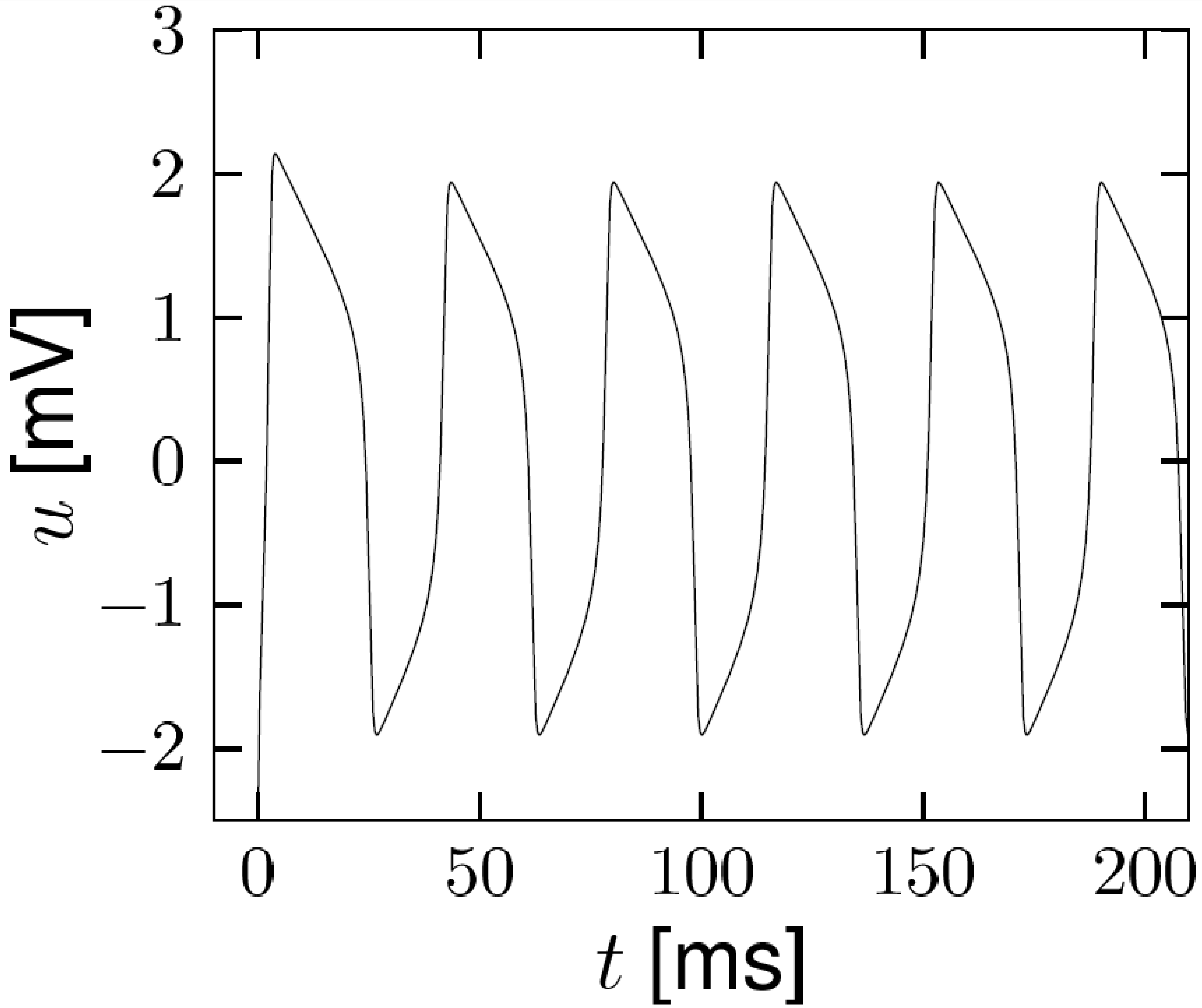
→ limit cycle



limit cycle

4.1. Limit Cycle





-unstable fixed point in 2D

-bounding box with inward flow

→ limit cycle *(Poincare Bendixson)*

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

In 2-dimensional equations,
a limit cycle must exist, if we can
find a surface

-containing one unstable fixed point
-no other fixed point
-bounding box with inward flow
→ limit cycle *(Poincare Bendixson)*

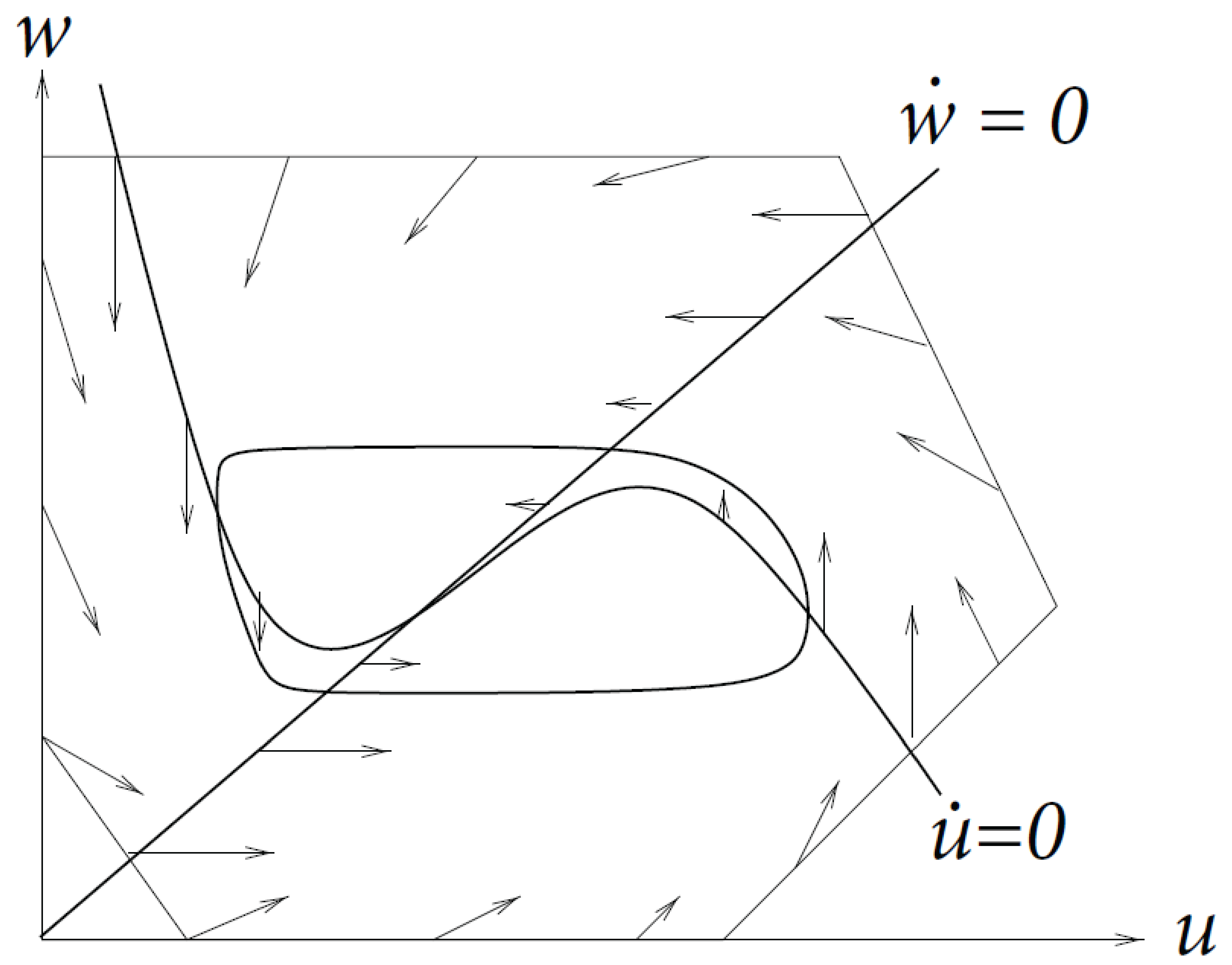


Image: Neuronal Dynamics, Gerstner et al., Cambridge Univ. Press (2014)

4.1 Type II Model

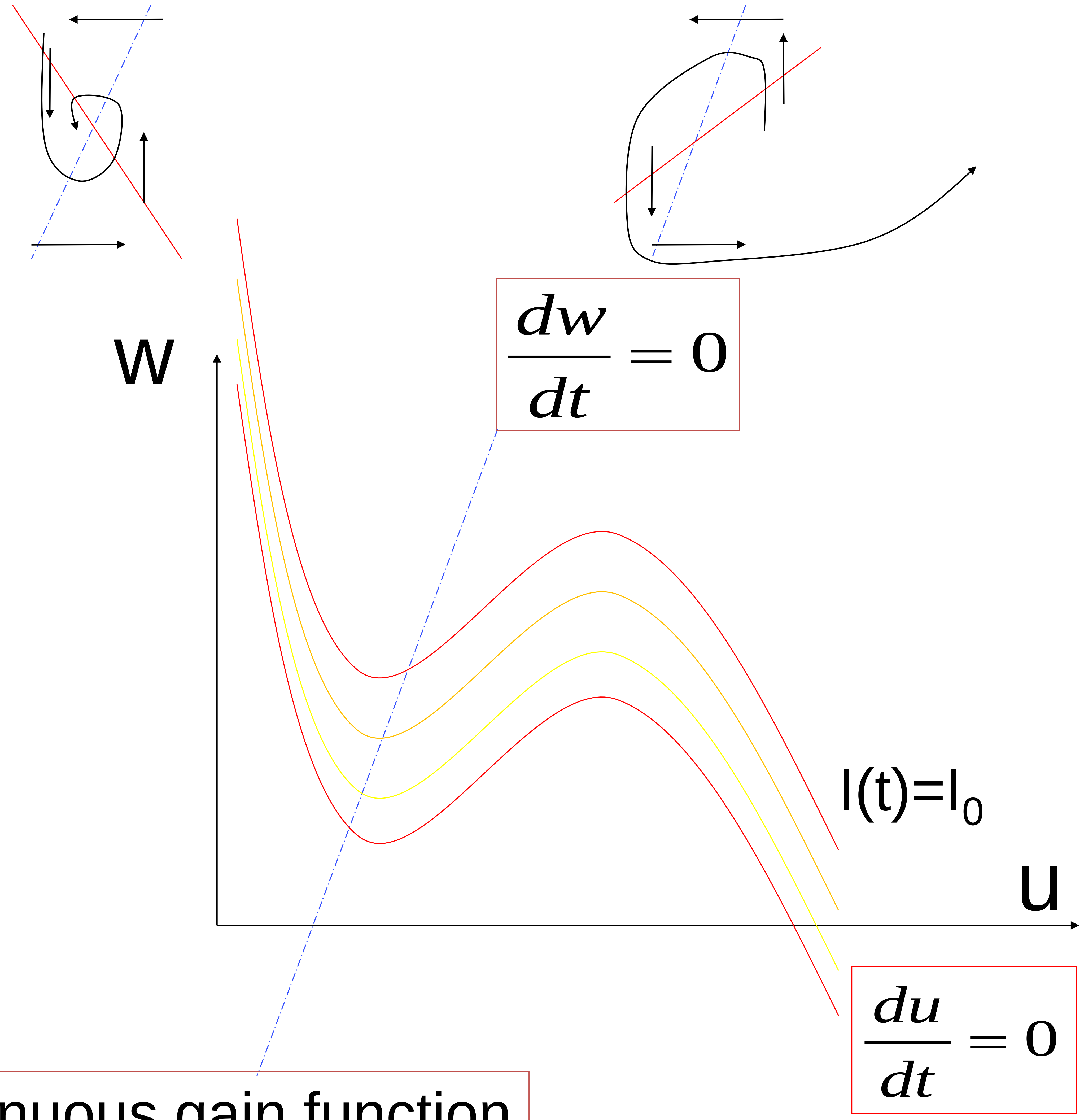
constant input

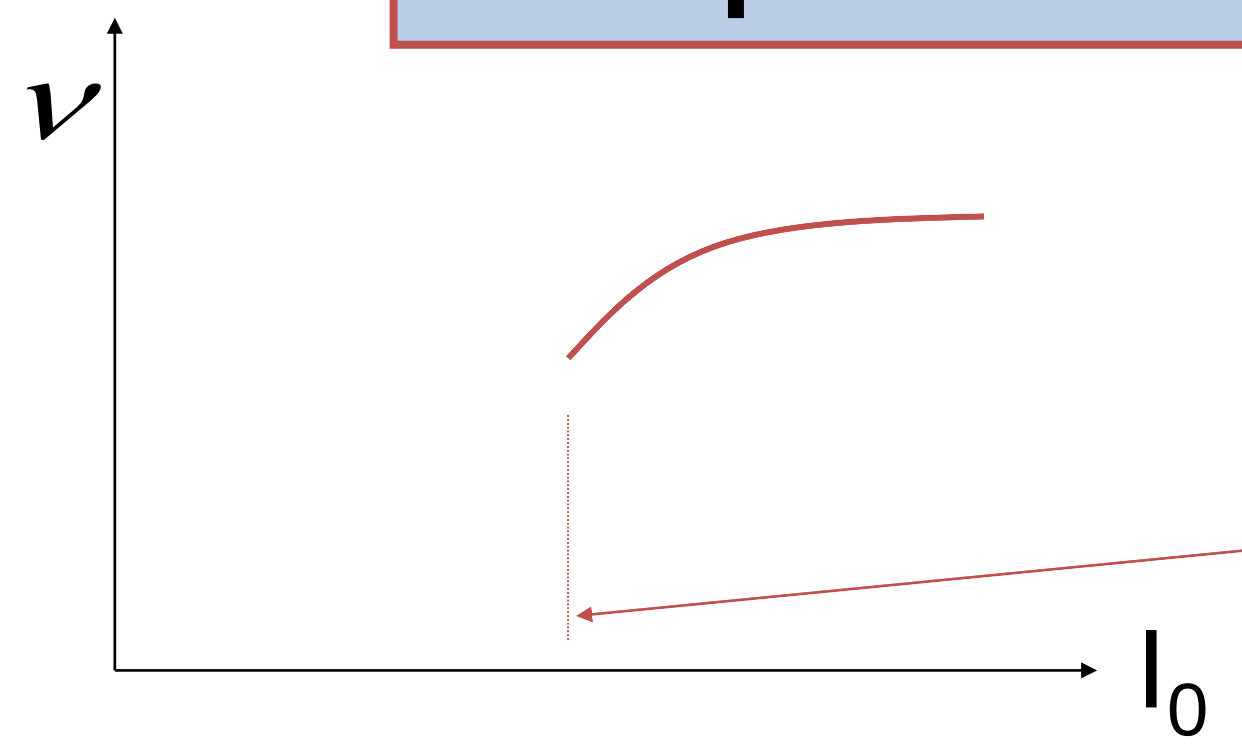
stimulus

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

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

Hopf bifurcation

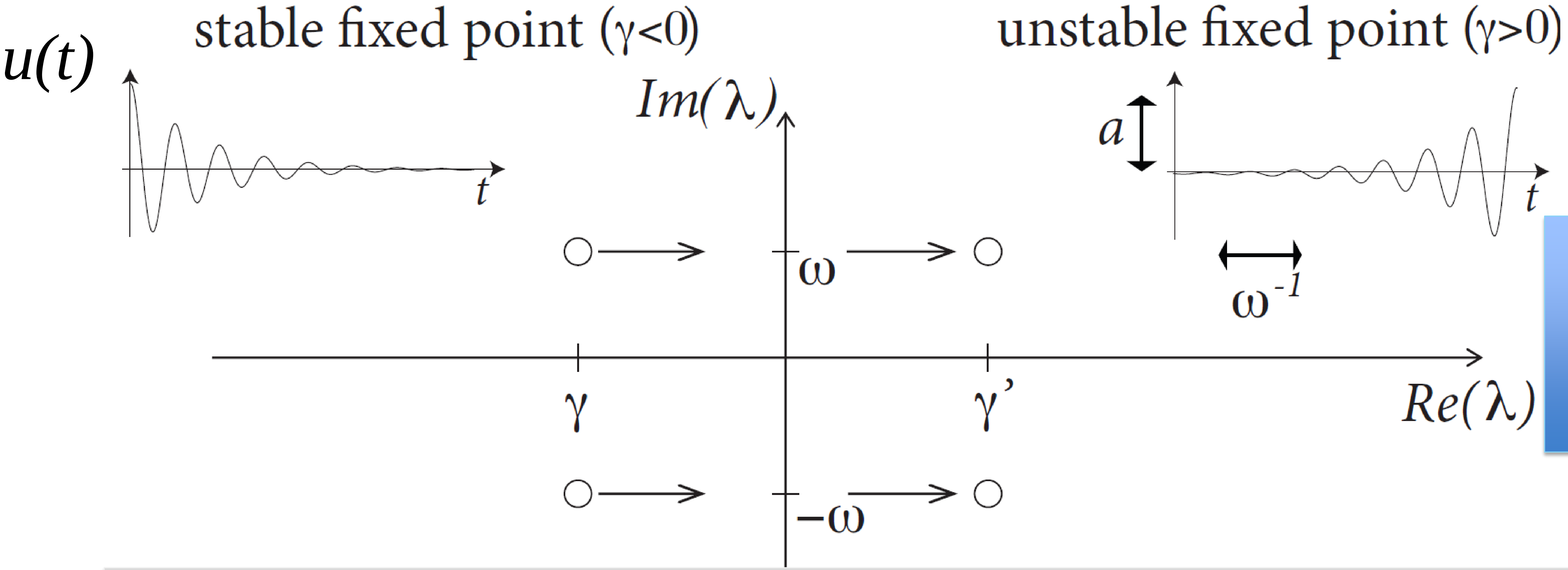




Discontinuous gain function

Stability lost → oscillation with finite frequency

4.1. Hopf bifurcation

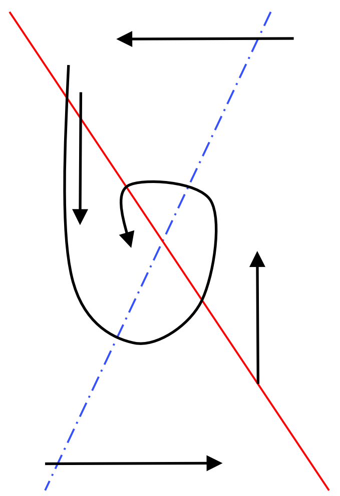


$$\lambda = \gamma + i\omega$$

$$\lambda = \gamma - i\omega$$

Blackboard

$\gamma < 0$



$\gamma > 0$

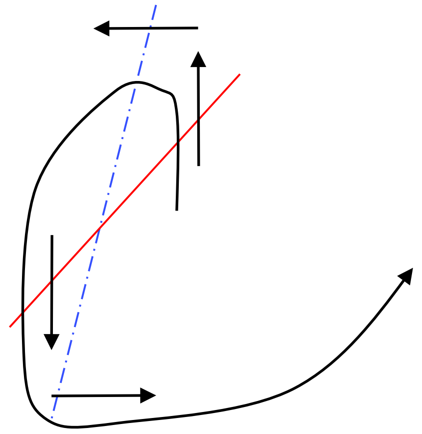
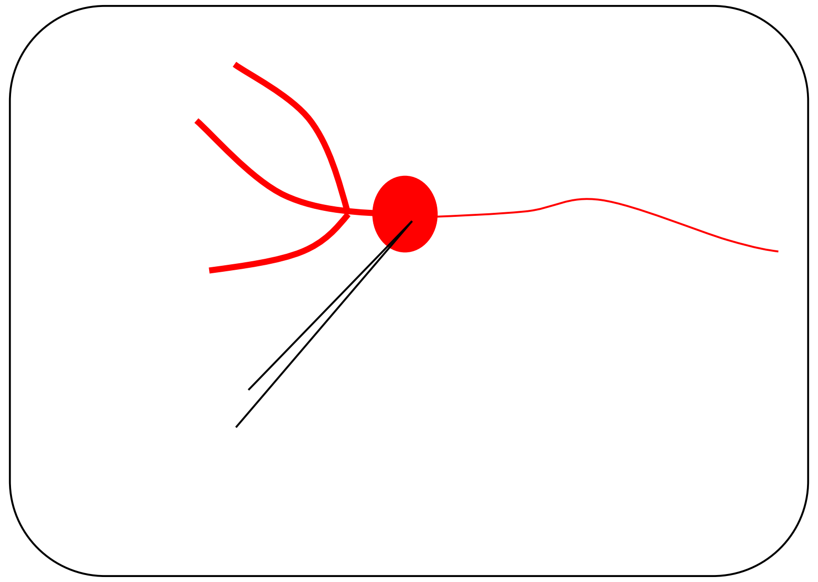
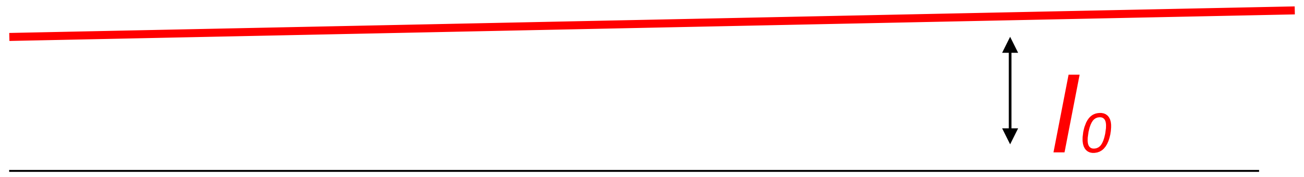


Image: Neuronal Dynamics, Gerstner et al., Cambridge Univ. Press (2014)

