Computational Neuroscience: Neuronal Dynamics

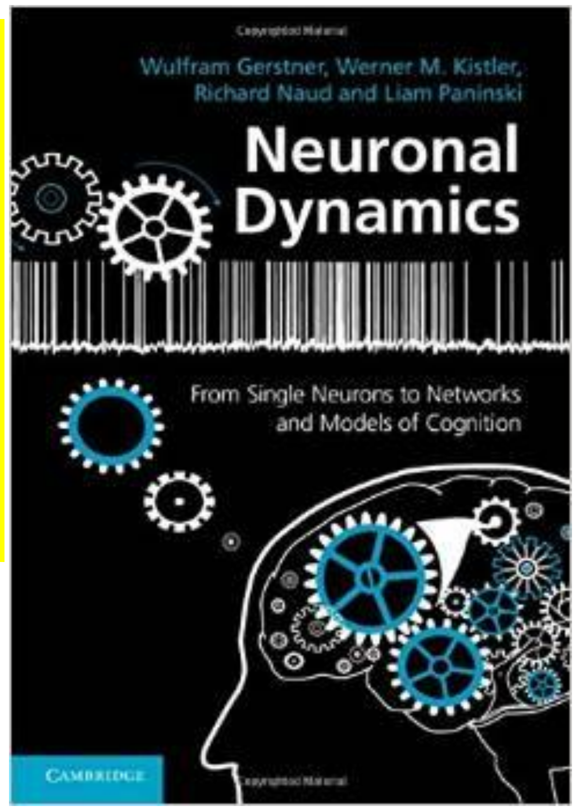
Week 3 – Reducing detail:

Two-dimensional neuron models

Wulfram Gerstner

EPFL, Lausanne, Switzerland

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



Cambridge Univ. Press

Lecture 4! of video series (first 100 minutes)

https://lcnwww.epfl.ch/gerstner/NeuronalDynamics-MOOCall.html

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

Week 3 – Quiz 3.1.

A - A biophysical point neuron model
with 3 ion channels,
each with activation and inactivation,
has a total number of equations
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Neuronal Dynamics – 3.1. Reduction of Hodgkin-Huxley model

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

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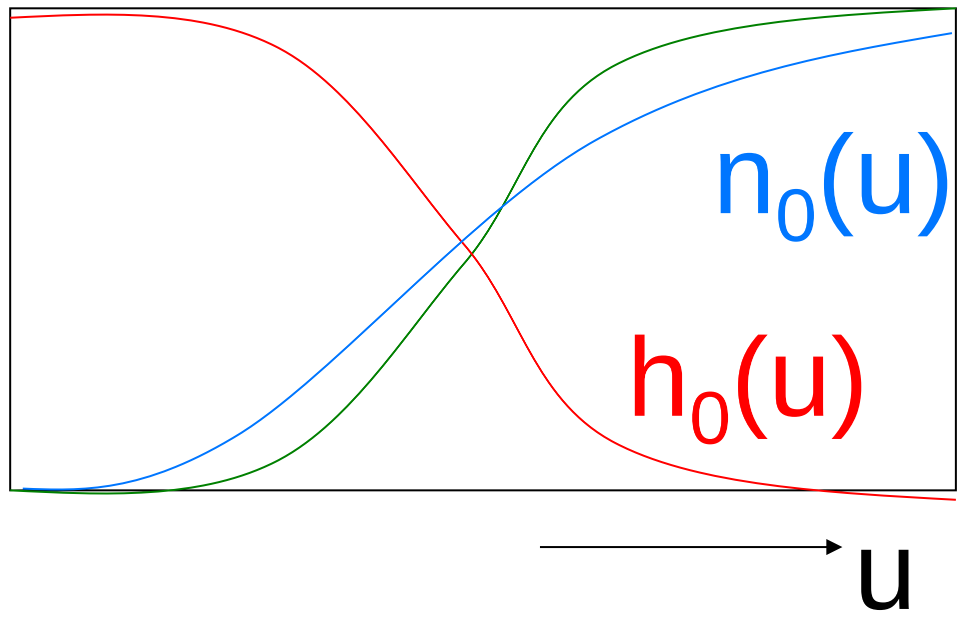