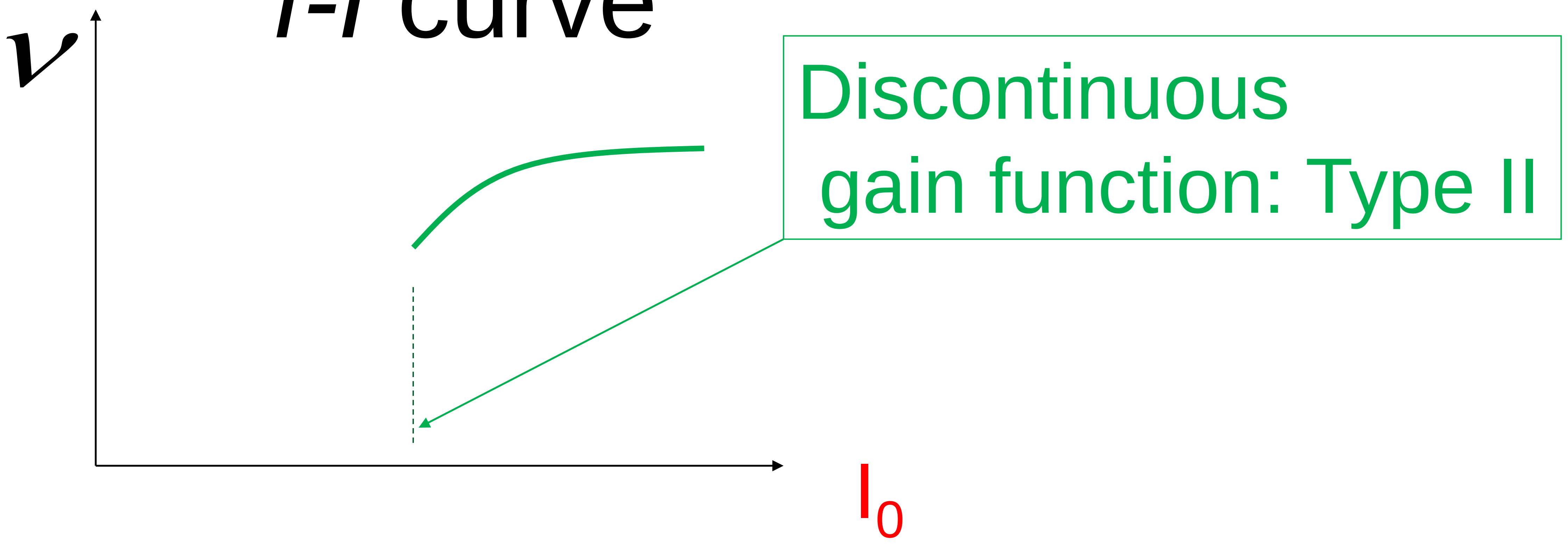
4.1. Hopf bifurcation: *f-I* -curve

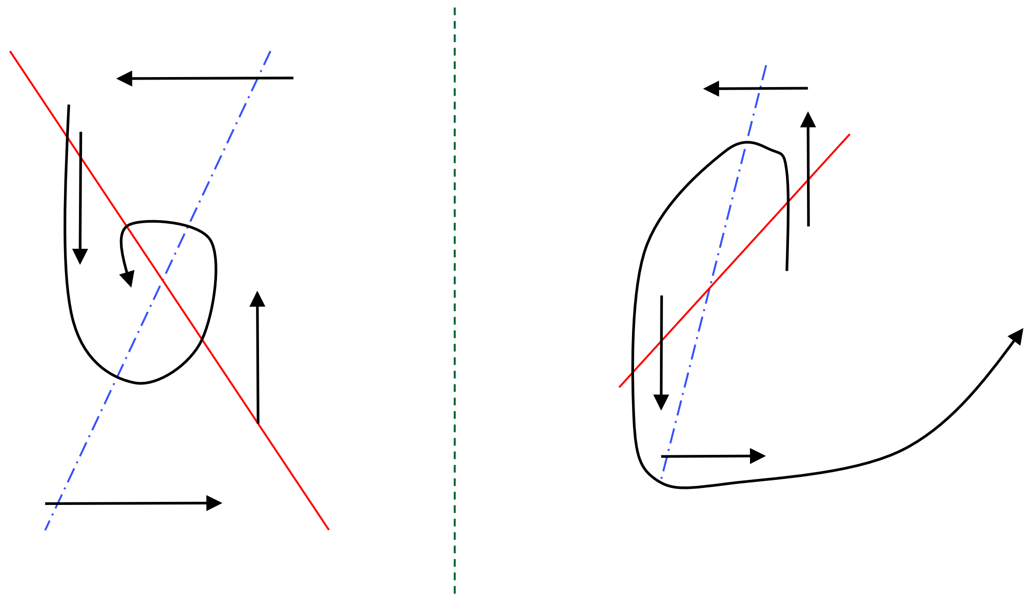


ramp input/
constant input



f-I curve

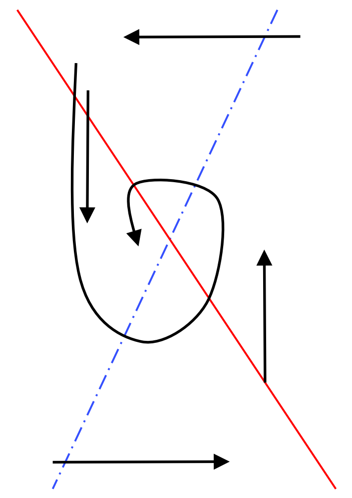


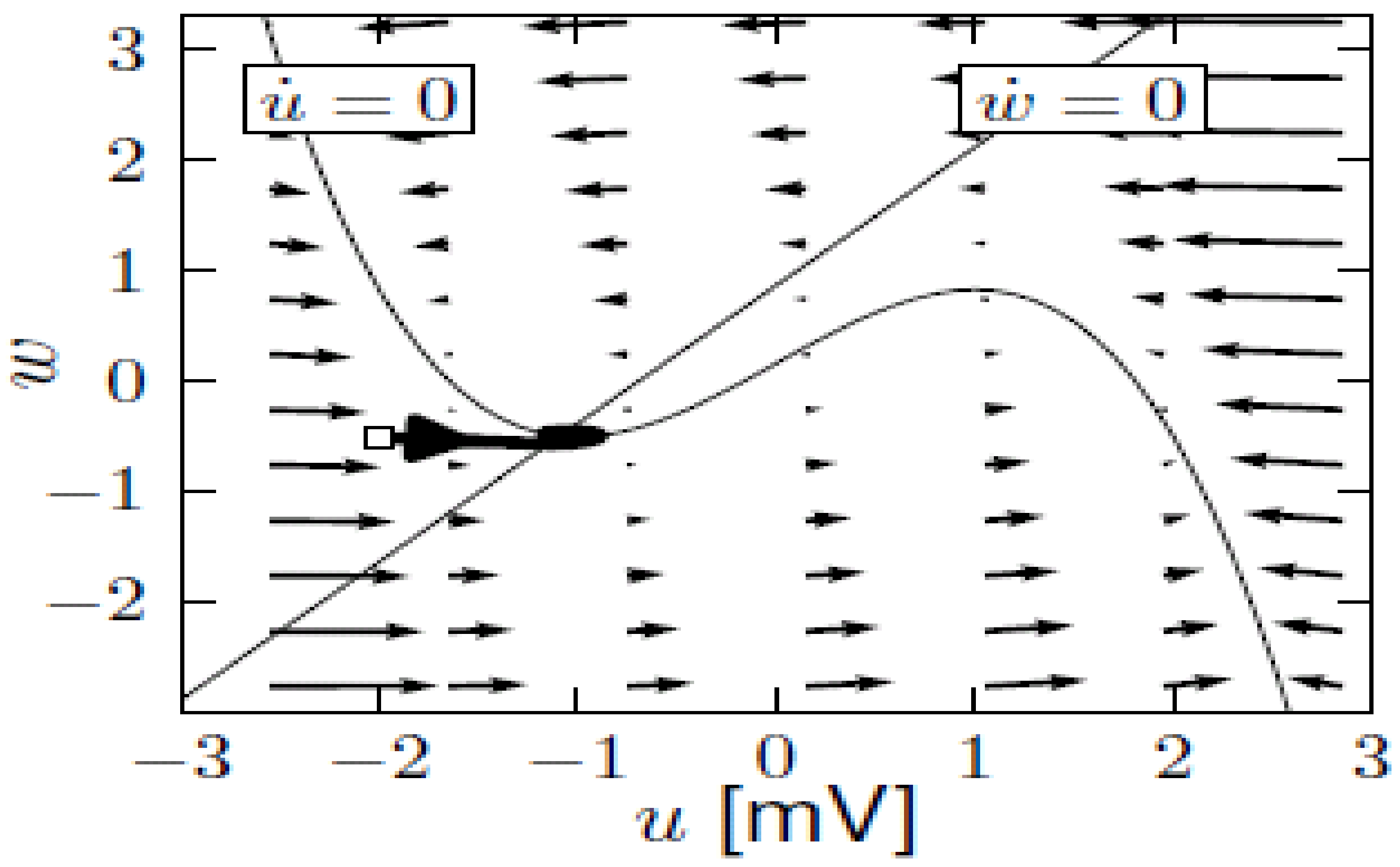


Stability lost → oscillation with finite frequency

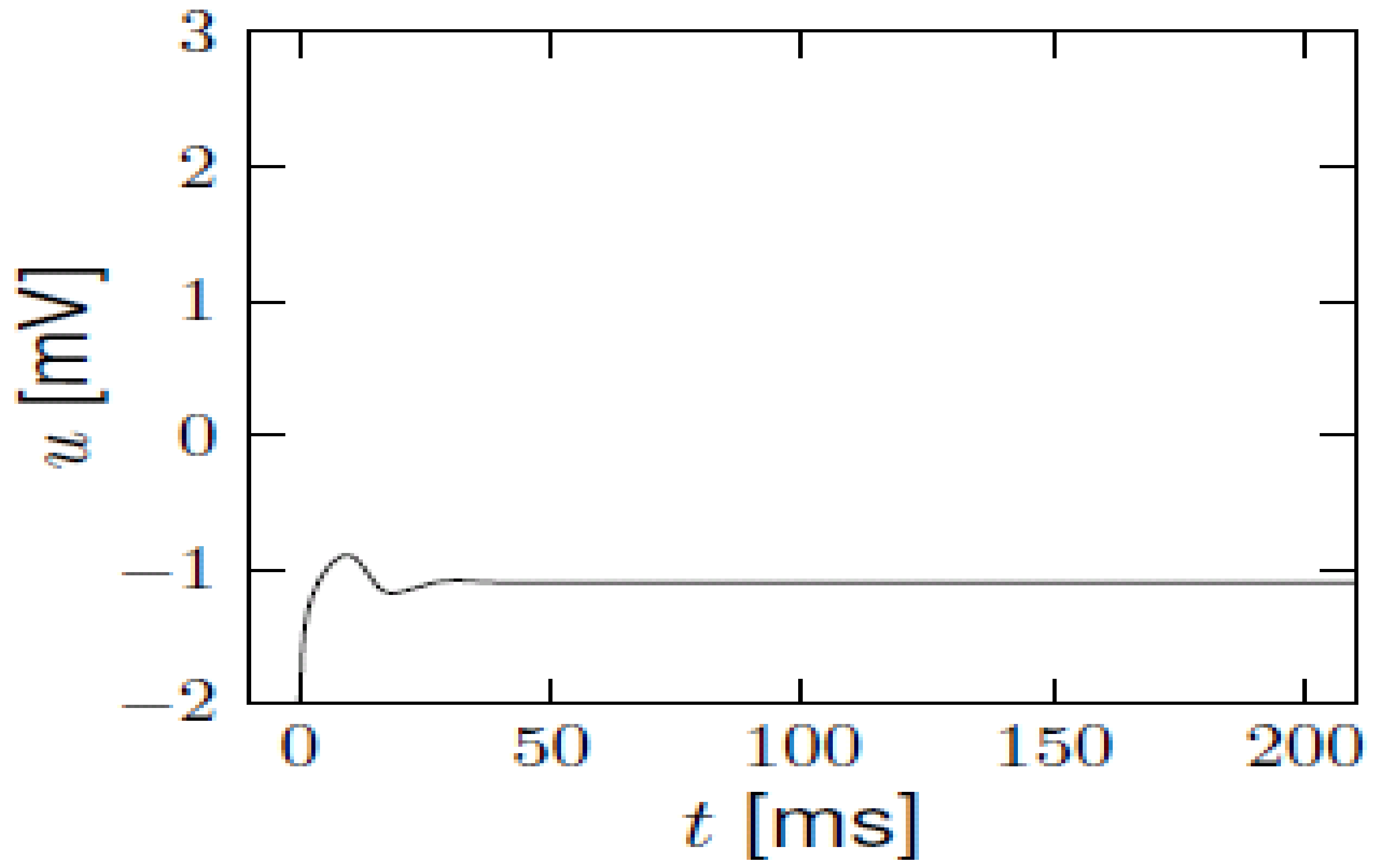
4.1 Example: FitzHugh-Nagumo / Hopf bifurcation

I=0

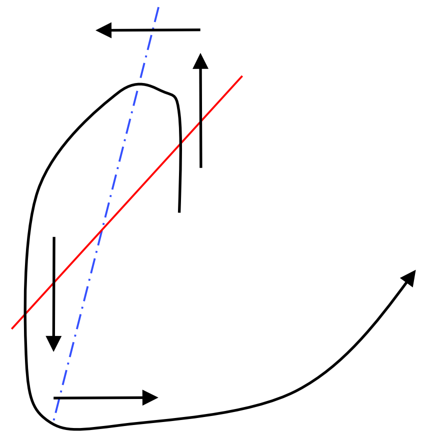


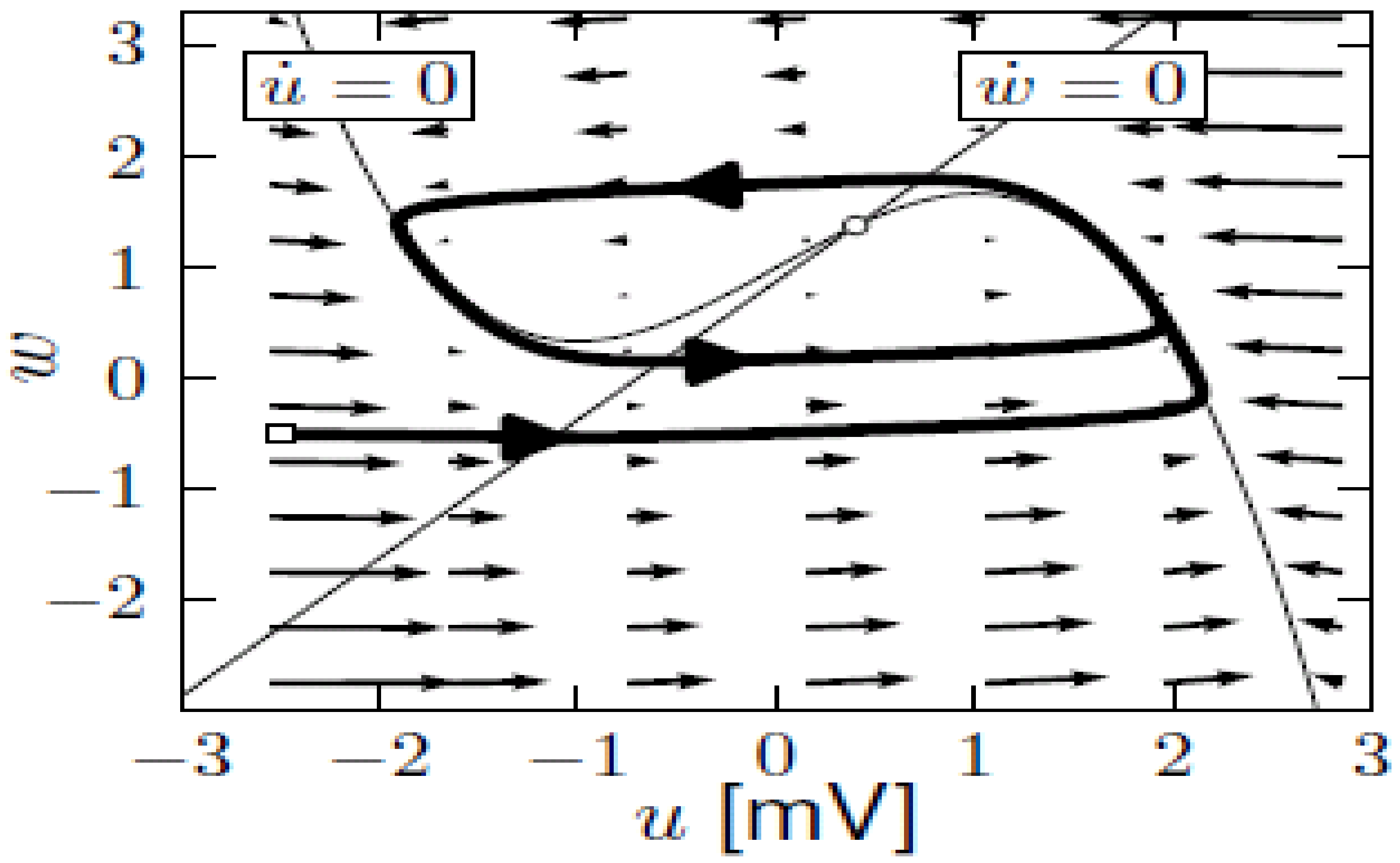


B

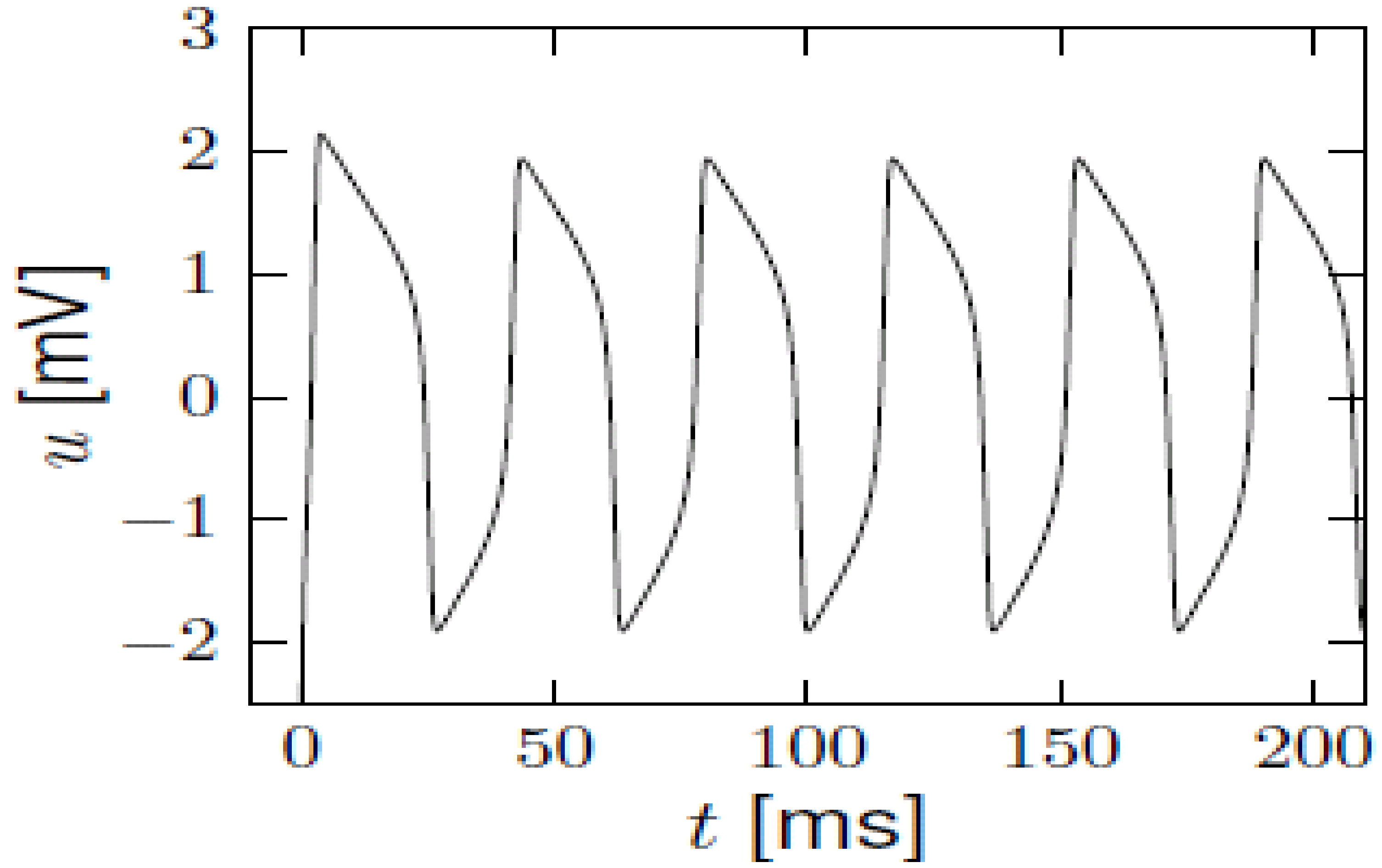


$I > I_c$

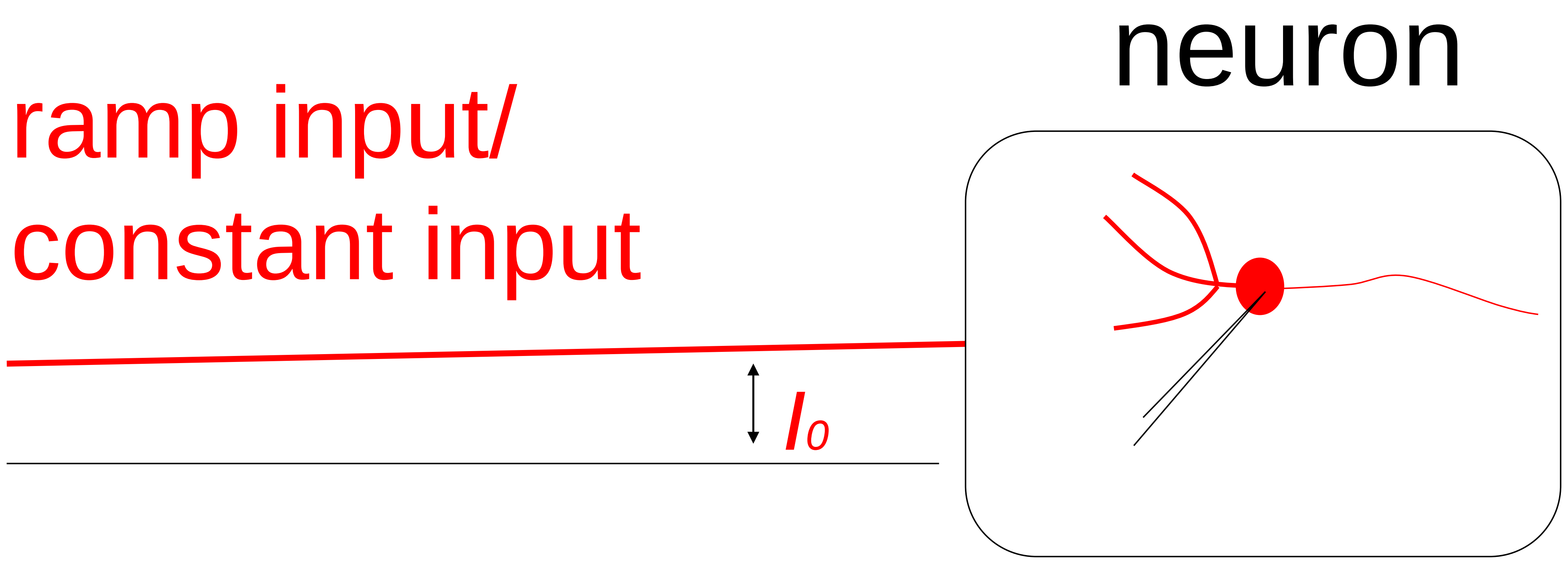




D

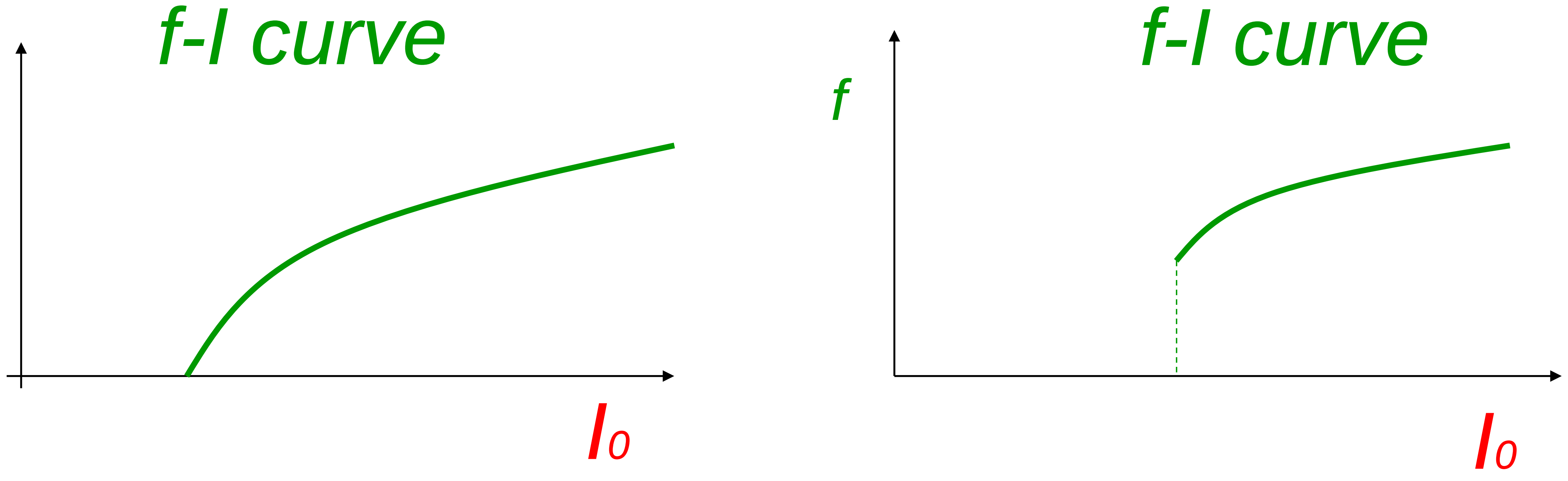


4.1. Type I and II Neuron Models



Now:
Type I model

Type I and type II models



4.1. Type I Neuron Models: saddle-node bifurcation

type I Model: 3 fixed points

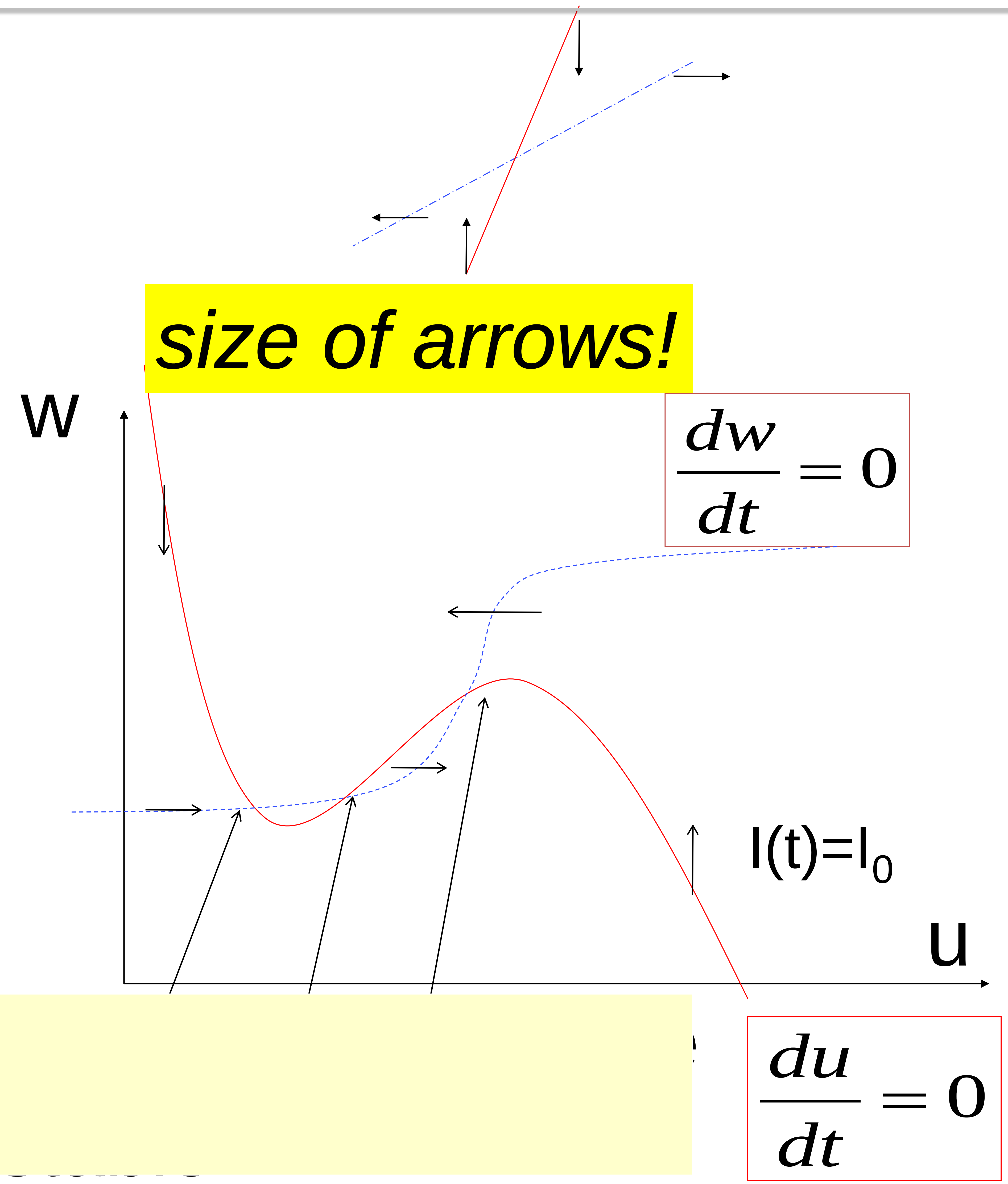
stimulus

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

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

apply constant stimulus I_0

Saddle-node bifurcation



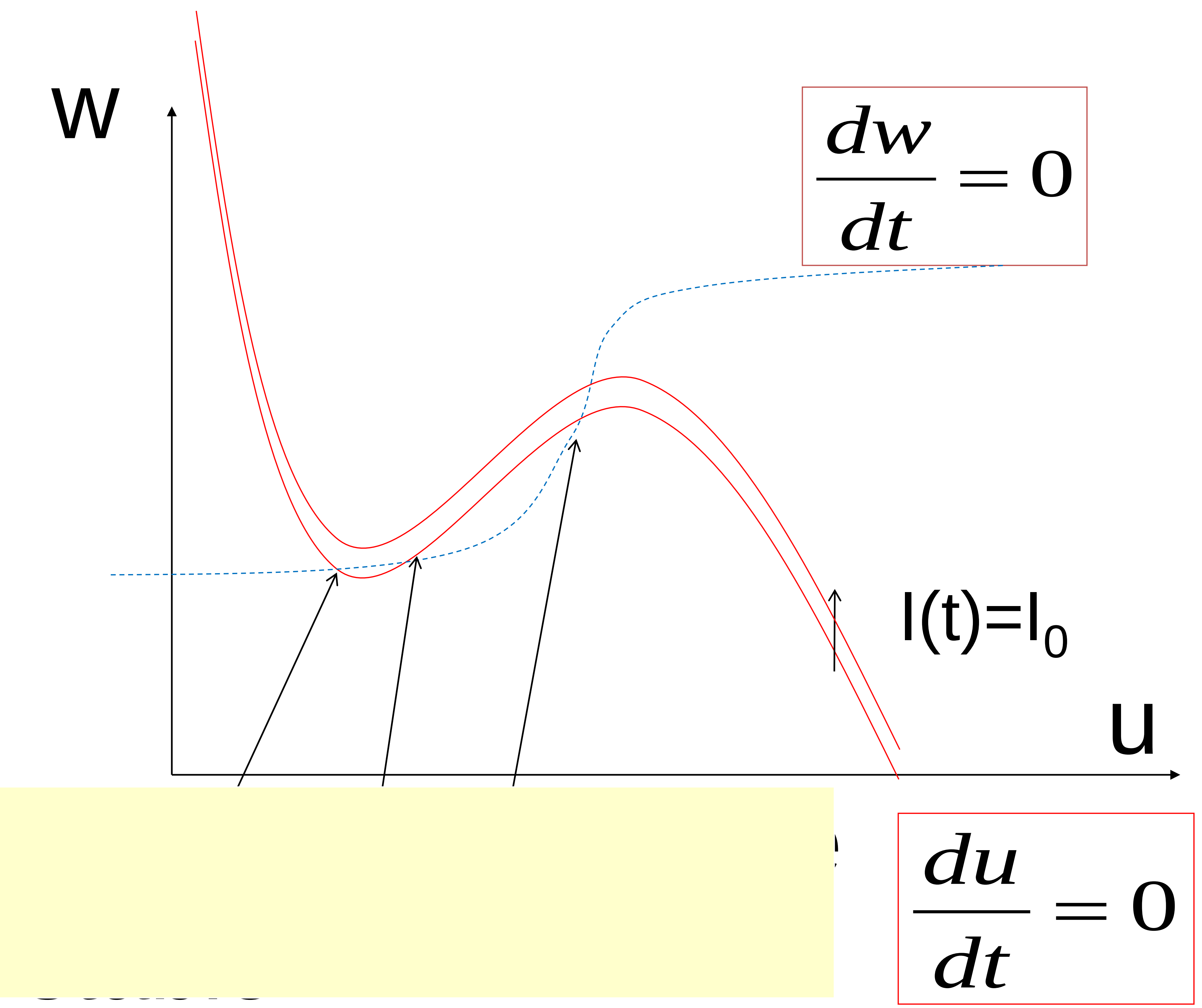
4.1. Type I Neuron Models: saddle-node bifurcation

stimulus

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

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

constant input



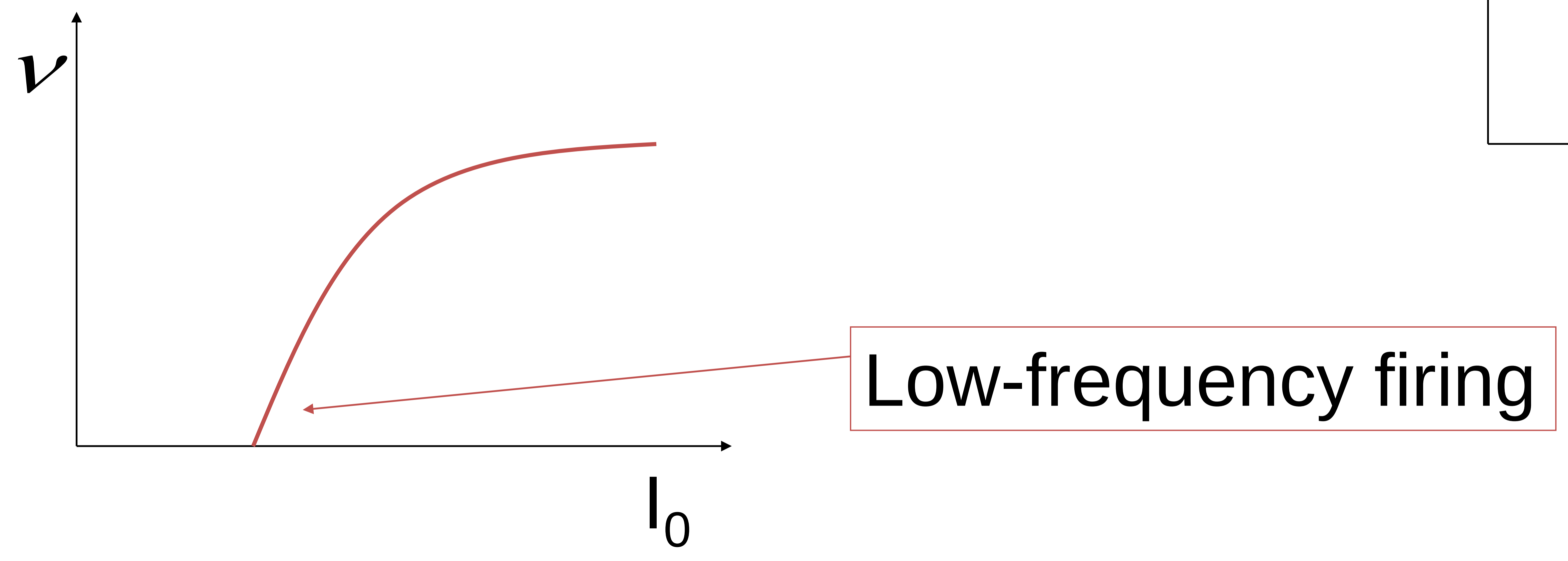
Blackboard:
- flow arrows,
- ghost/ruins

4.1. Type I Neuron Models: saddle-node bifurcation

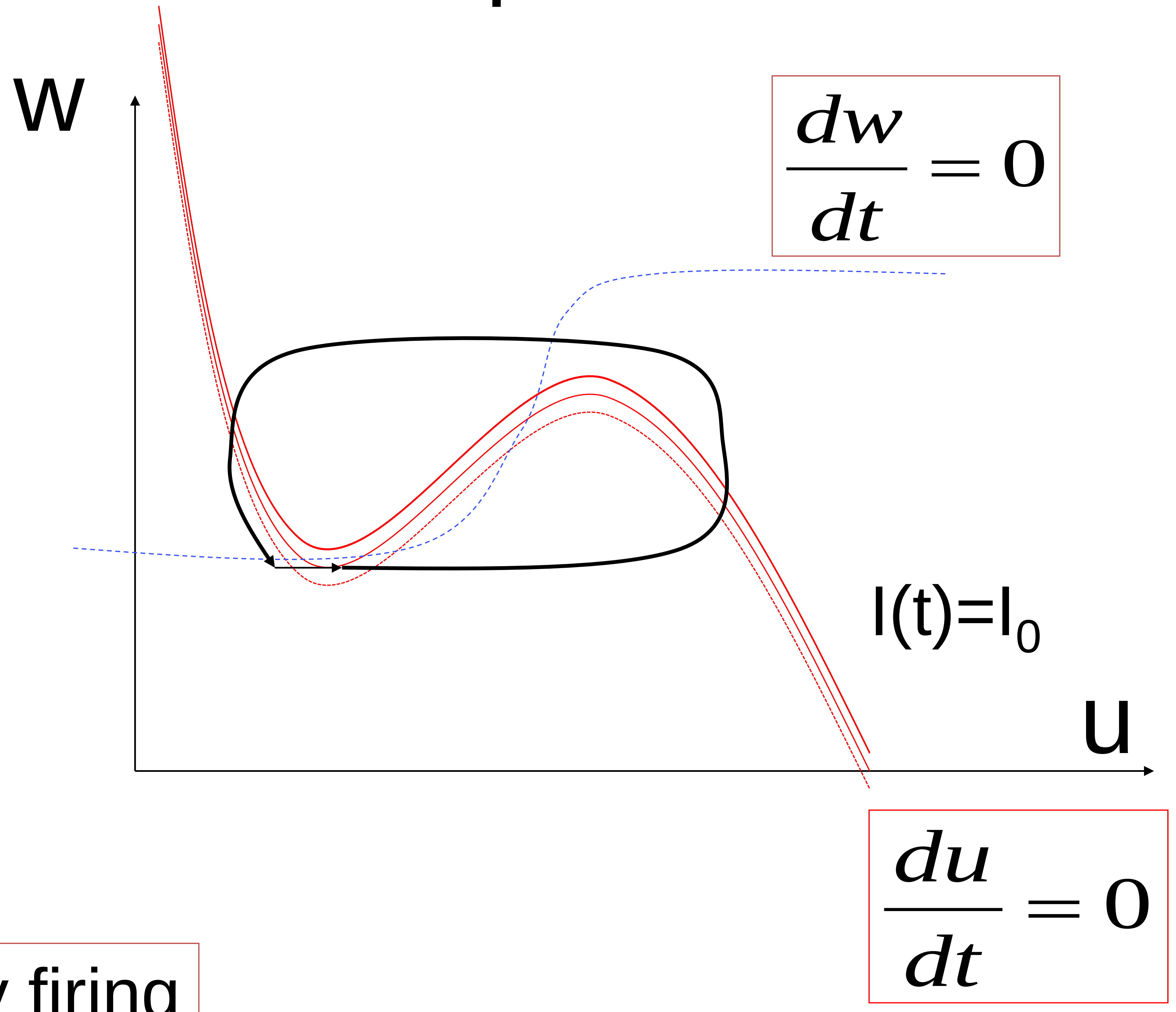
stimulus

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

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



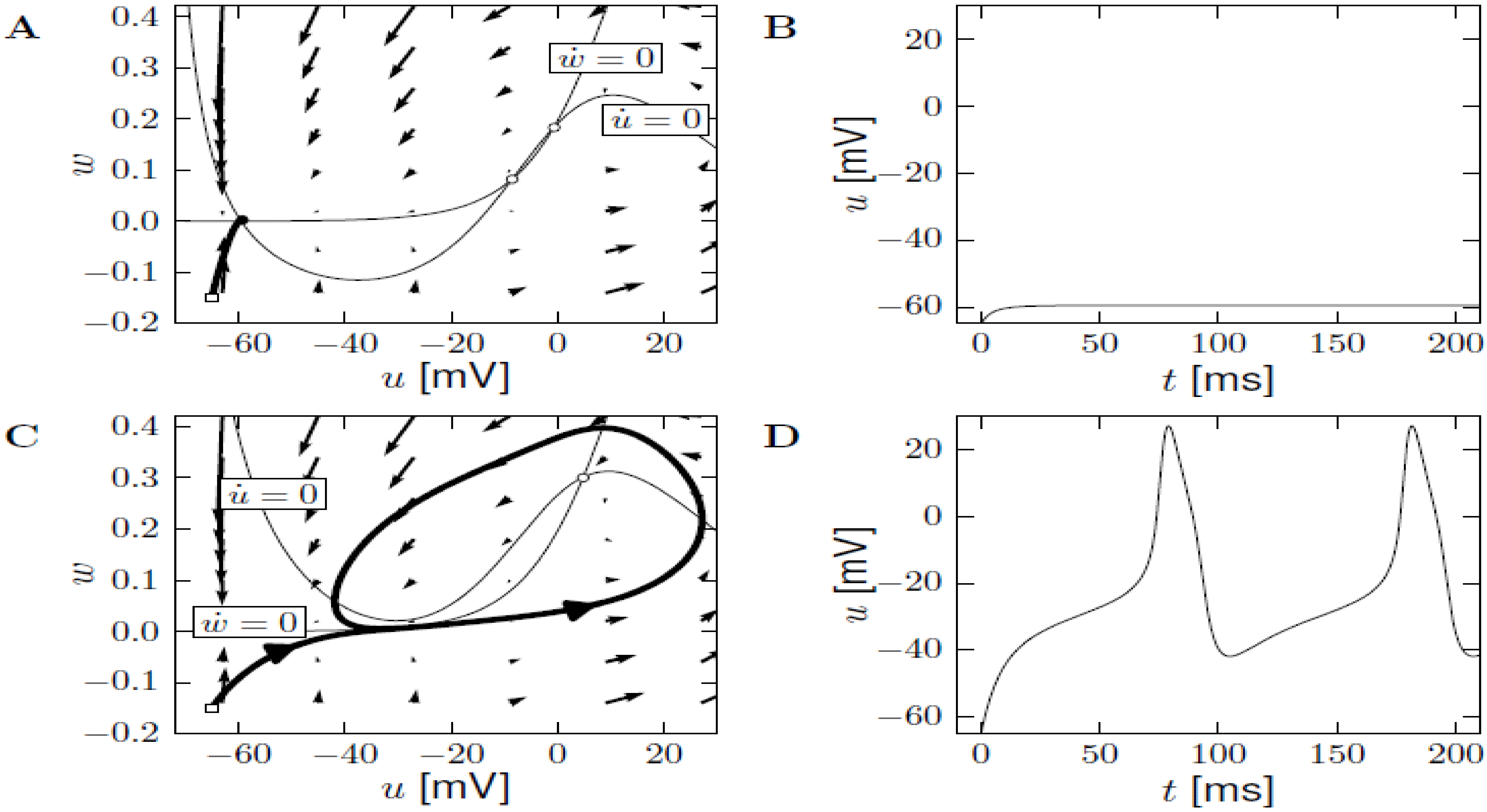
constant input



4.1. Example: Morris-Lecar as type I Model

I=0

I>I_c



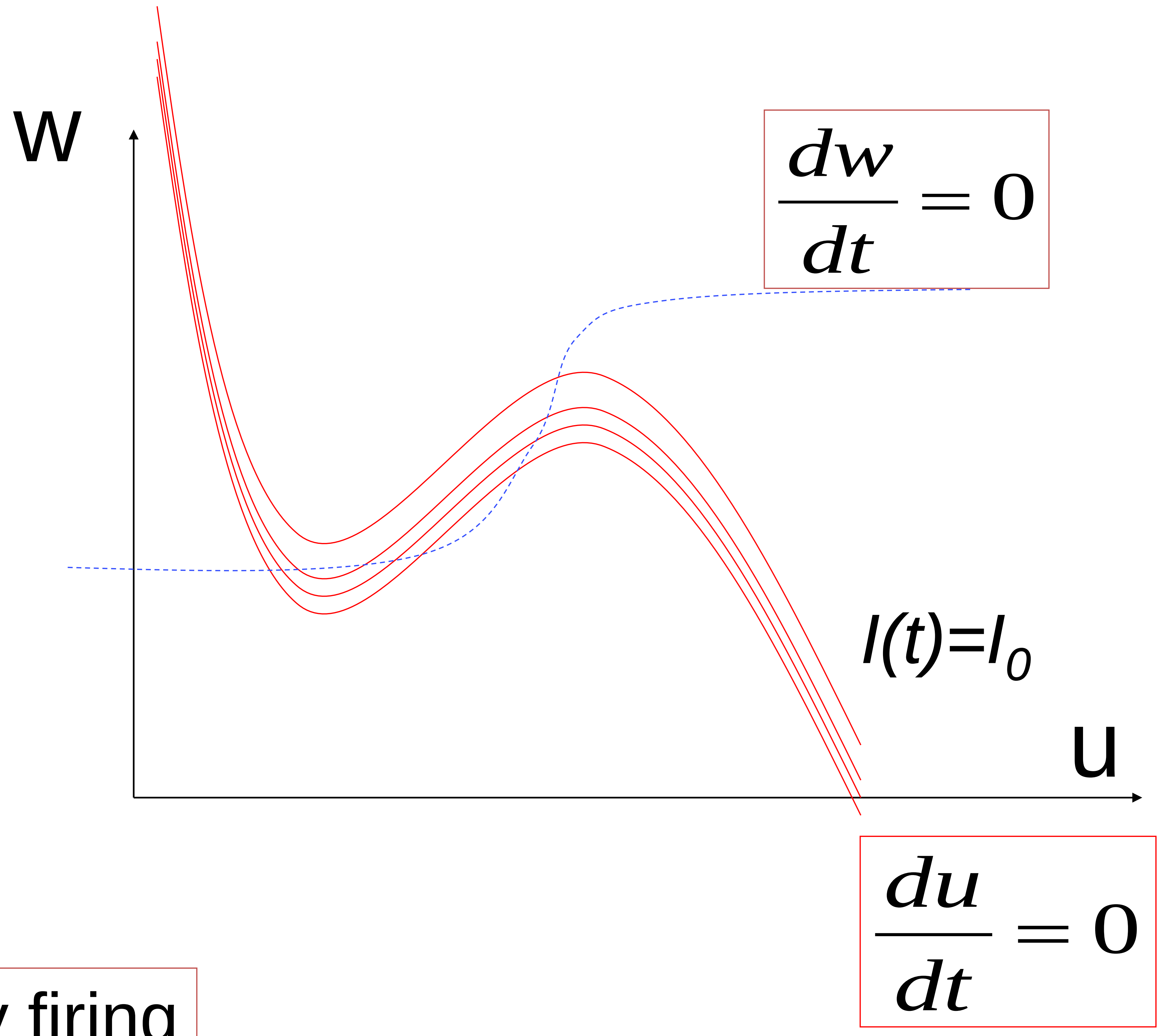
4.1. Example: Morris-Lecar as type I Model

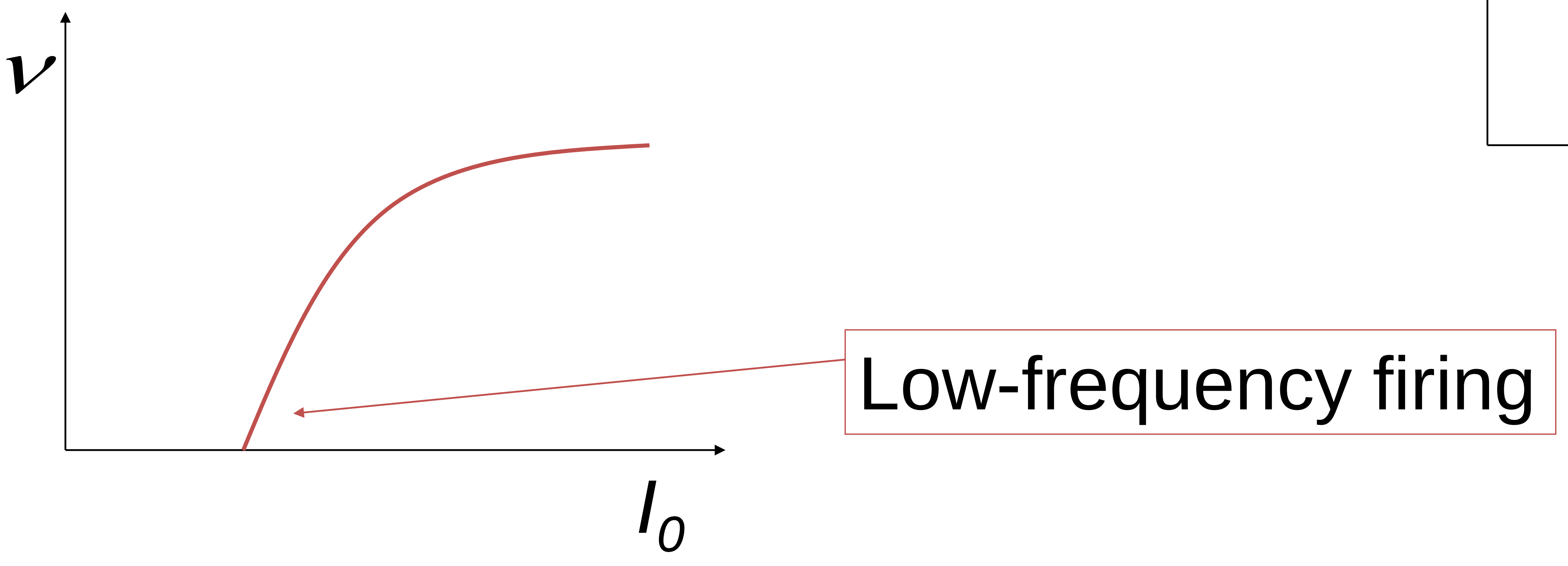
stimulus

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

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

$$w_0(u) = 0.5[1 + \tanh(\tfrac{u-\theta}{d})]$$





4.1. Type I and II Neuron Models

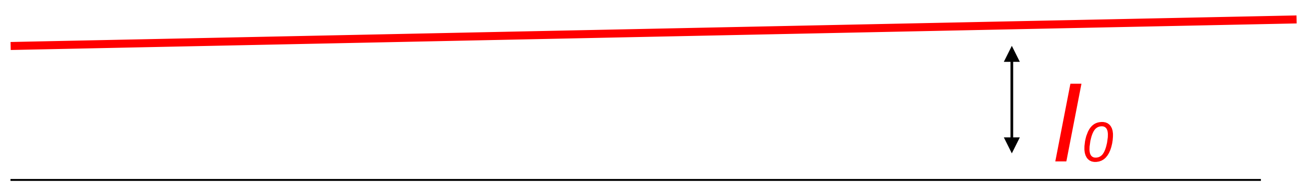
Response at firing threshold?

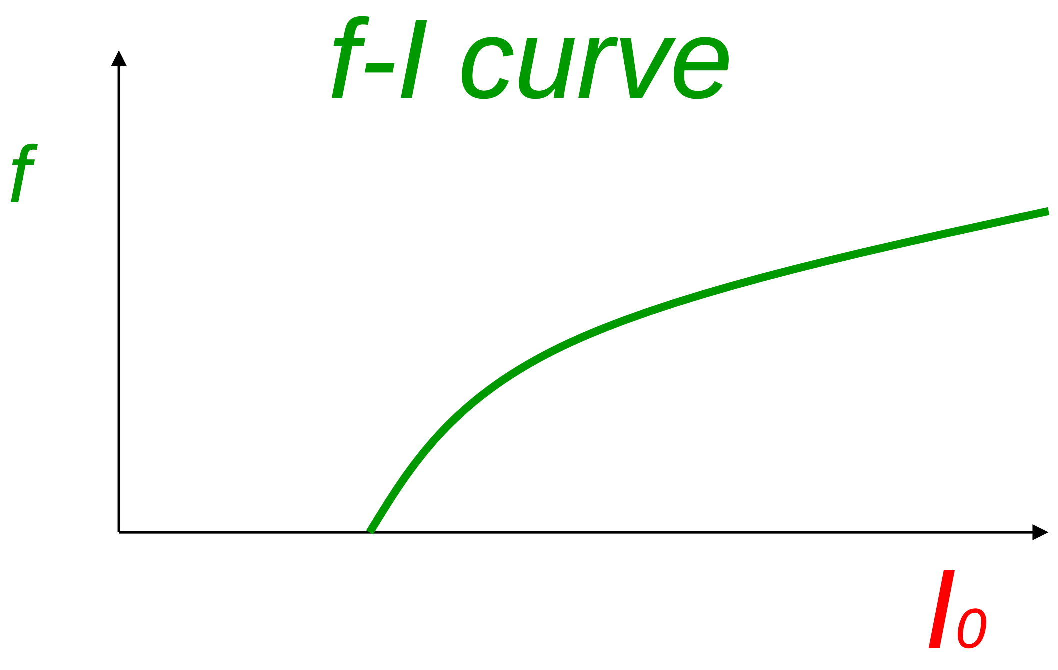
Type I	type II

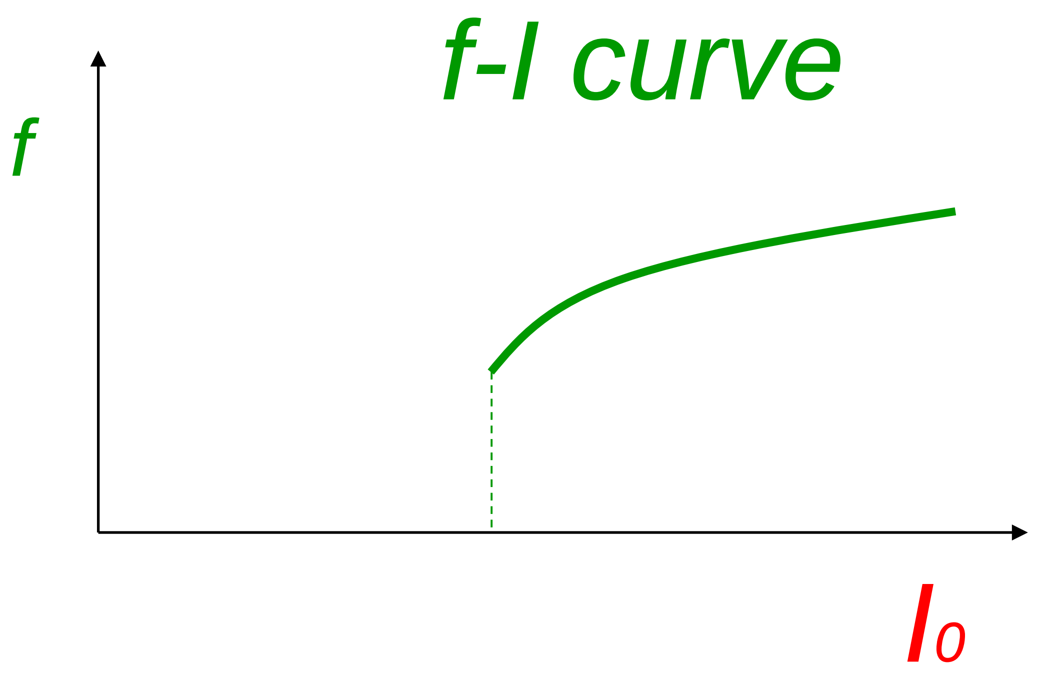
Saddle-Node
Onto limit cycle

For example:
Subcritical Hopf

ramp input/
constant input







4.1. Type I and II Neuron Models

2-dimensional equation

stimulus

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

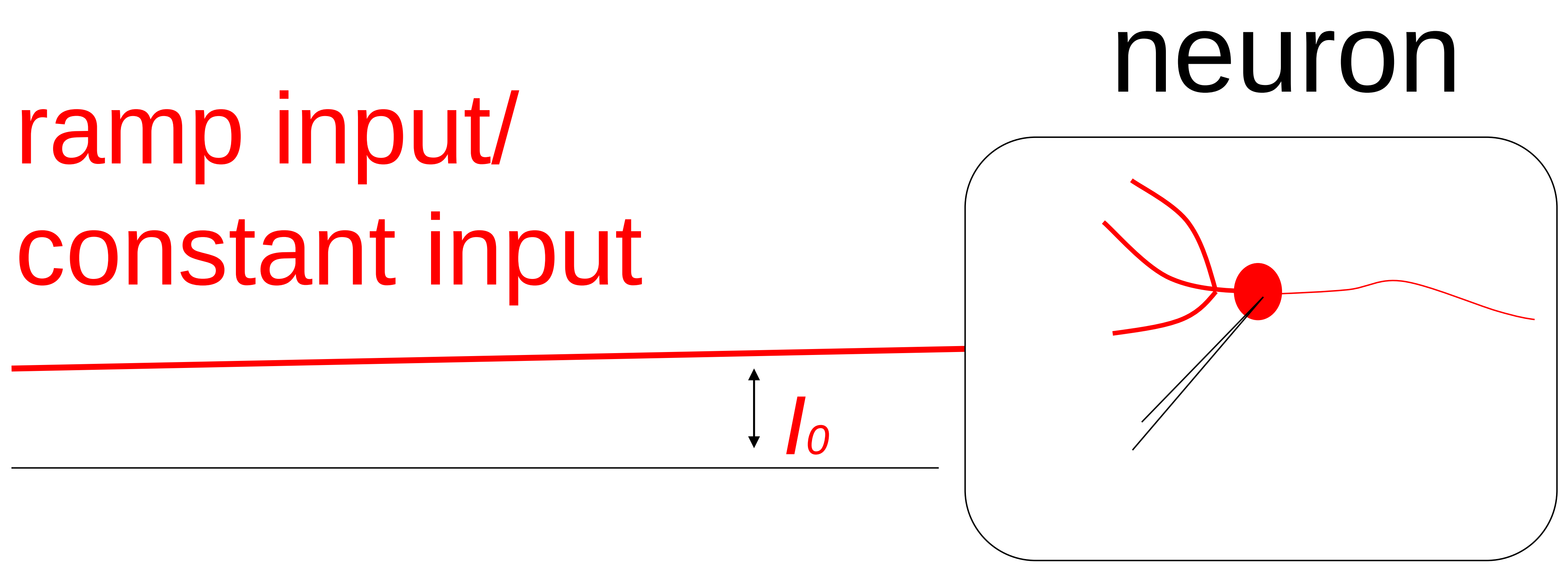
$$\tau_w \frac{dw}{dt} = G(u,w)$$

Enables graphical analysis!

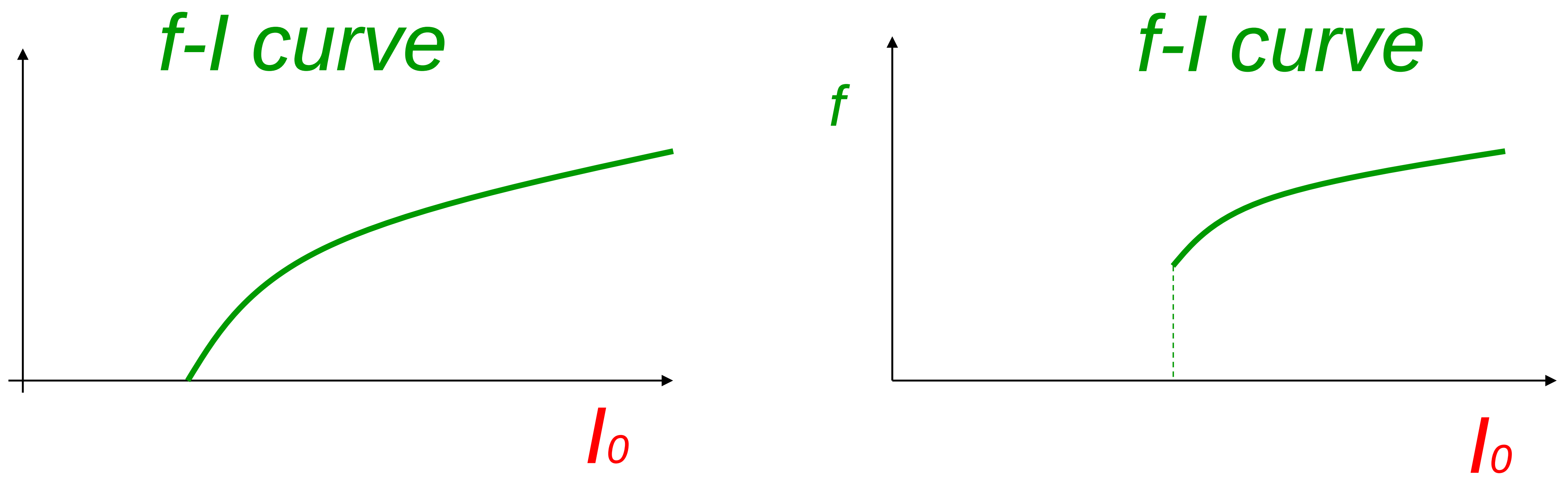
Constant input

→ repetitive firing (or not)

→ limit cycle (or not)



Type I and type II models



Neuronal Dynamics – Quiz 4.1.

A. 2-dimensional neuron model with (supercritical) saddle-node-onto-limit cycle bifurcation

[ ] The neuron model is of type II, because there is a jump in the f-I curve

[ ] The neuron model is of type I, because the f-I curve is continuous

[ ] The neuron model is of type I, if the limit cycle passes through a regime where the flow is very slow.

B. Threshold in a 2-dimensional neuron model with subcritical Hopf bifurcation

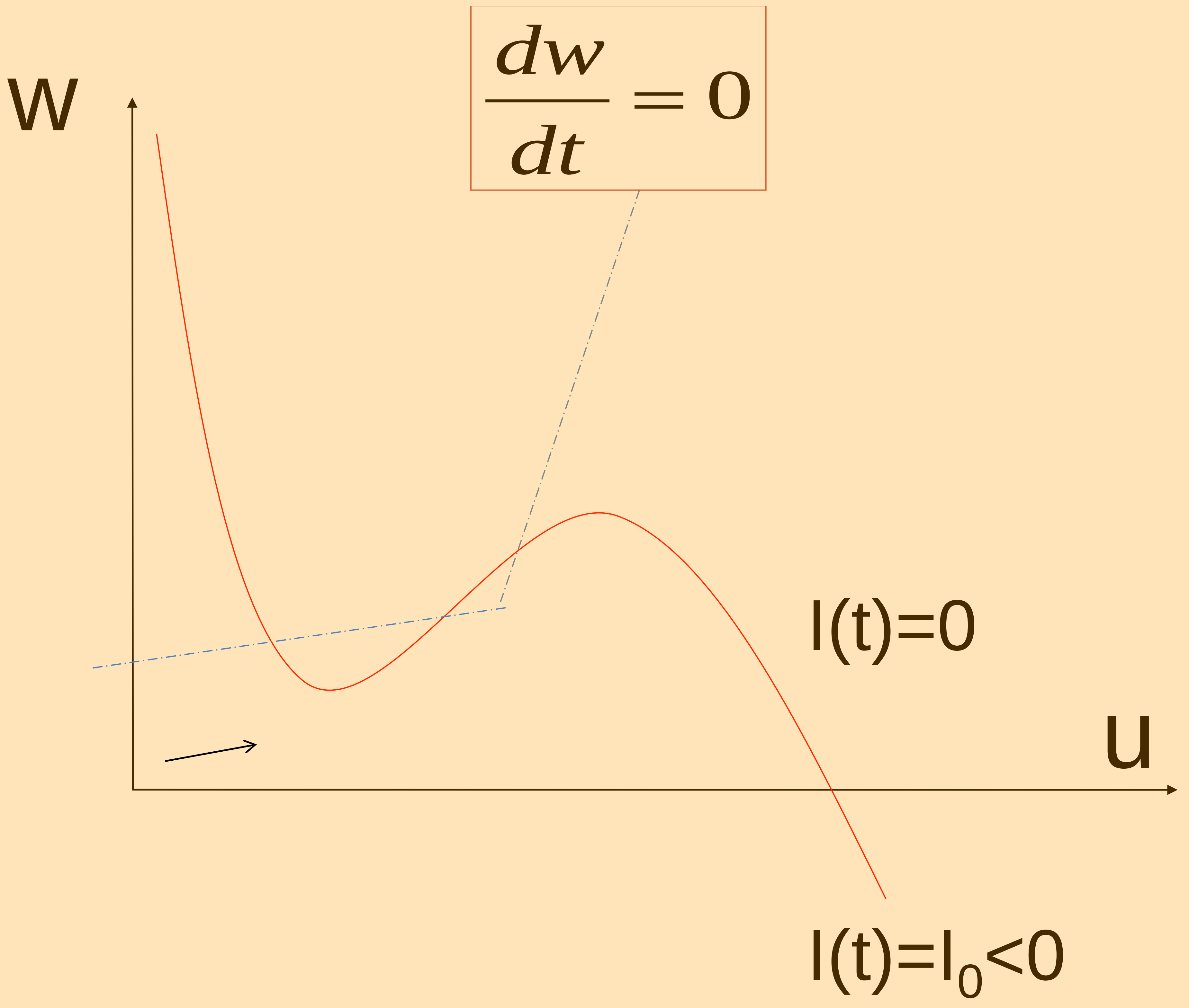
[ ] The neuron model is of type II, because there is a jump in the f-I curve

[ ] The neuron model is of type I, because the f-I curve is continuous

[ ] starting with zero current, and slowly increasing the current, is this true?

“ in the regime below the Hopf bifurcation, the neuron is at rest or will necessarily converge to the resting state”

Week 4 - Exercise 1 and 2: NOW!



Next lecture at 11:15

Now exercises

Week 4 – part 2: Pulse input in 2D Neuron Models

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Biological Modeling of Neural Networks

Week 4
Reducing detail:
Analysis of 2D models

Wulfram Gerstner

EPFL, Lausanne, Switzerland

√ 3.1 From Hodgkin-Huxley to 2D

√ 3.2 Phase Plane Analysis

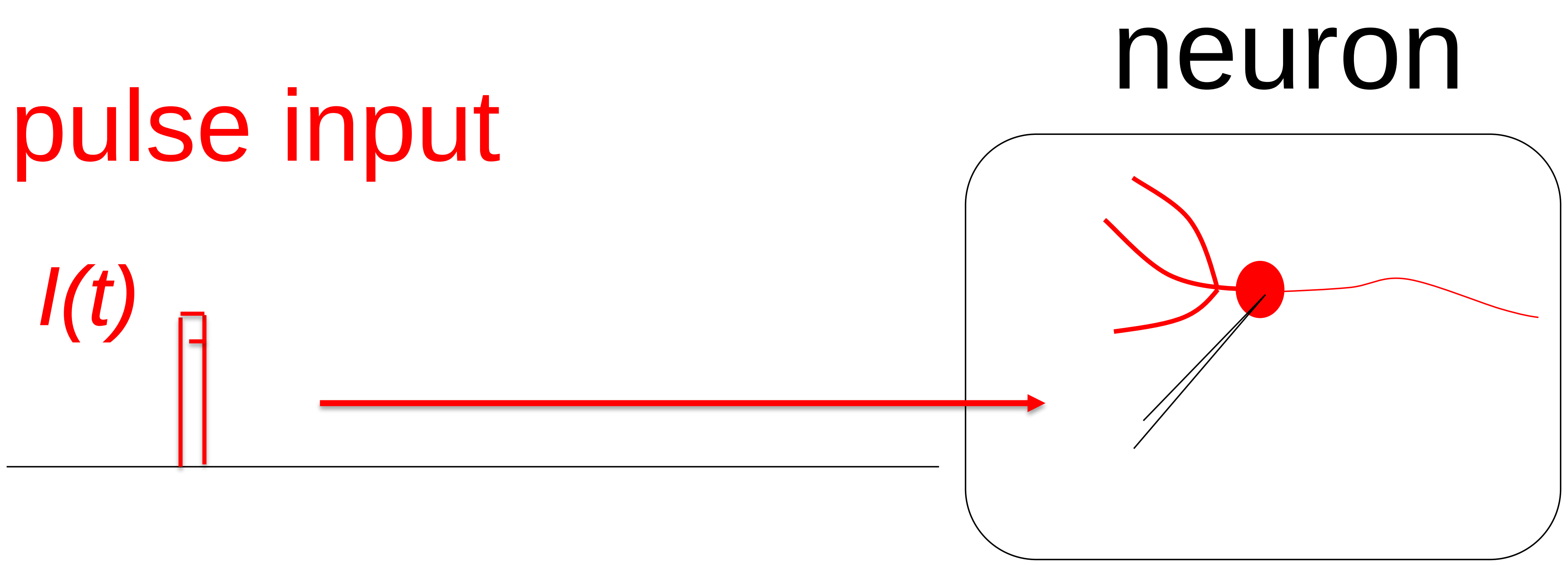
√ 3.3 Analysis of a 2D Neuron Model

4.1 Type I and II Neuron Models
- limit cycles

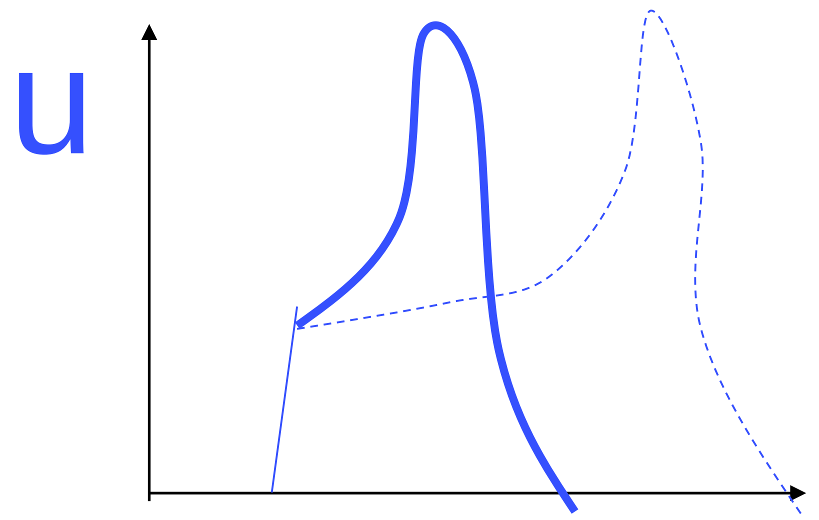
4.2 Pulse input
- where is the firing threshold?
- separation of time scales

4.3. Further reduction to 1 dim
- nonlinear integrate-and-fire (again)

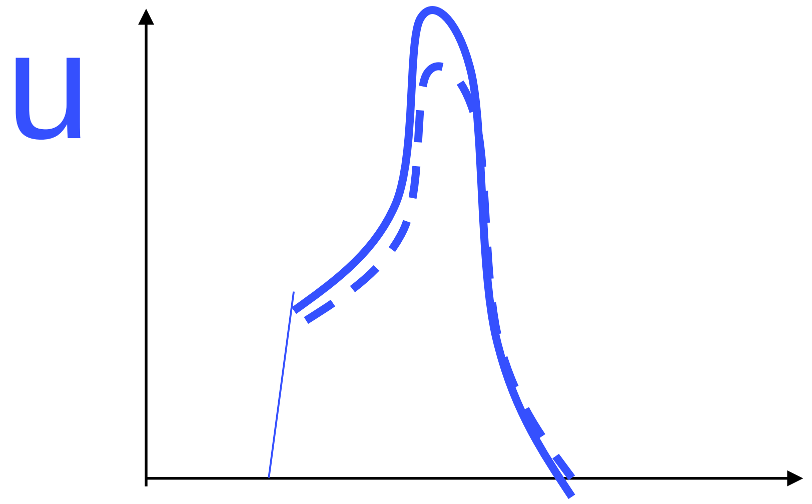
4.2. Threshold for Pulse Input in 2dim. Neuron Models



Delayed spike



Reduced amplitude



Review from 4.1 Bifurcations, simplifications

Bifurcations in neural modeling,
Type I/II neuron models,
Canonical simplified models

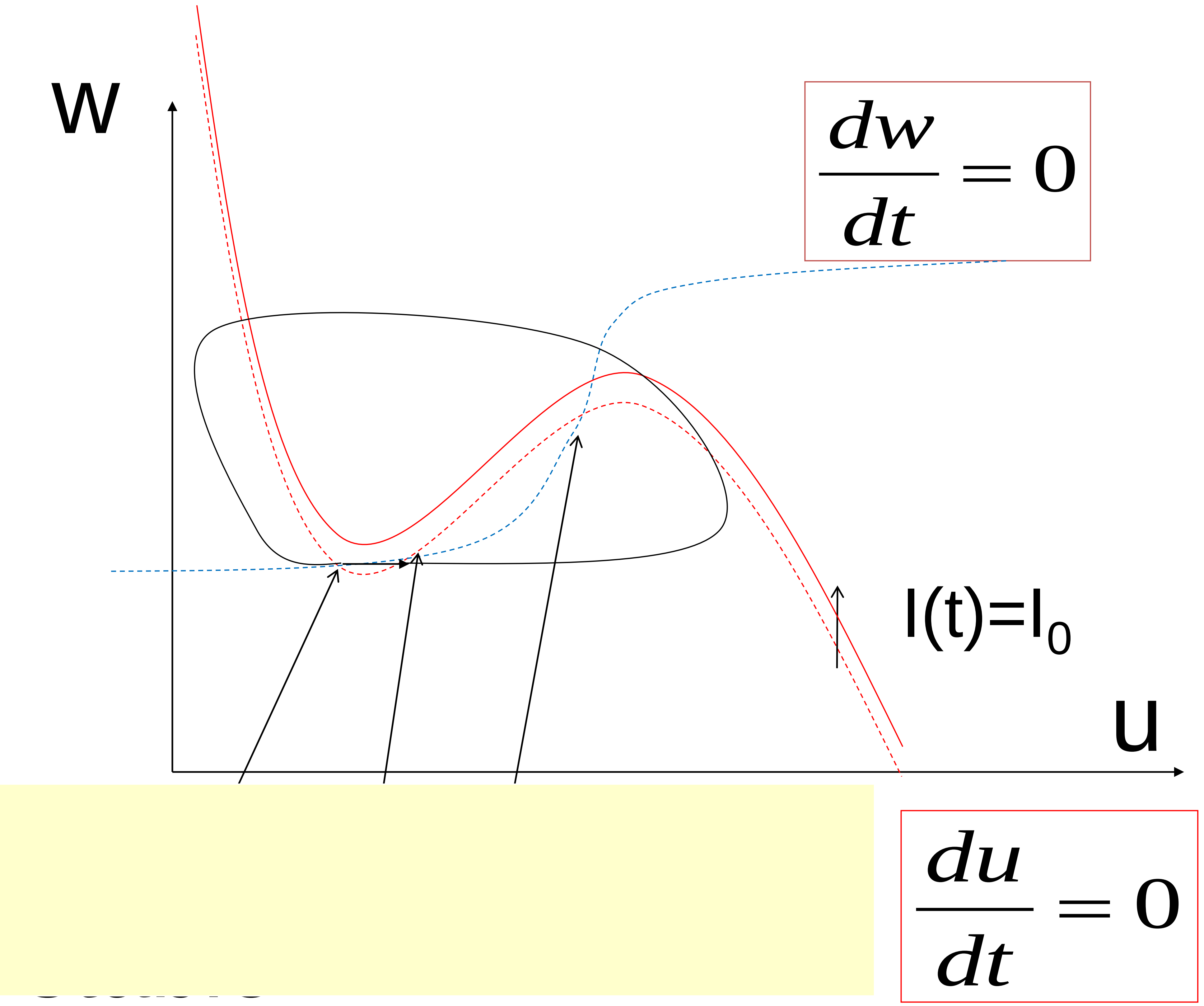
Nancy Koppell,
Bart Ermentrout,
John Rinzel,
Eugene Izhikevich
and many others

Review from 4.1: Saddle-node onto limit cycle bifurcation

stimulus

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

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



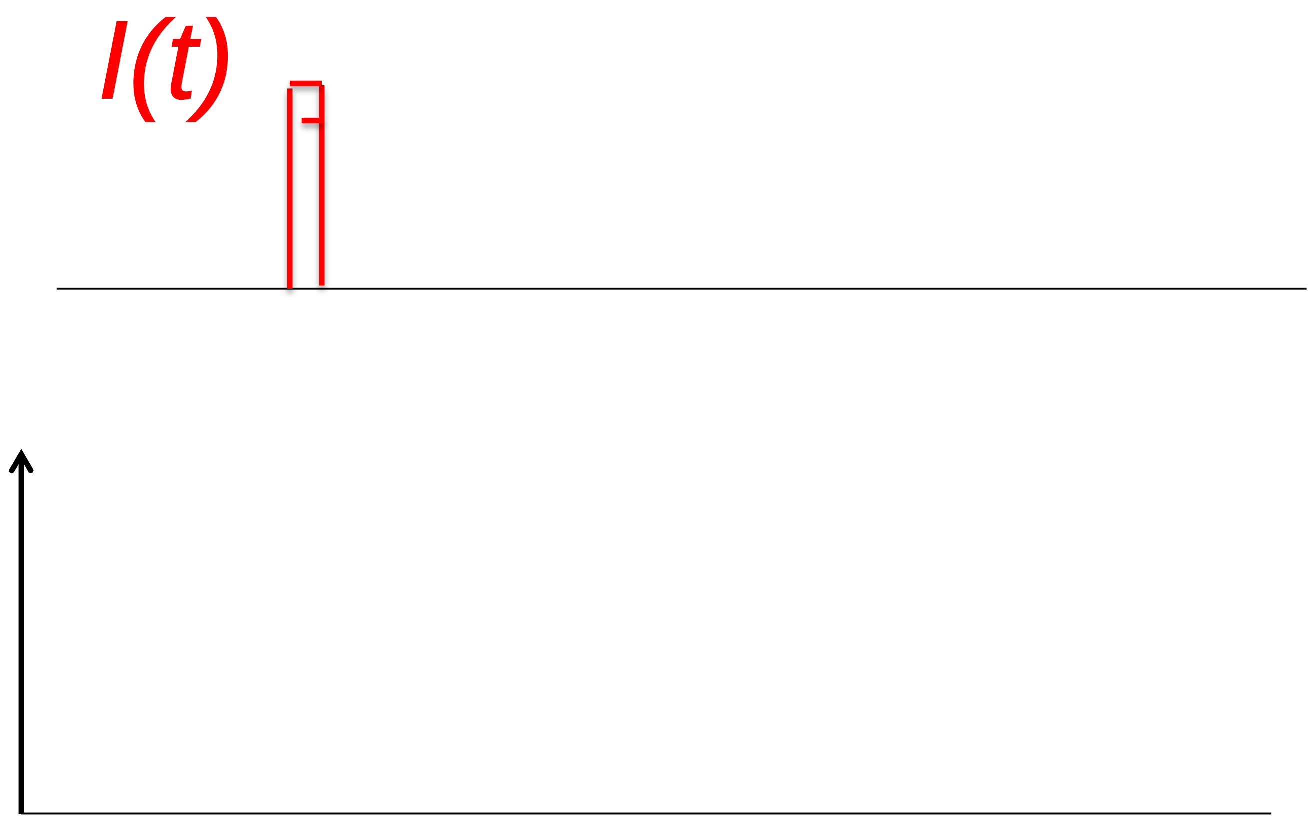
4.2 Threshold for Pulse input

stimulus

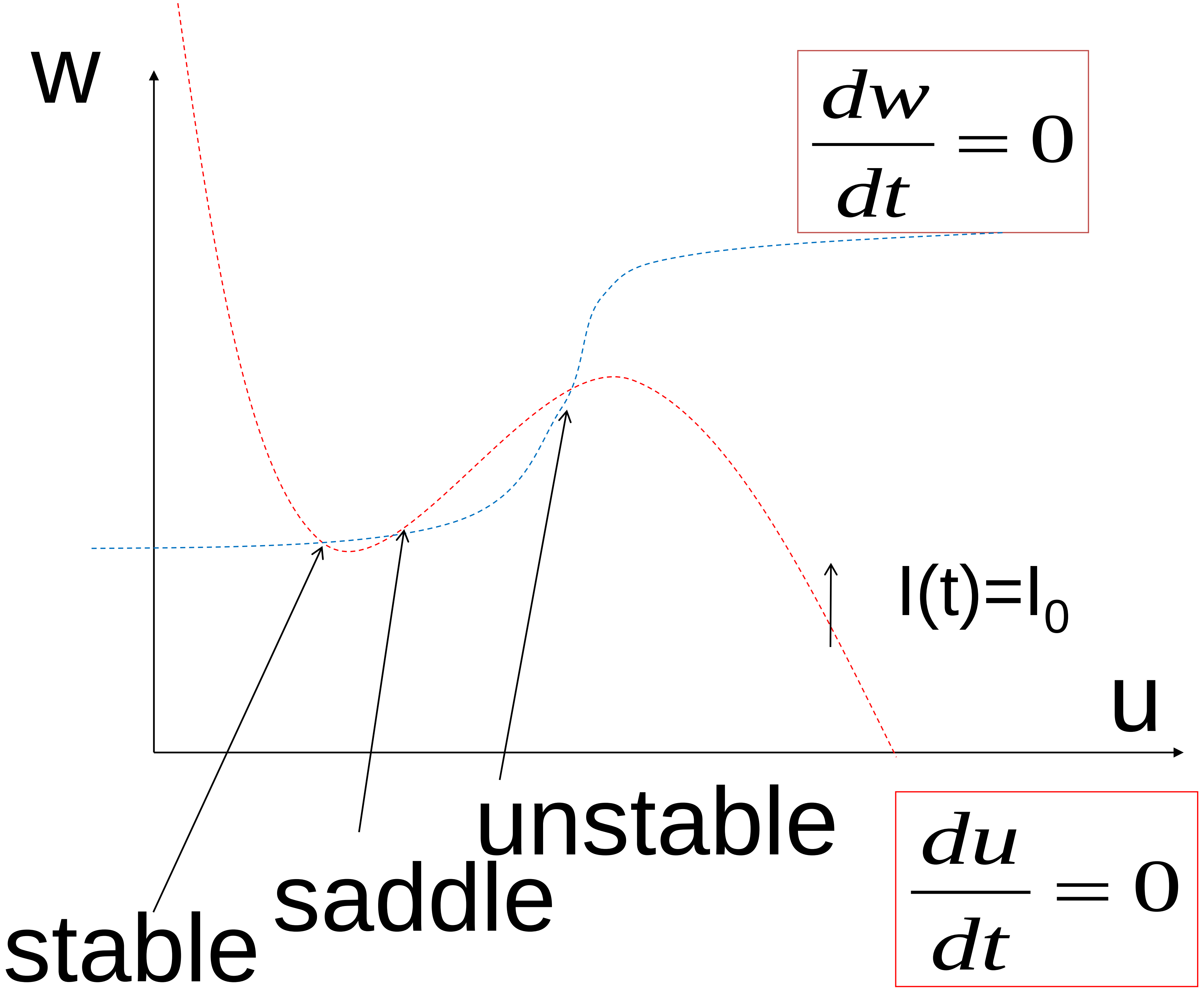
$$\tau \frac{du}{dt} = F(u,w) + RI(t)$$

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

pulse input



Blackboard:
Saddle, stable manifold,
Slow response



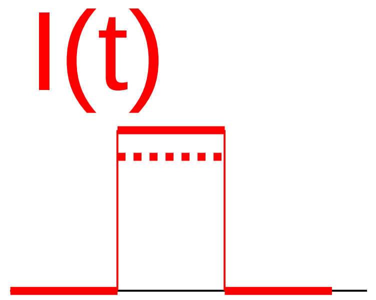
4.2 Type I model: Pulse input

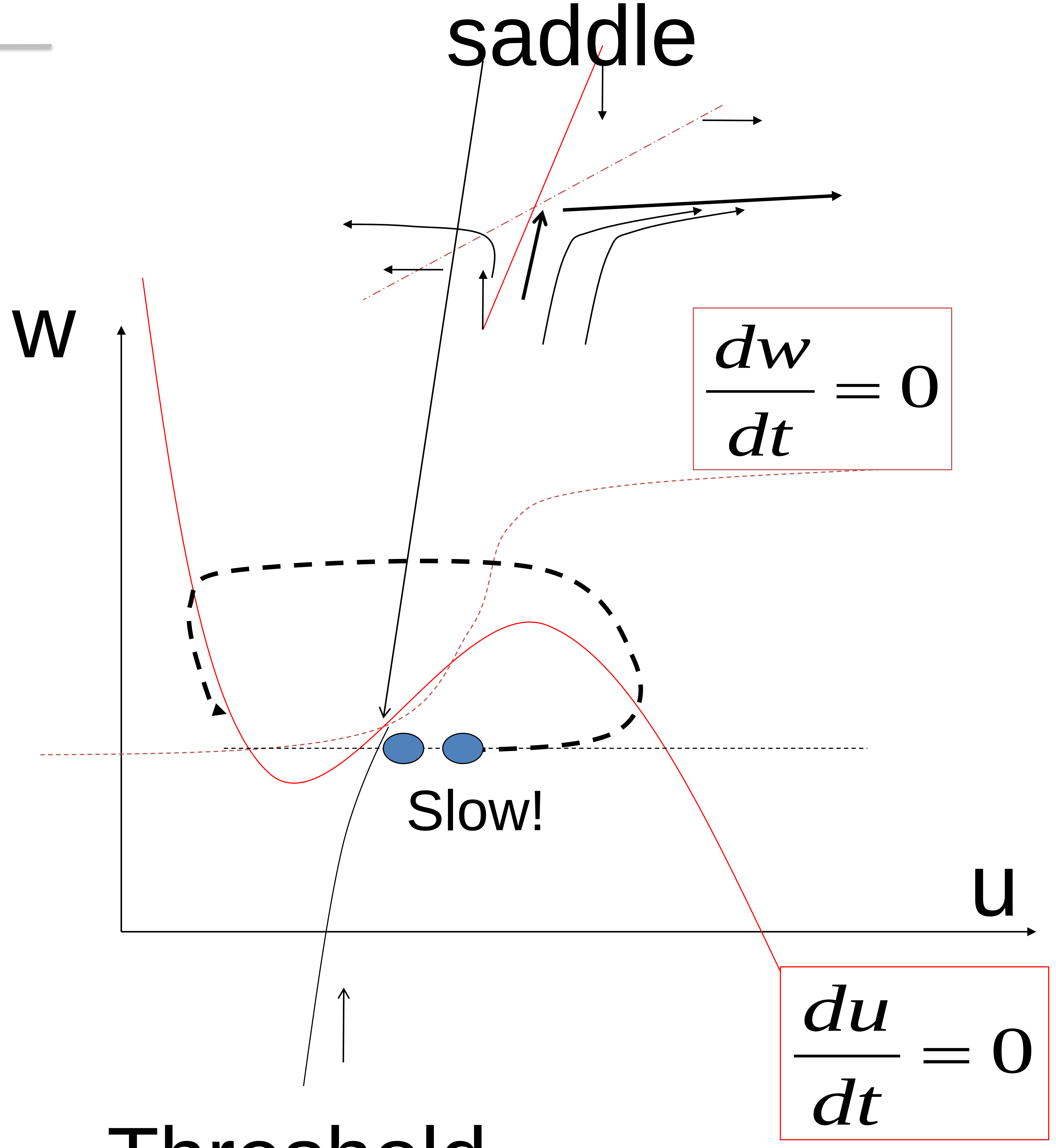
stimulus

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

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

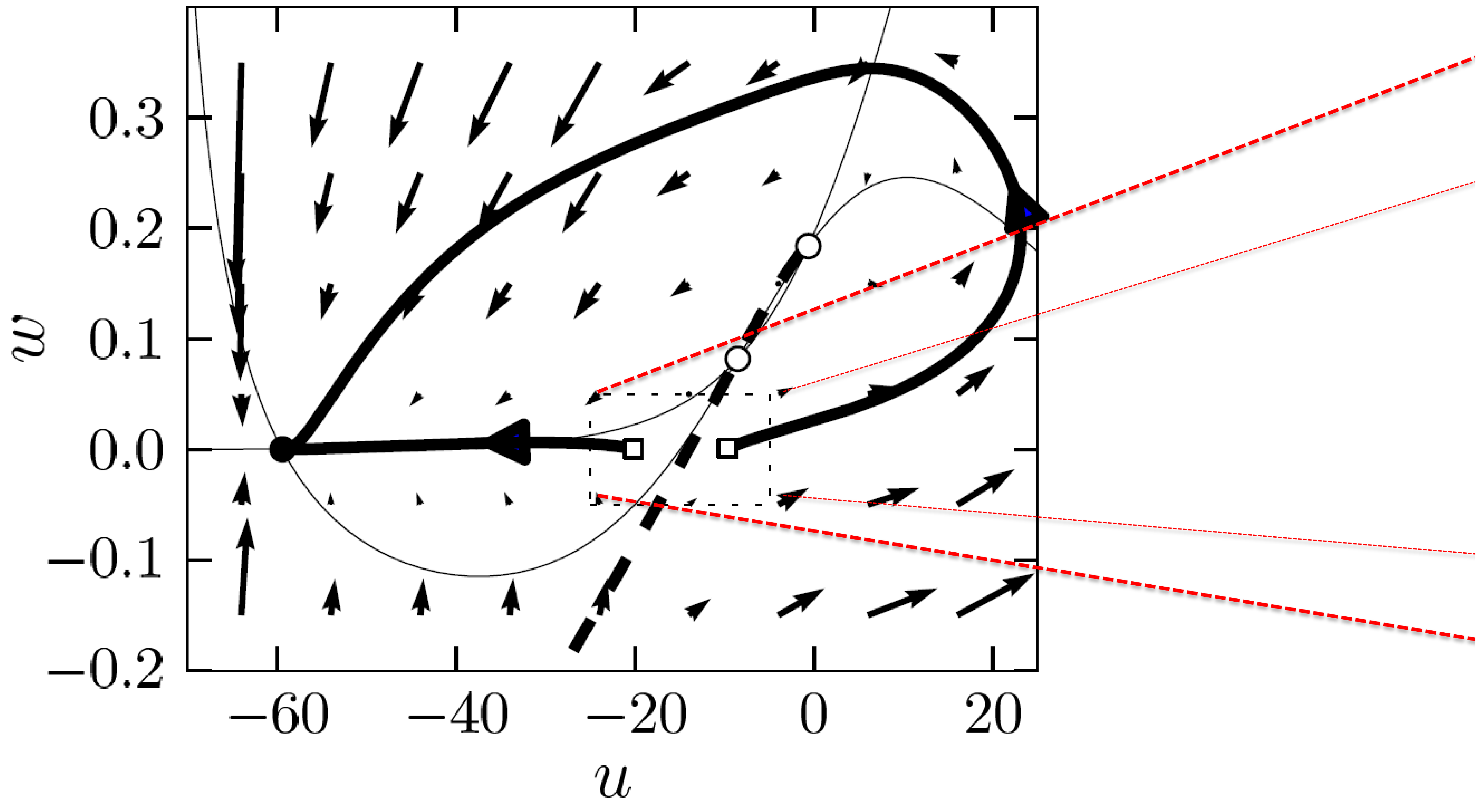
pulse input





Threshold
for pulse input

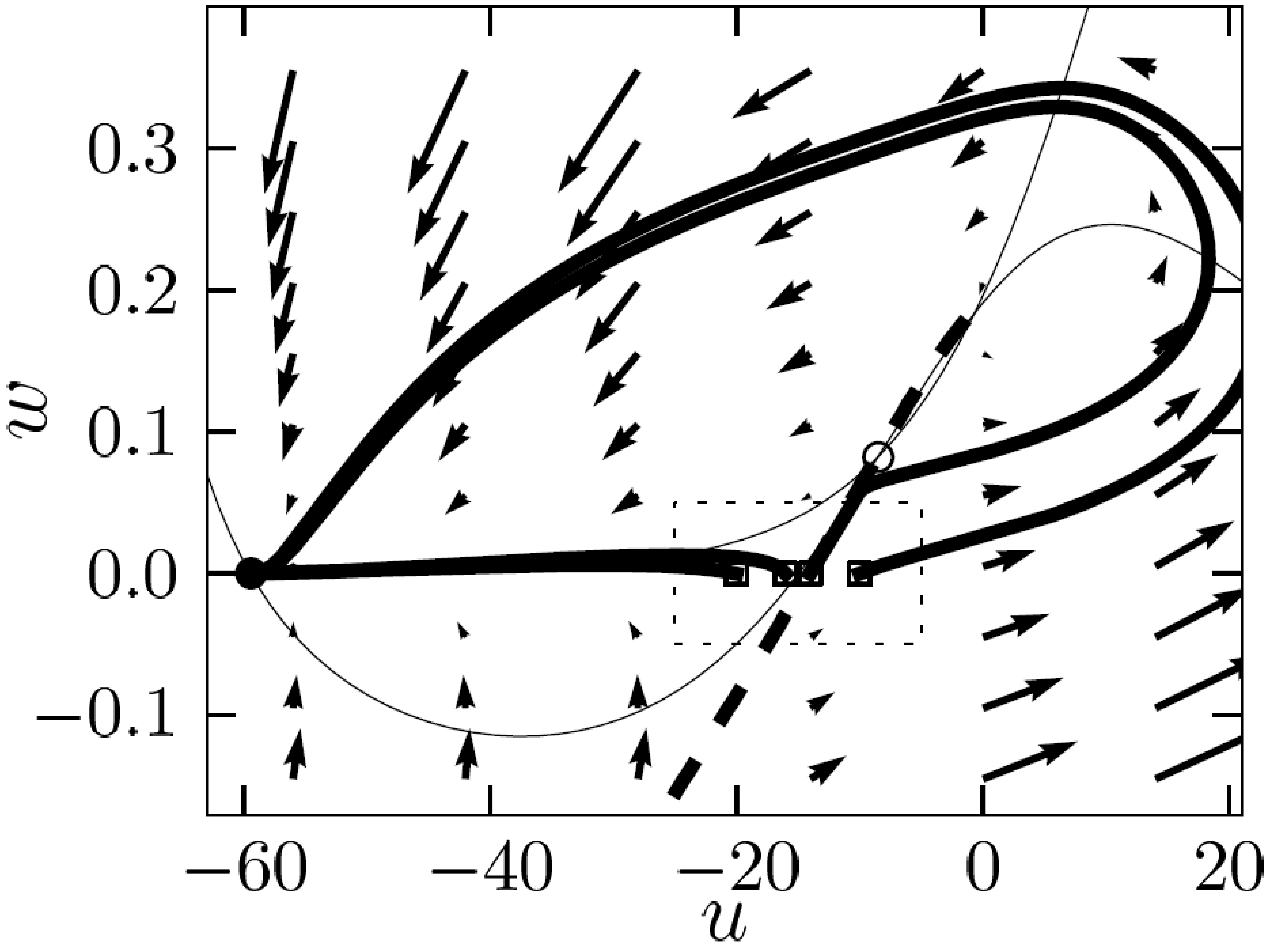
4.1 Type I model: Threshold for Pulse input

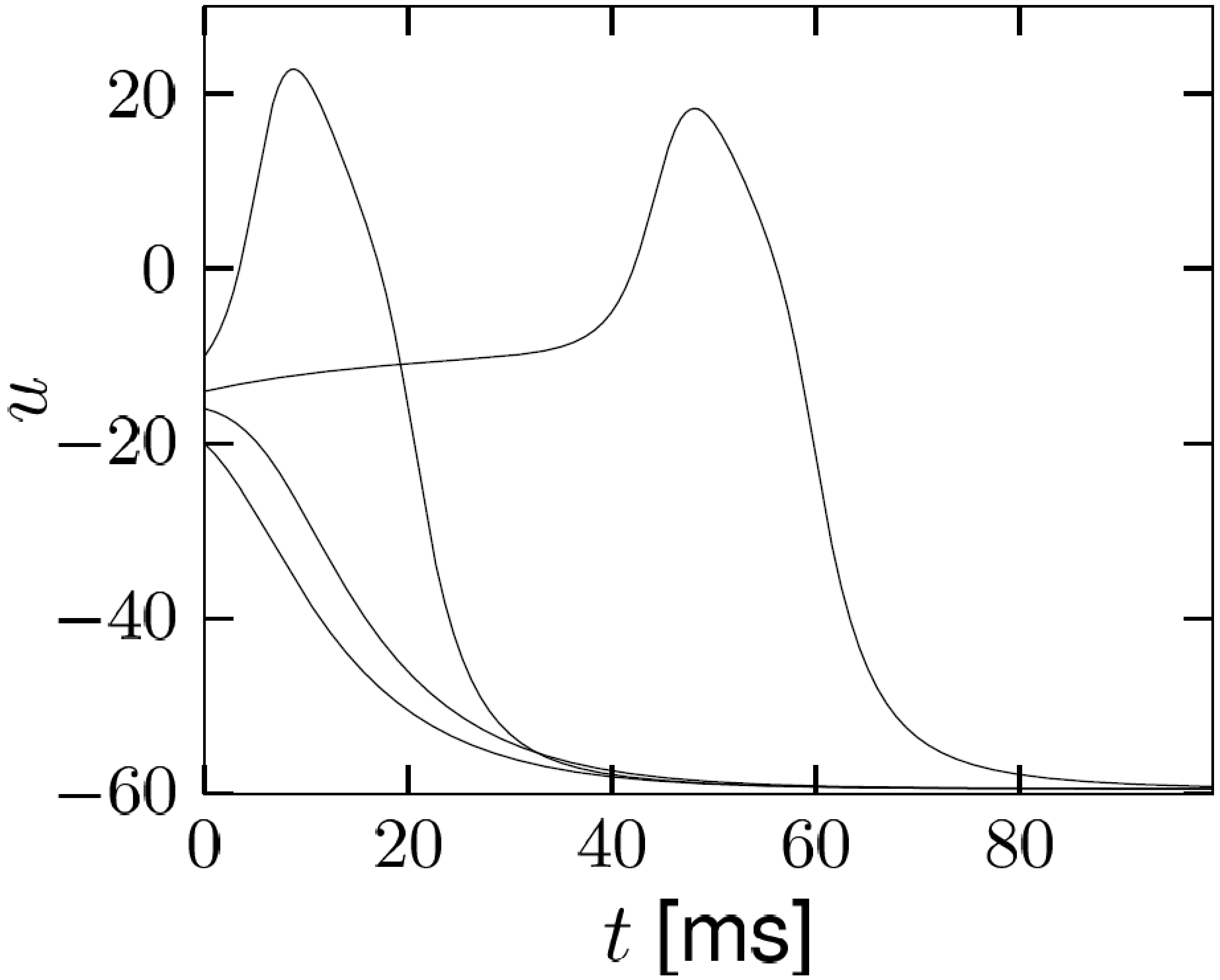


Stable manifold plays role of 'Threshold' (for pulse input)

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

4.1 Type I model: Delayed spike initation for Pulse input

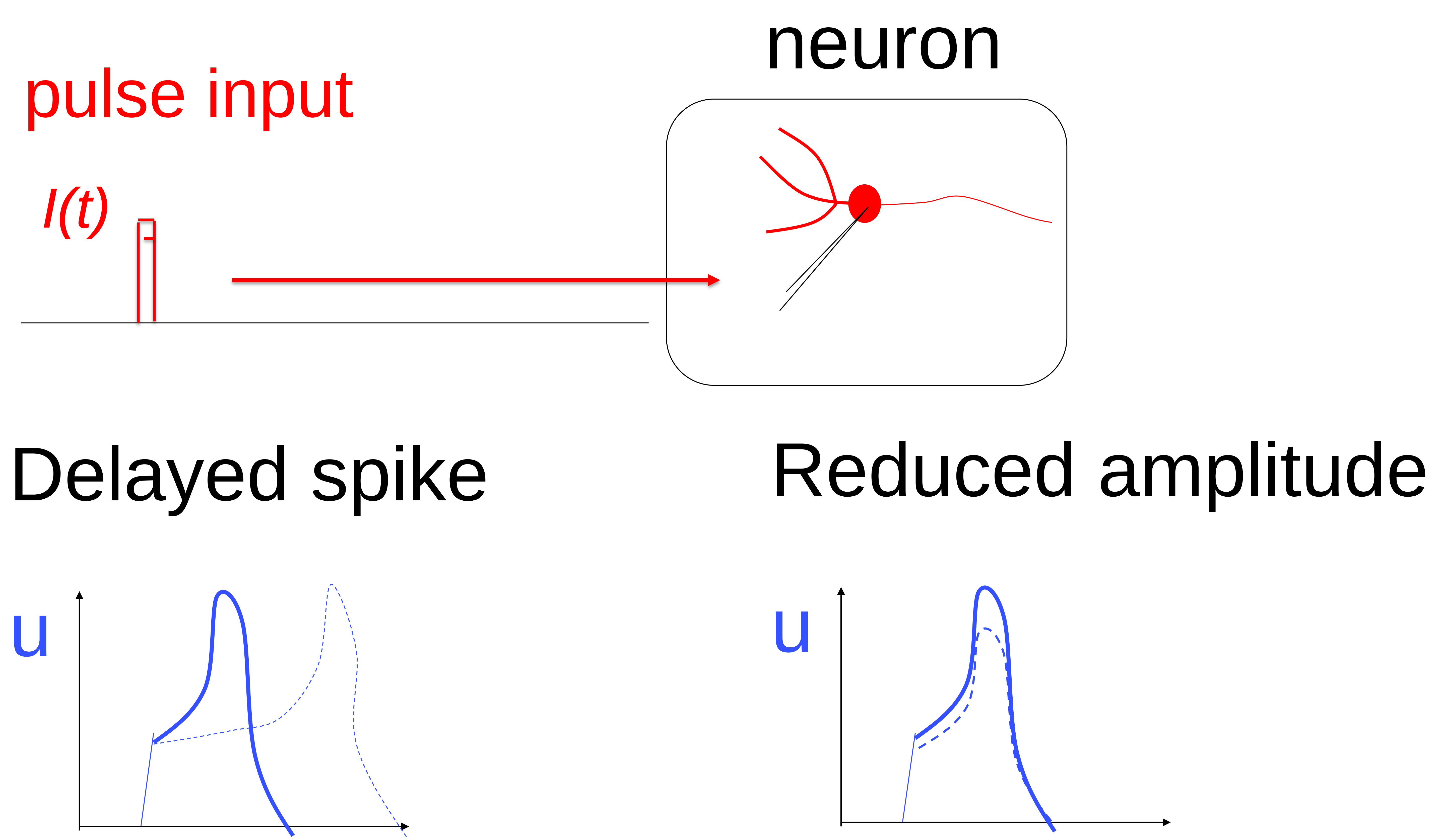




Delayed spike initiation close to ‘Threshold’ (for pulse input)

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

4.2 Threshold for pulse input in 2dim. Neuron Models



NOW: model with subc. Hopf

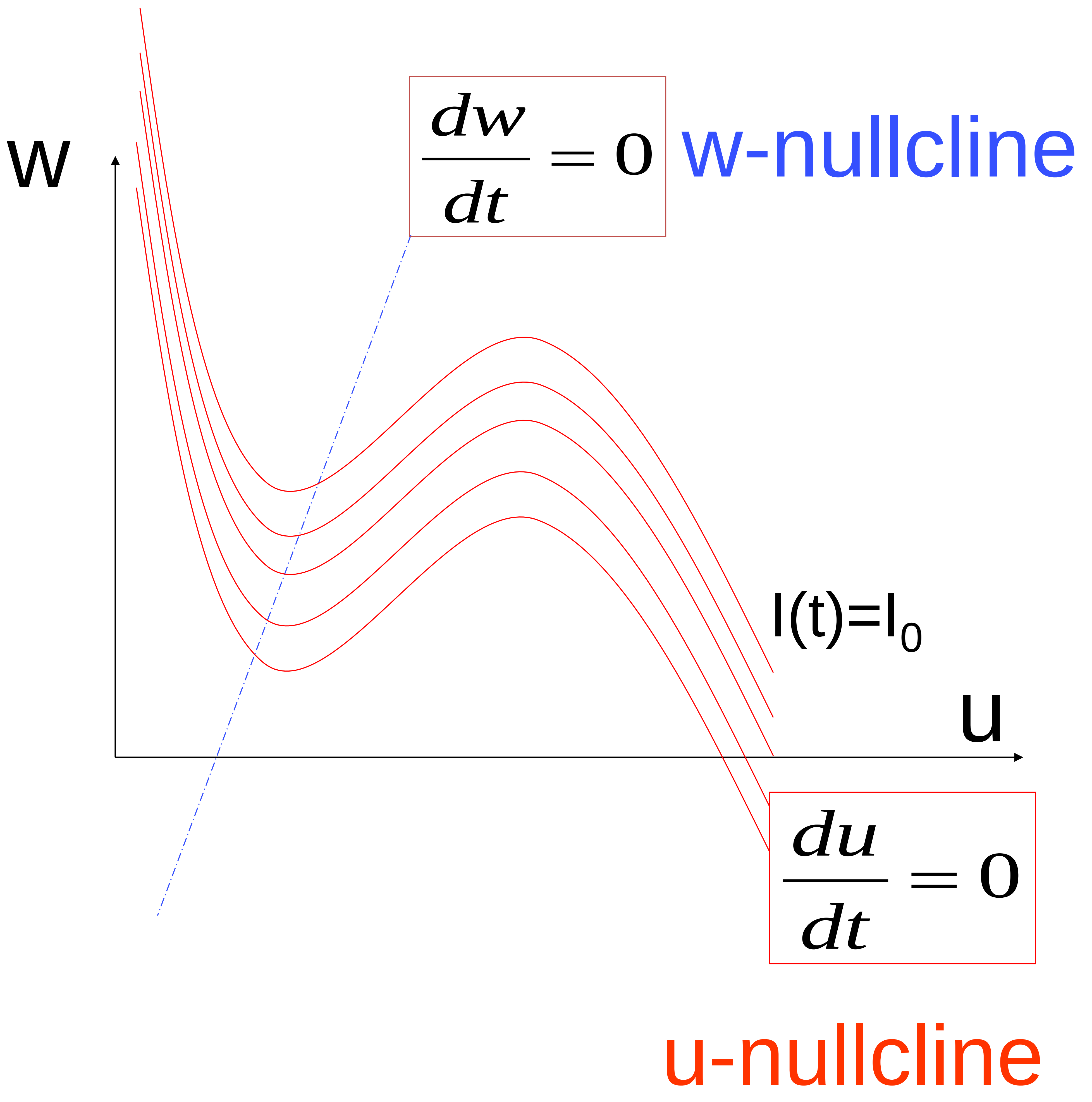
Review from 4.1: FitzHugh-Nagumo Model: Hopf bifurcation

stimulus

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

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

apply constant stimulus I_0



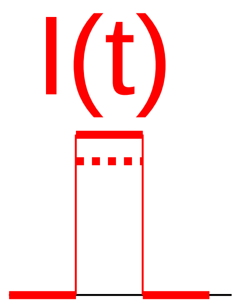
4.2 FitzHugh-Nagumo Model with pulse input

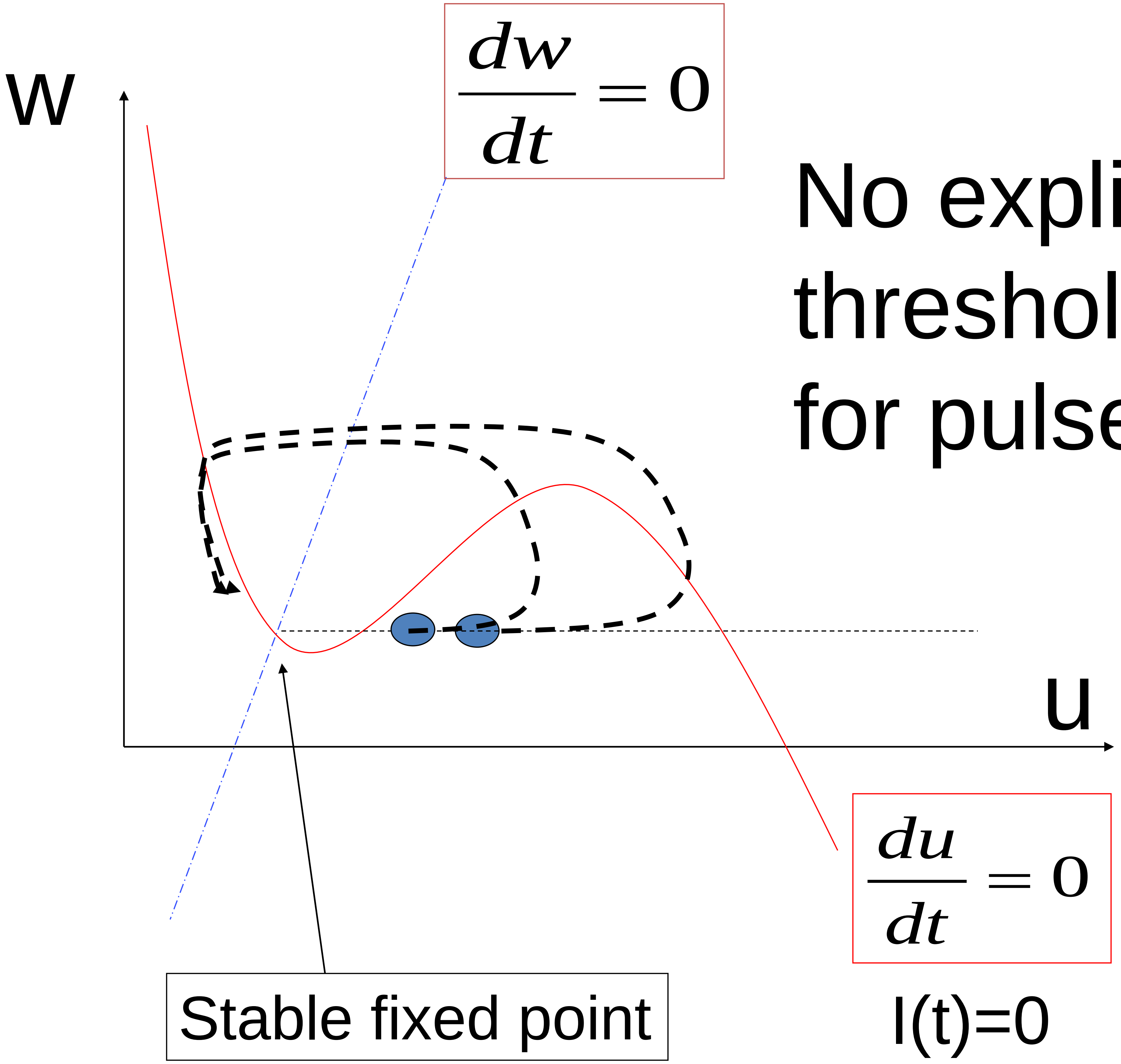
stimulus

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

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

pulse input





No explicit threshold for pulse input

Week 4 – part 2: Threshold for pulse input in 2D models

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Biological Modeling of Neural Networks

Week 4

Reducing detail:

Analysis of 2D models

Wulfram Gerstner

EPFL, Lausanne, Switzerland

√ 3.1 From Hodgkin-Huxley to 2D

√ 3.2 Phase Plane Analysis

√ 3.3 Analysis of a 2D Neuron Model

√ 4.1 Type I and II Neuron Models
- limit cycles

4.2 Pulse input
- √ where is the firing threshold?
- separation of time scales

4.3. Further reduction to 1 dim
- nonlinear integrate-and-fire (again)

4.2 Separation of time scales, example FitzHugh-Nagumo Model

stimulus

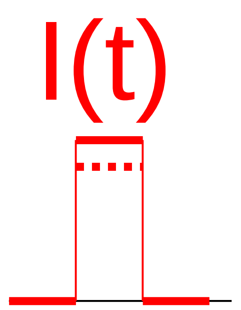
$$\tau \frac{du}{dt} = F(u,w) + RI(t)$$

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

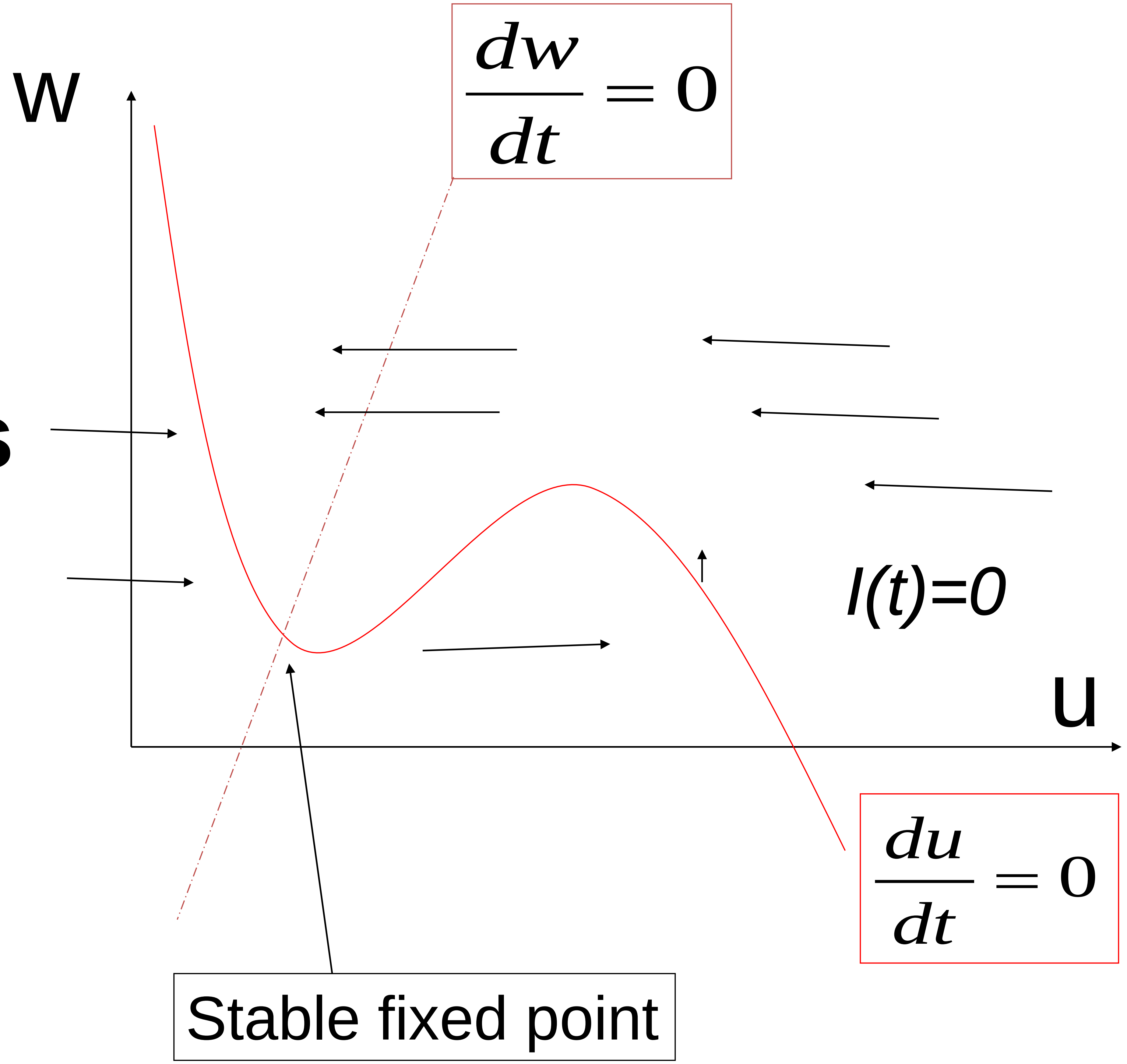
Separation of time scales

$$\tau_w >> \tau_u$$

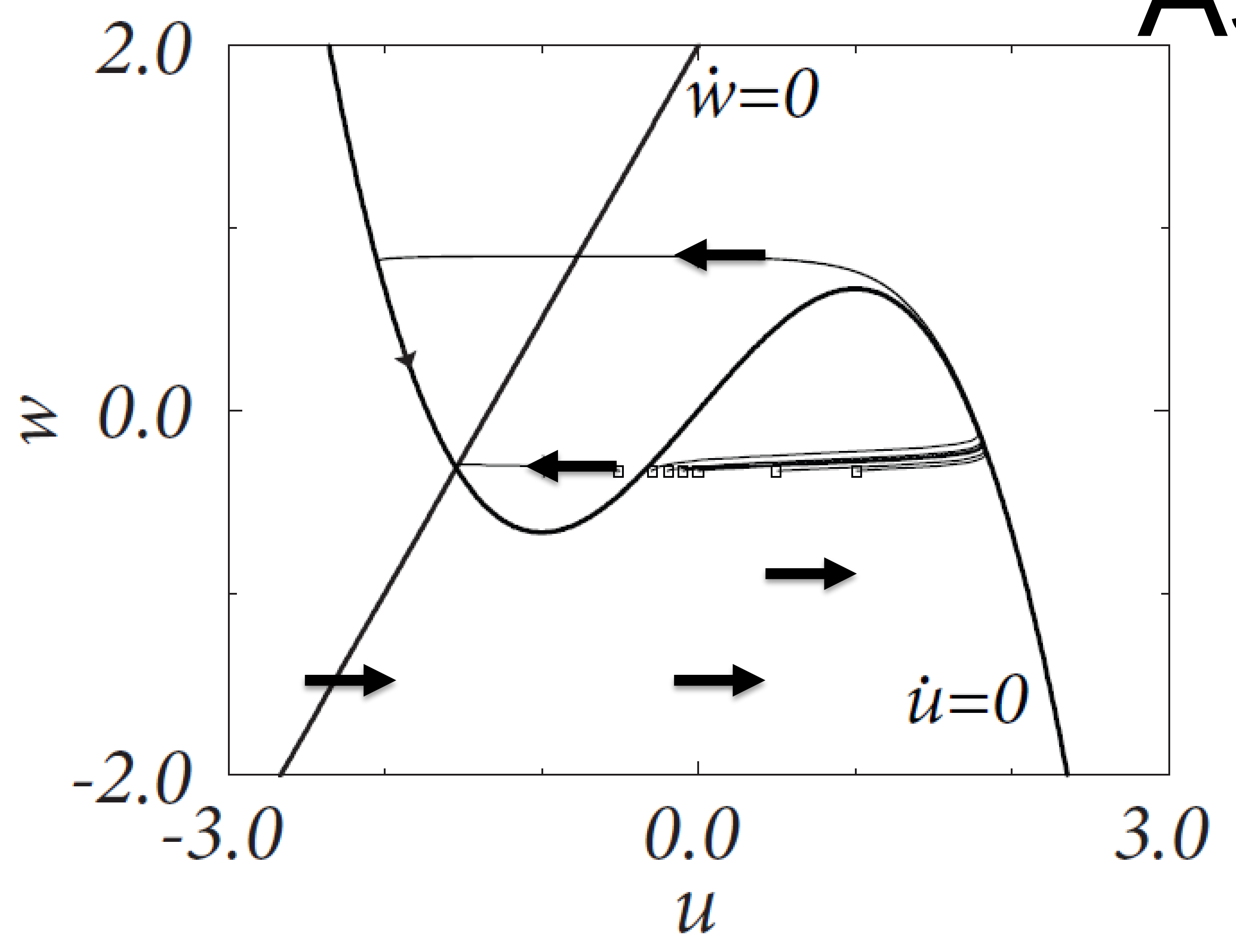
pulse input



blackboard

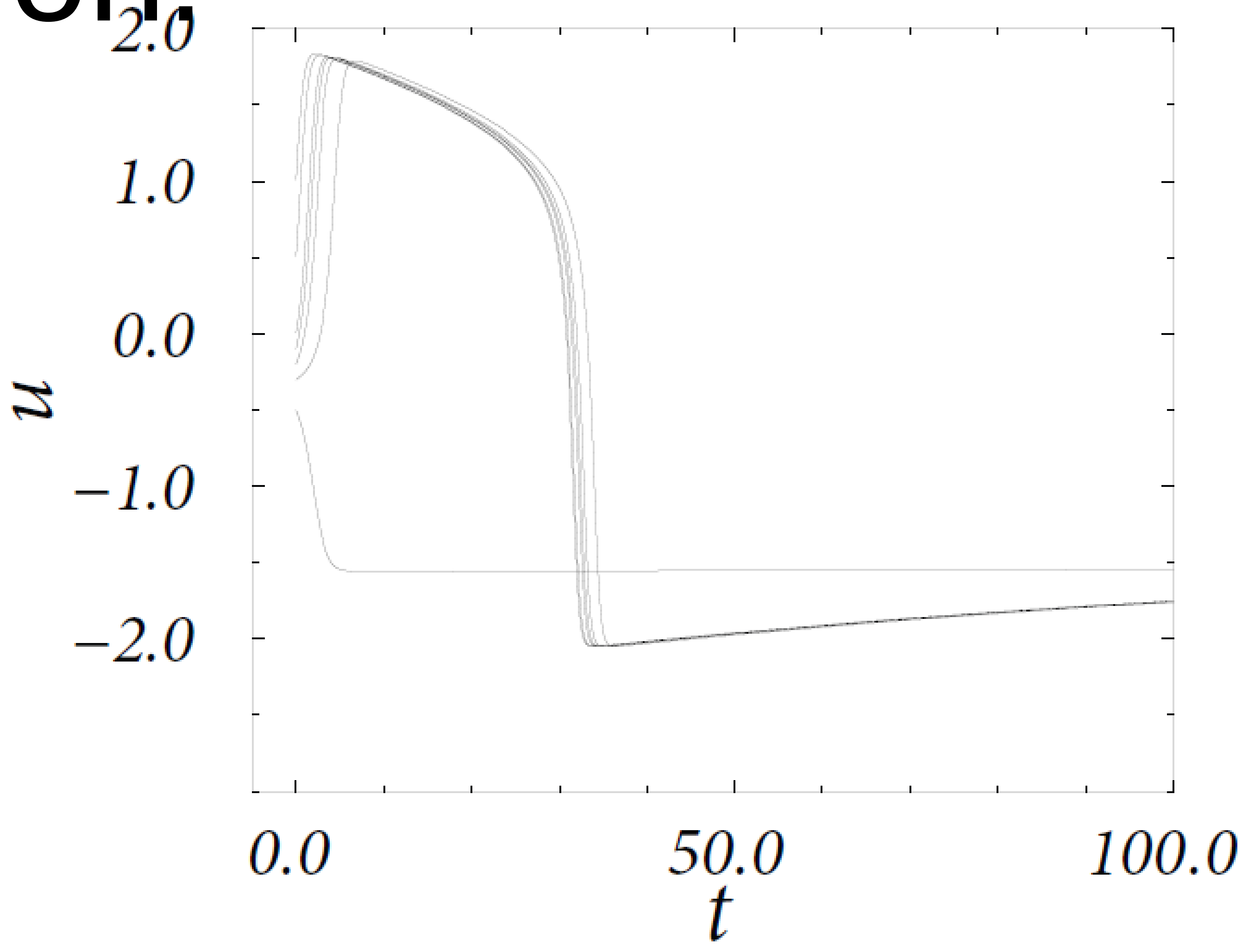


4.2 FitzHugh-Nagumo model: Threshold for Pulse input



Assumption:

$\tau_w >> \tau_u$



Middle branch of u-nullcline plays role of
'Threshold' (for pulse input)

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

4.2 Detour: Separation fo time scales in 2dim models

stimulus

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

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

Assumption:

$$\tau_w >> \tau_u$$

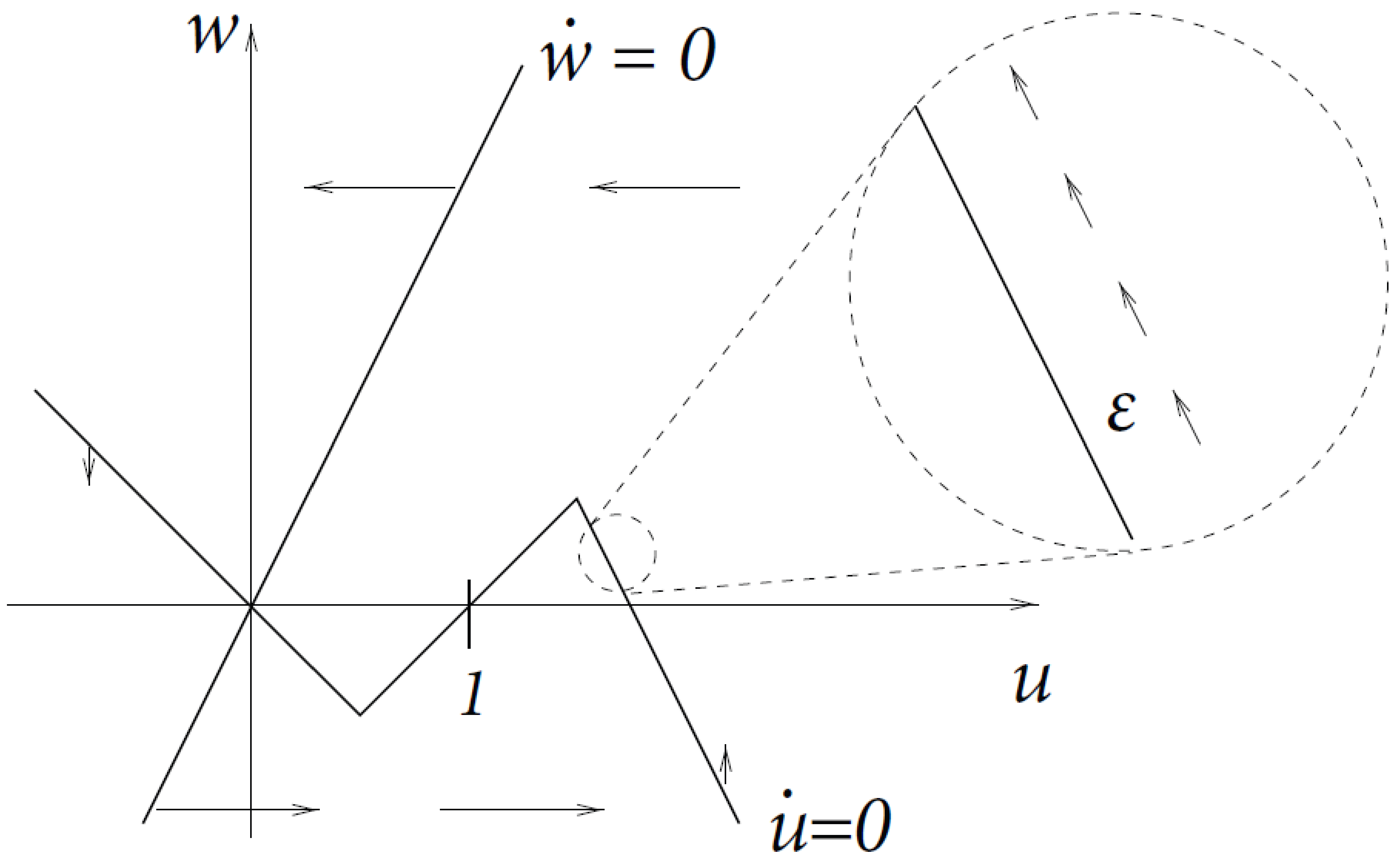
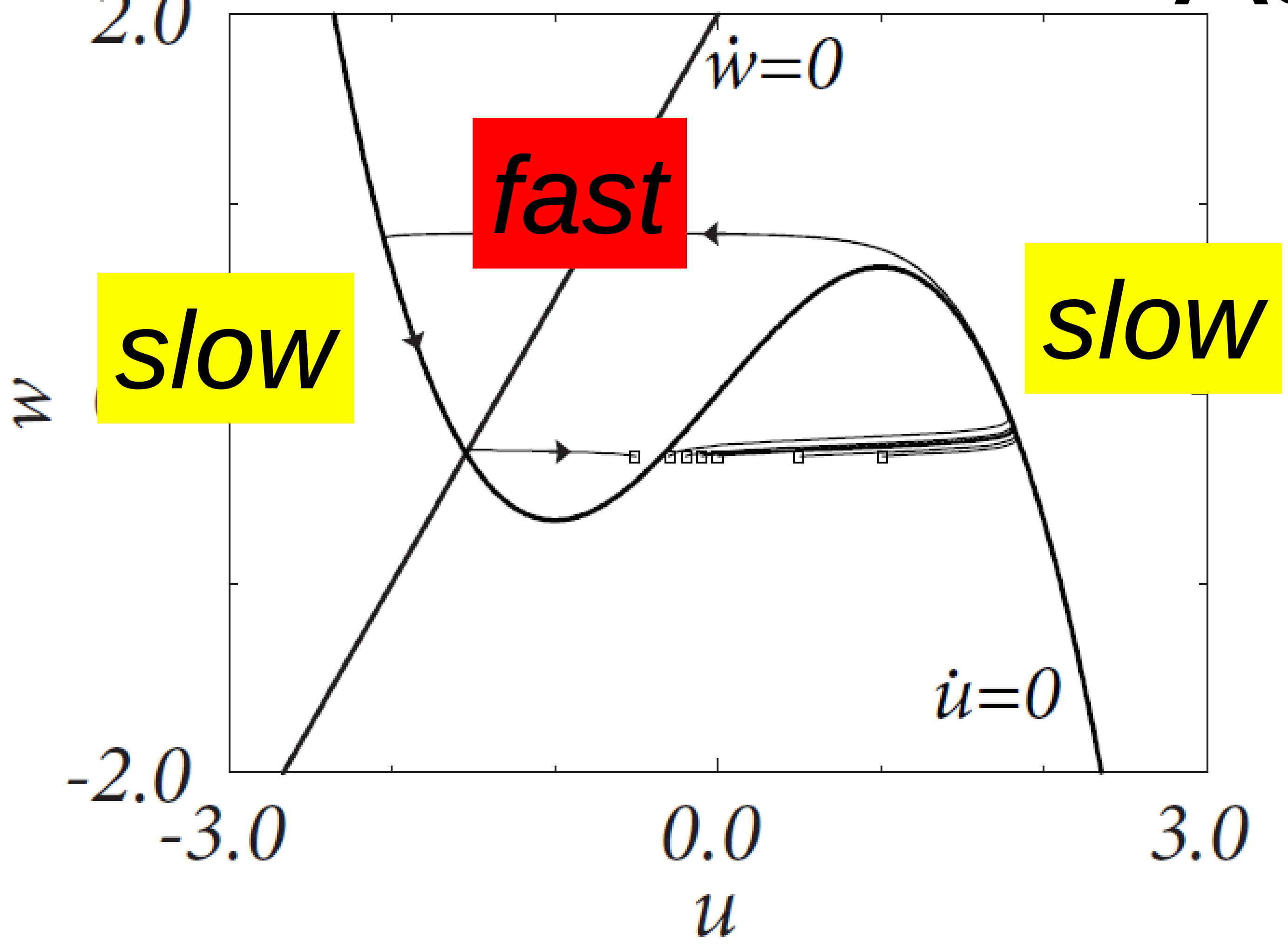
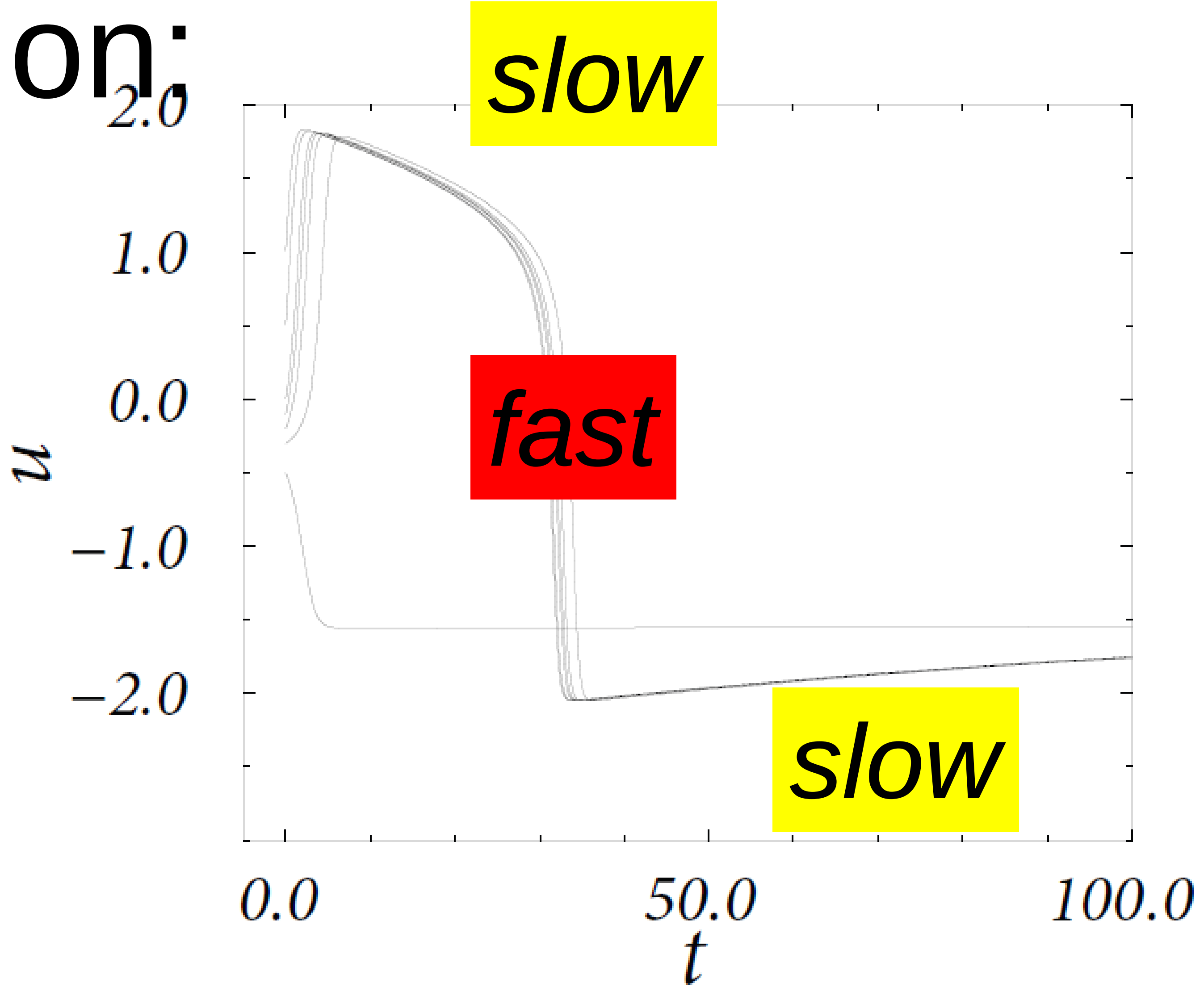


Image: Neuronal Dynamics, Gerstner et al., Cambridge Univ. Press (2014)

4.2 FitzHugh-Nagumo model: Threshold for Pulse input

Assumption: $\tau_w \gg \tau_u$





trajectory

- -follows u-nullcline: slow
- -jumps between branches: fast

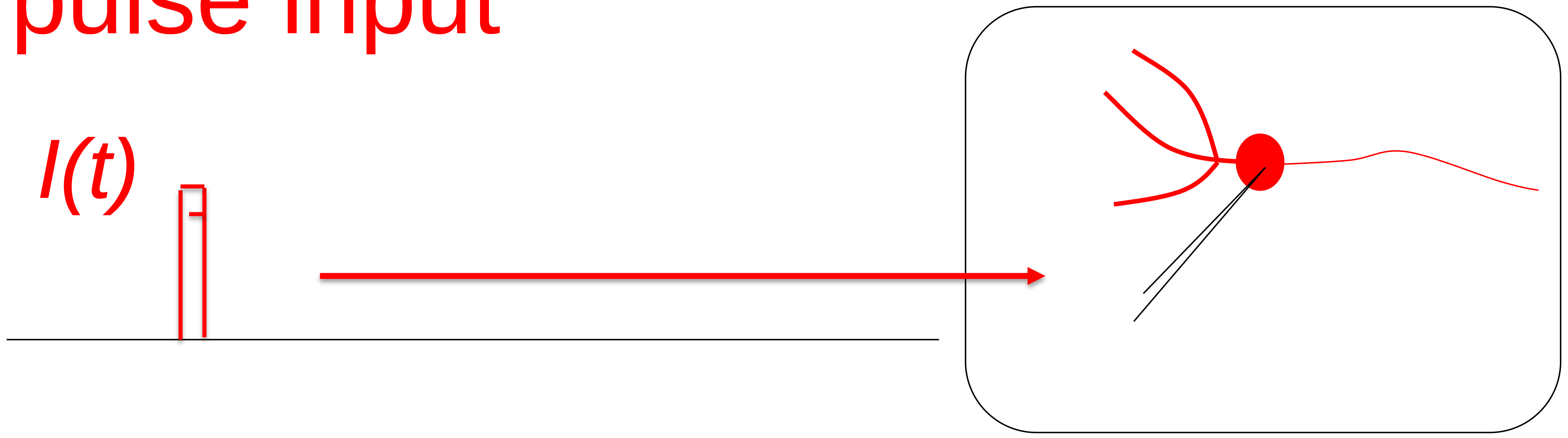
Image: Neuronal Dynamics, Gerstner et al., Cambridge Univ. Press (2014)

4.2 Threshold for pulse input in 2dim. Neuron Models

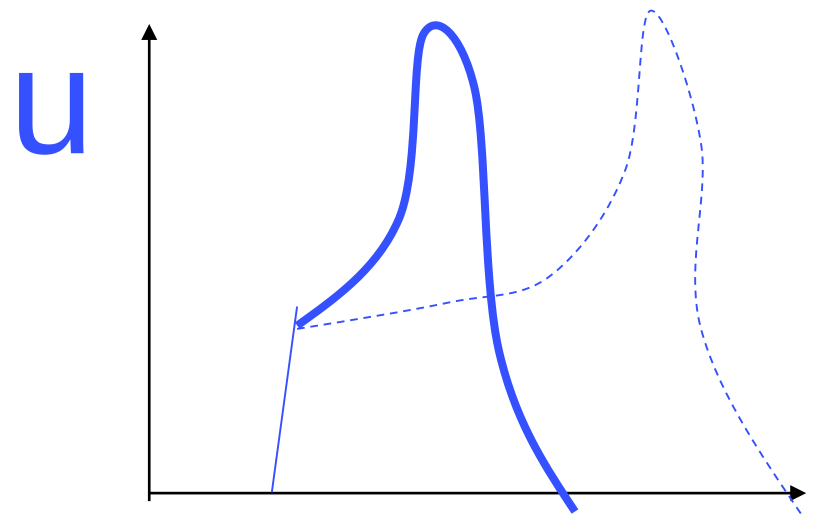
Biological input scenario

pulse input

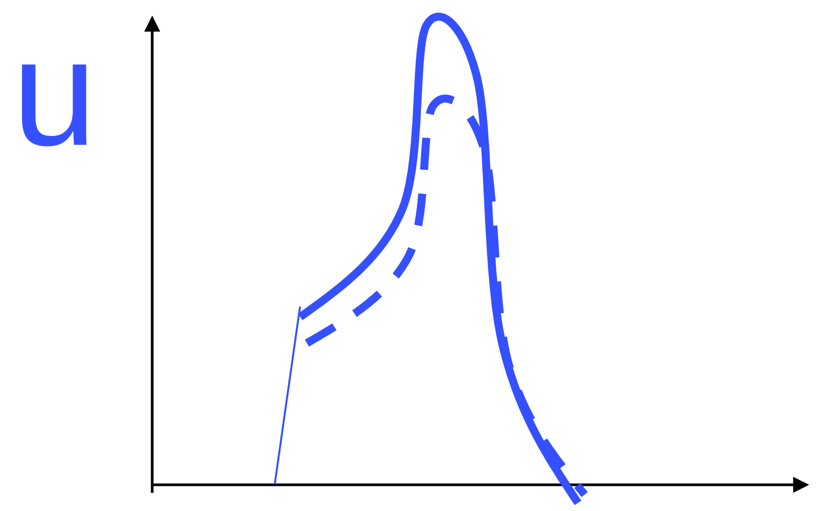
neuron



Delayed spike



Reduced amplitude



Mathematical explanation:
Graphical analysis in 2D

Week 4– Quiz 4.2.

A. Threshold in a 2-dimensional neuron model with saddle-node bifurcation

[ ] The voltage threshold for repetitive firing is always the same as the voltage threshold for pulse input.

[ ] in the regime below the saddle-node bifurcation, the voltage threshold for repetitive firing is given by the stable manifold of the saddle.

[ ] in the regime below the saddle-node bifurcation, the voltage threshold for action potential firing in response to a short pulse input is given by the middle branch of the u-nullcline.

[ ] in the regime below the saddle-node bifurcation, the voltage threshold for action potential firing in response to a short pulse input is given by the stable manifold of the saddle point.

B. Threshold in a 2-dimensional neuron model with subcritical Hopf bifurcation

[ ] in the regime below the bifurcation, a voltage threshold for action potential firing in response to a short pulse input exists only if $\tau_w >> \tau_u$

Week 4: Reducing Detail – 2D models

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Biological Modeling of Neural Networks

Week 4

Reducing detail:

Analysis of 2D models

Wulfram Gerstner

EPFL, Lausanne, Switzerland

√ 3.1 From Hodgkin-Huxley to 2D

√ 3.2 Phase Plane Analysis

√ 3.3 Analysis of a 2D Neuron Model

4.1 Type I and II Neuron Models
- limit cycles

4.2 Pulse input
- where is the firing threshold?
- separation of time scales

4.3. Further reduction to 1 dim
- nonlinear integrate-and-fire (again)

4.3. Further reduction to 1 dimension

stimulus

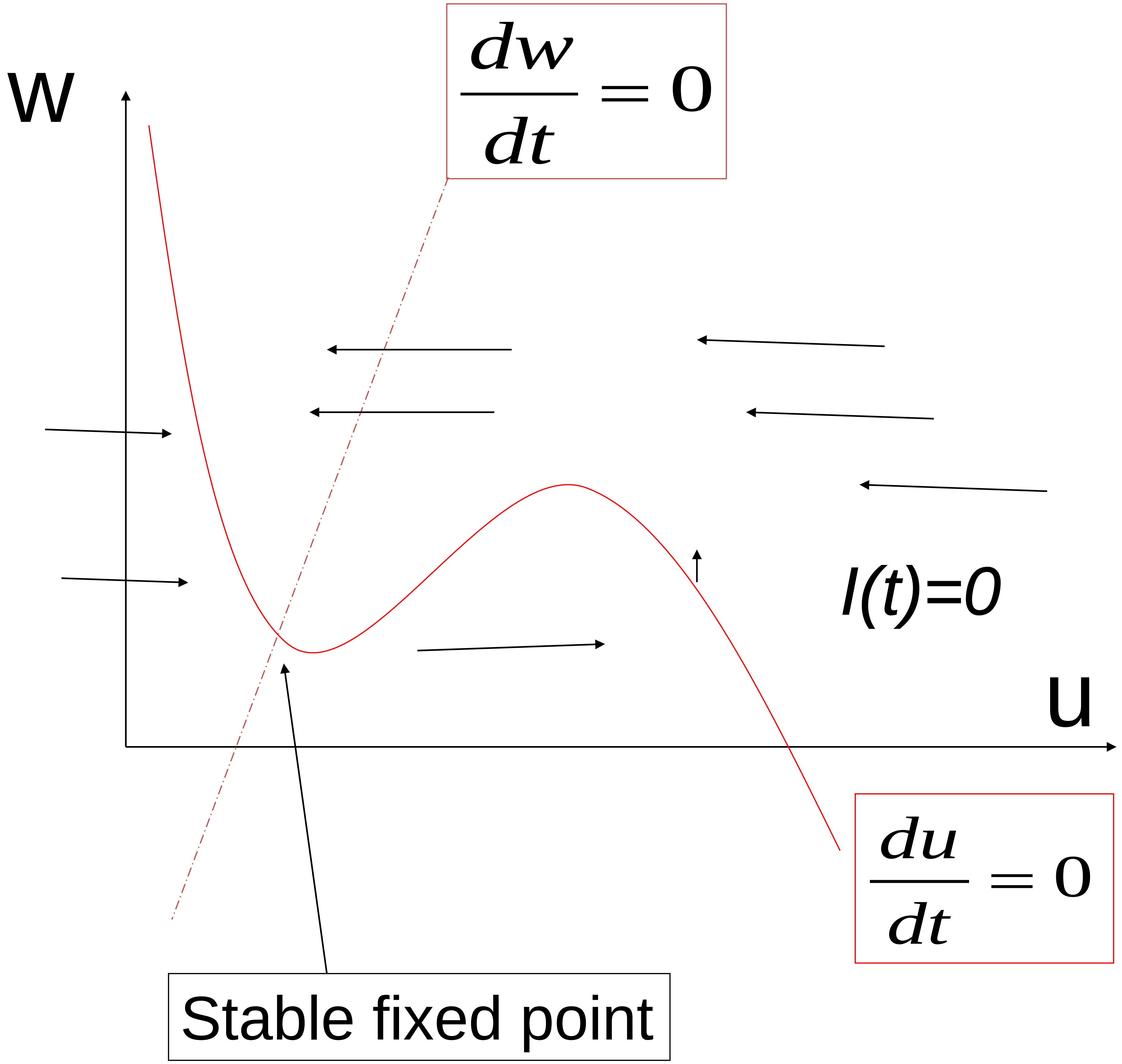
$$\tau \frac{du}{dt} = F(u,w) + I(t)$$

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

Separation of time scales

$$\tau_w >> \tau_u$$

→ Flux nearly horizontal



4.3. Further reduction to 1 dimension

2-dimensional equation

stimulus

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

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

slow!

Separation of time scales

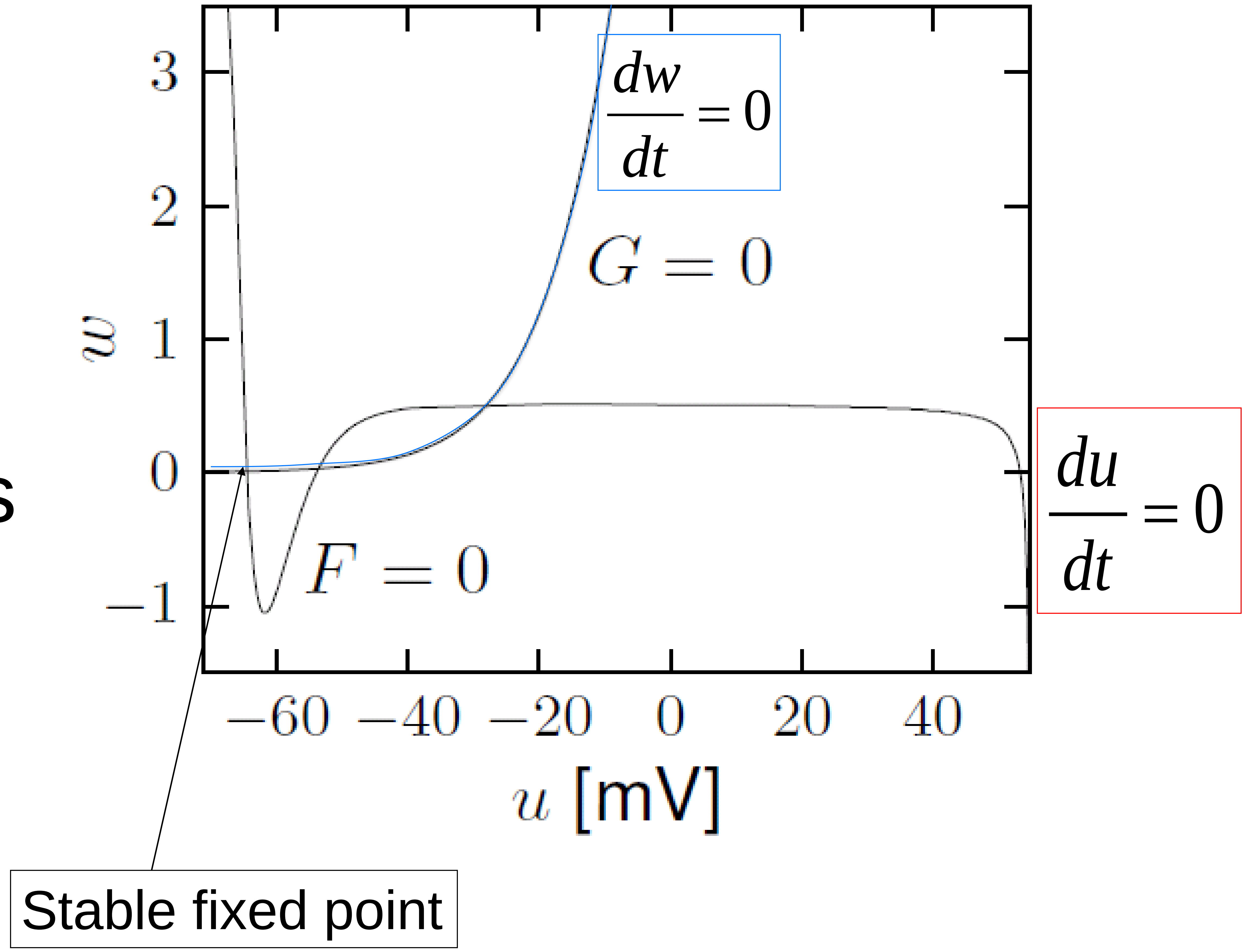
-*w* is nearly constant (most of the time)

4.3. Further reduction to 1 dimension

Hodgkin-Huxley reduced to 2dim

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

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



Separation of time scales

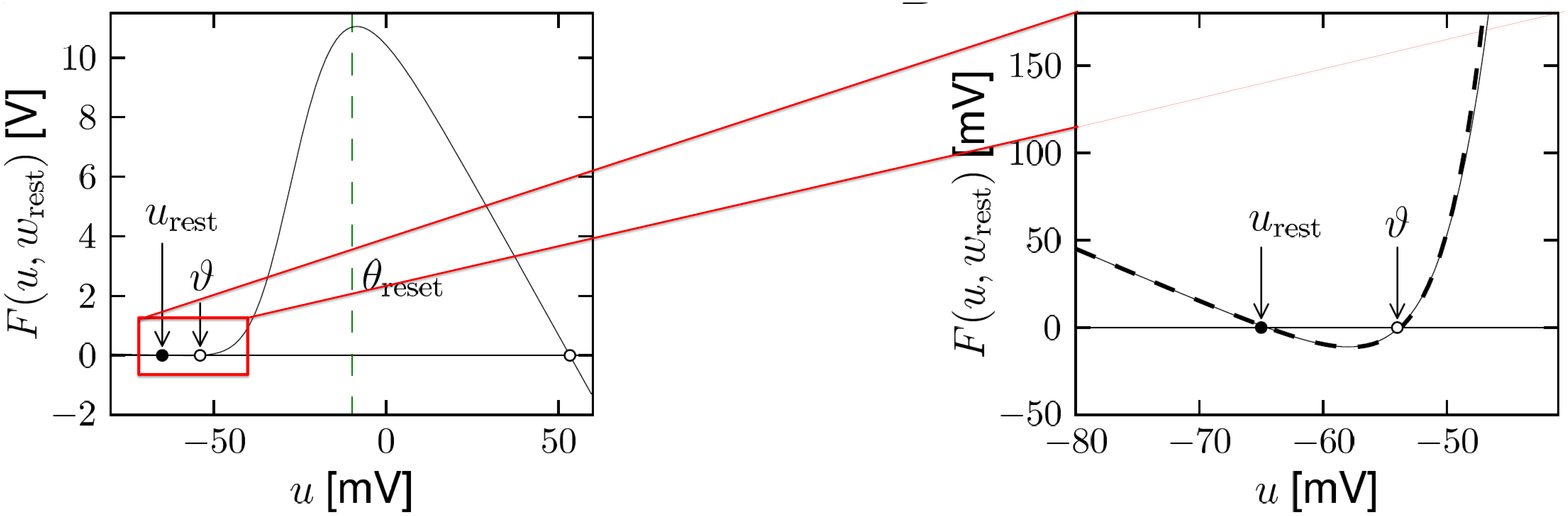
$$\tau_w >> \tau_u$$

$$\tau_w \frac{dw}{dt} \approx 0 \rightarrow \; w \approx w_{rest}$$

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

During preparation/initation of spike

4.3. Spike initiation: Nonlinear Integrate-and-Fire Model



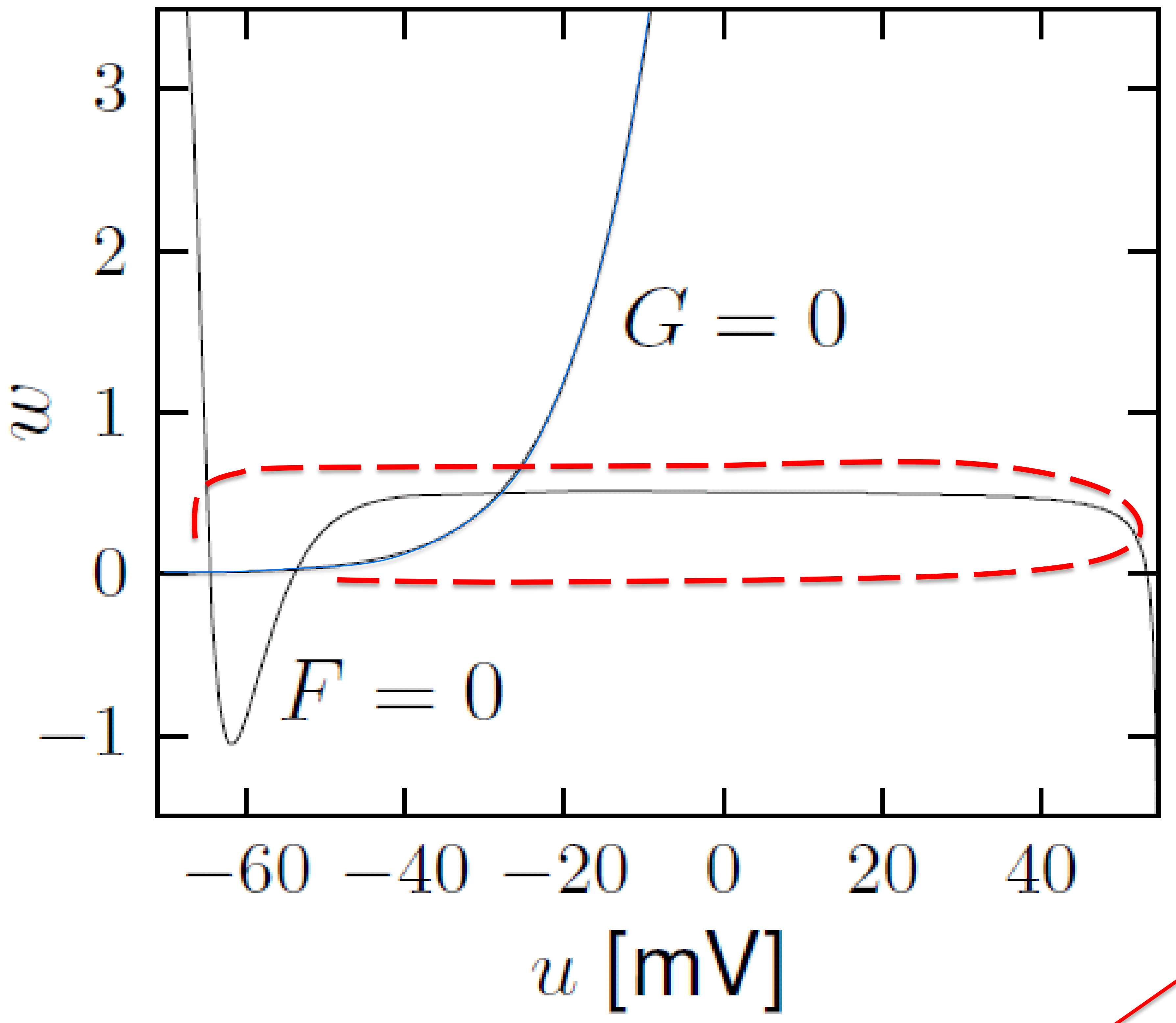
$$\tau \frac{du}{dt} = F(u, w_{rest}) + RI(t) = f(u) + RI(t)$$

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

→ Nonlinear I&F (see week 1!)

During spike initiation, the 2D models with separation of time scales can be reduced to a 1D model equivalent to nonlinear integrate-and-fire

4.3. 2D model, after spike initiation



Relevant during spike and downswing of AP

2-dimensional equation

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

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

Separation of time scales

-*w* is constant (if not firing)

$$\tau \frac{du}{dt} = f(u) + RI(t)$$

Integrate-and-fire: threshold+reset for AP

4.3. From 2D to Nonlinear Integrate-and-Fire Model

2-dimensional equation

2dimensional Model

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

Relevant during spike and downswing of AP →

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

Separation of time scales

-w is constant (if not firing)

Nonlinear Integrate-and-Fire Model

w-dynamics replaced by Threshold and reset in Integrate-and-ire

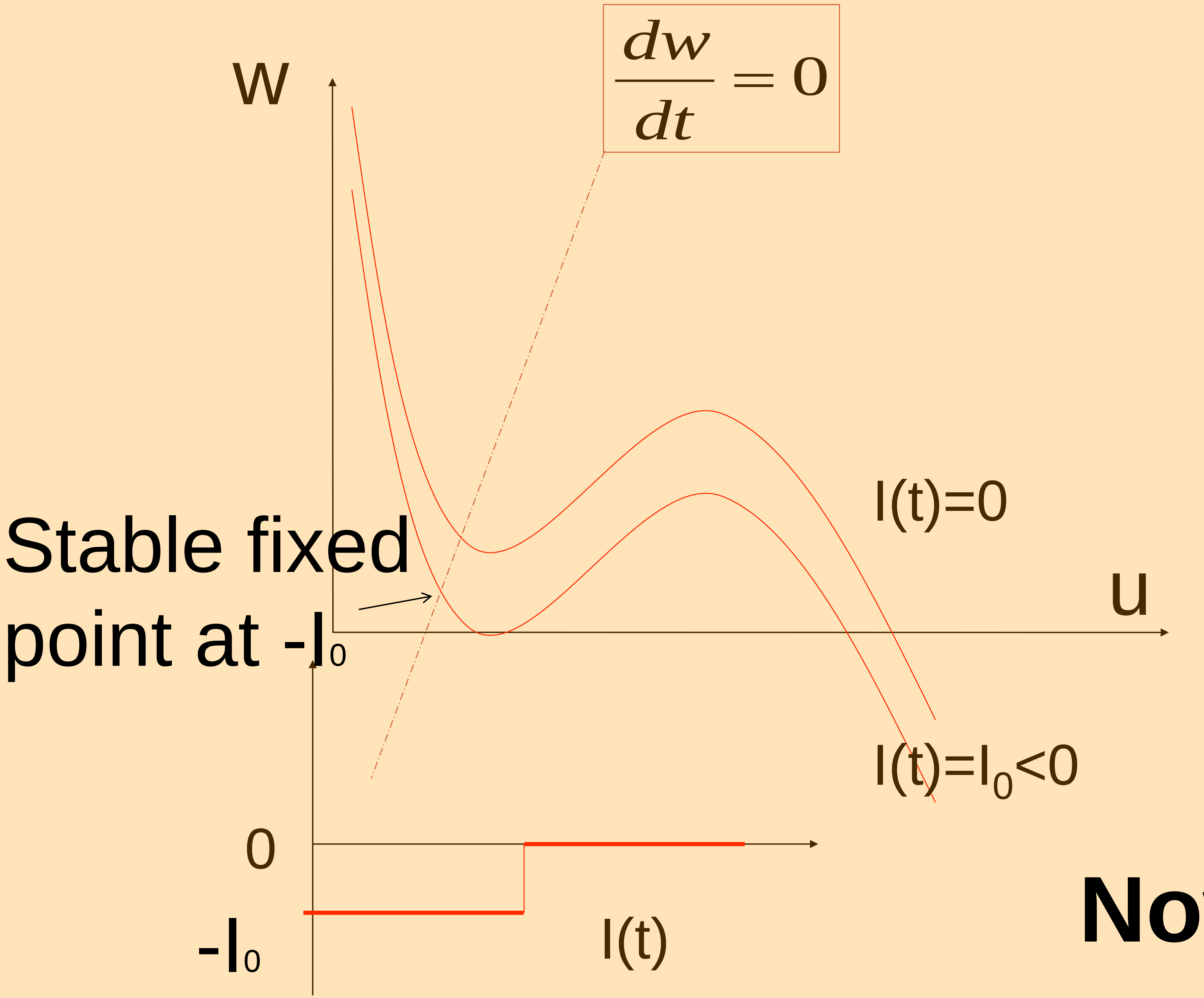
$$\tau \frac{du}{dt} = f(u) + RI(t)$$

Linear plus exponential

Exercise 2 and 3: NOW!

inhibitory rebound

Assume separation of time scales



Now exercises

Neuronal Dynamics – Literature for week 3 and 4.1

Reading: W. Gerstner, W.M. Kistler, R. Naud and L. Paninski,
Neuronal Dynamics: from single neurons to networks and models of cognition. Chapter 4 Cambridge Univ. Press, 2014
OR J. Rinzel and G.B. Ermentrout, (1989). Analysis of neuronal excitability and oscillations. In Koch, C. Segev, I., editors, *Methods in neuronal modeling*. MIT Press, Cambridge, MA.

Selected references.

-Ermentrout, G. B. (1996). *Type I membranes, phase resetting curves, and synchrony*. Neural Computation, 8(5):979-1001.
-Fourcaud-Trocme, N., Hansel, D., van Vreeswijk, C., and Brunel, N. (2003). *How spike generation mechanisms determine the neuronal response to fluctuating input.* J. Neuroscience, 23:11628-11640.
-Badel, L., Lefort, S., Berger, T., Petersen, C., Gerstner, W., and Richardson, M. (2008). Biological Cybernetics, 99(4-5):361-370.
- E.M. Izhikevich, Dynamical Systems in Neuroscience, MIT Press (2007)

The END

The END

4.3. Nonlinear Integrate-and-Fire Model

Exponential integrate-and-fire model (EIF)

$$f(u) = -(u - u_{rest}) + \Delta \exp\left(\frac{u-\vartheta}{\Delta}\right)$$

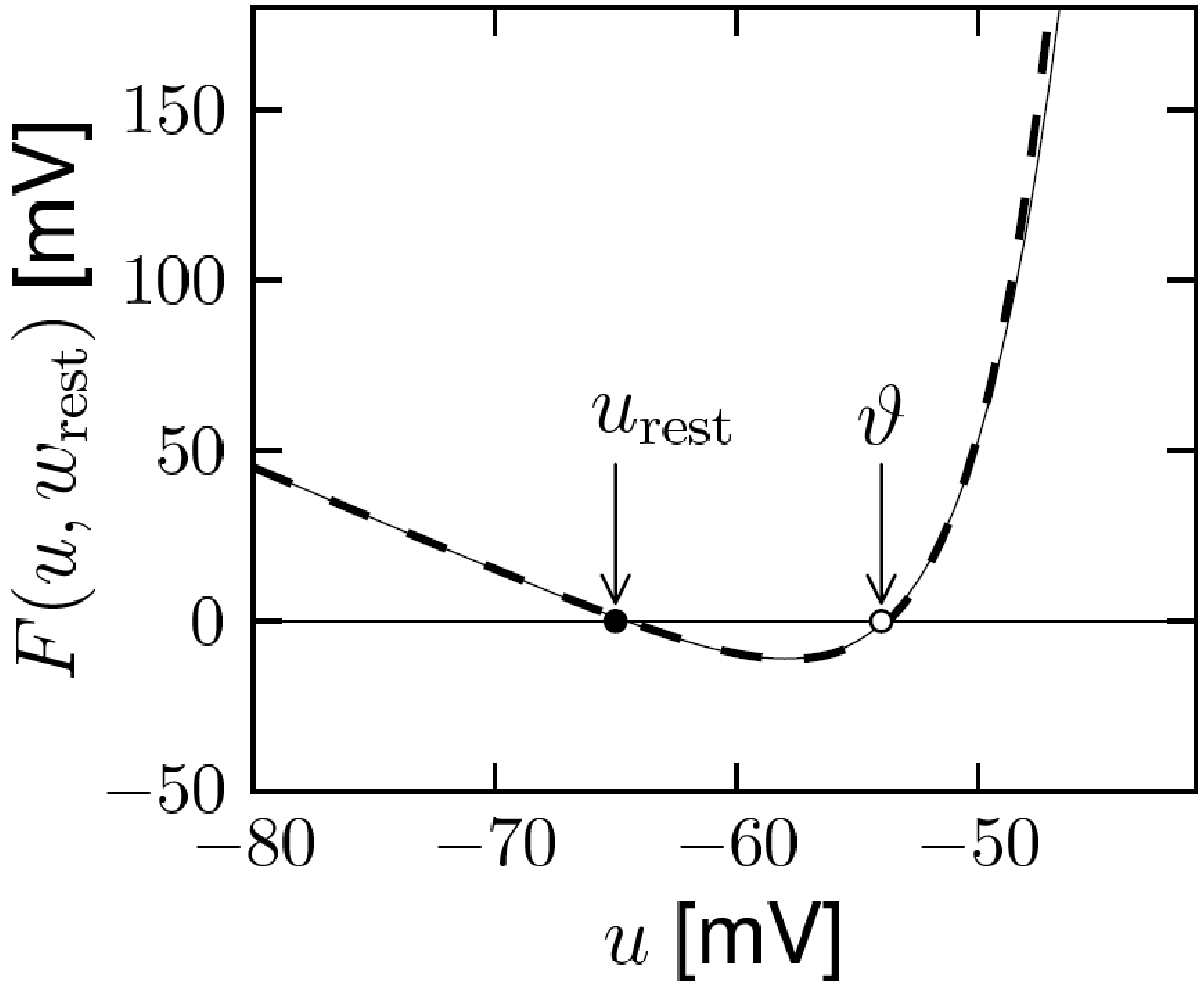


Image: Neuronal Dynamics, Gerstner et al., Cambridge Univ. Press (2014)

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

→ Nonlinear I&F (see week 1!)

Direct derivation from Hodgkin-Huxley

$$C\frac{du}{dt} = -g_{Na}\, m^3\, h\,(u - E_{Na}) - g_K n^4\,(u - E_K) - g_l(u - E_l) + I(t)$$

$$C\frac{du}{dt} = -g_{Na}[m_0(u)]^3 h_{rest}(u - E_{Na}) - g_K[n_{rest}]^4(u - E_K) - g_l(u - E_l) + I(t)$$

Fourcaud-Trocme et al, J. Neurosci. 2003

$$f(u) = -(u - u_{rest}) + \Delta\exp(\tfrac{u-\vartheta}{\Delta})$$

$$\tau\frac{du}{dt} = F(u, h_{rest}, n_{rest}) + RI(t) = f(u) + RI(t)$$

gives expon. I&F

Neuronal Dynamics – Quiz 4.3.

A. Exponential integrate-and-fire model.

The model can be derived

[ ] from a 2-dimensional model, assuming that the auxiliary variable w is constant.

[ ] from the HH model, assuming that the gating variables h and n are constant.

[ ] from the HH model, assuming that the gating variables m is constant.

[ ] from the HH model, assuming that the gating variables m is instantaneous.

B. Reset.

[ ] In a 2-dimensional model, the auxiliary variable w is necessary to implement a reset of the voltage after a spike

[ ] In a nonlinear integrate-and-fire model, the auxiliary variable w is necessary to implement a reset of the voltage after a spike

[ ] In a nonlinear integrate-and-fire model, a reset of the voltage after a spike is implemented algorithmically/explicitly