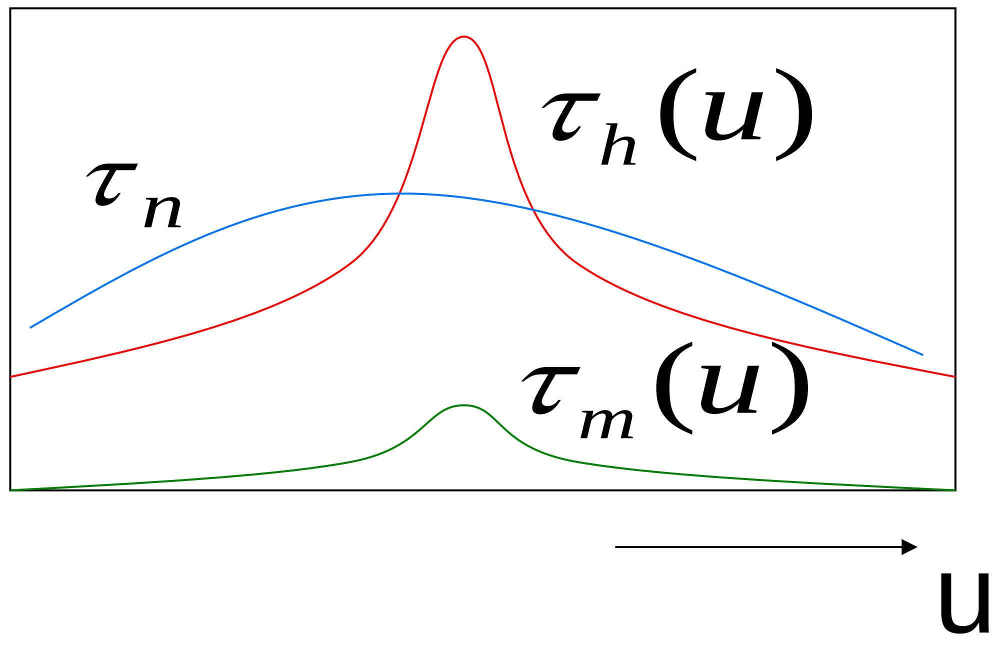

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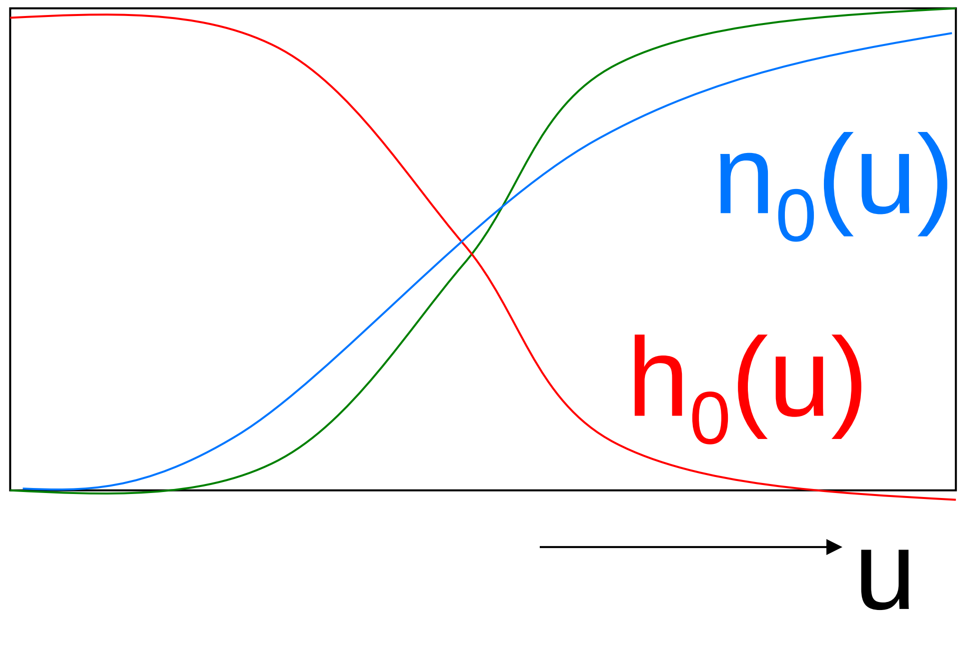

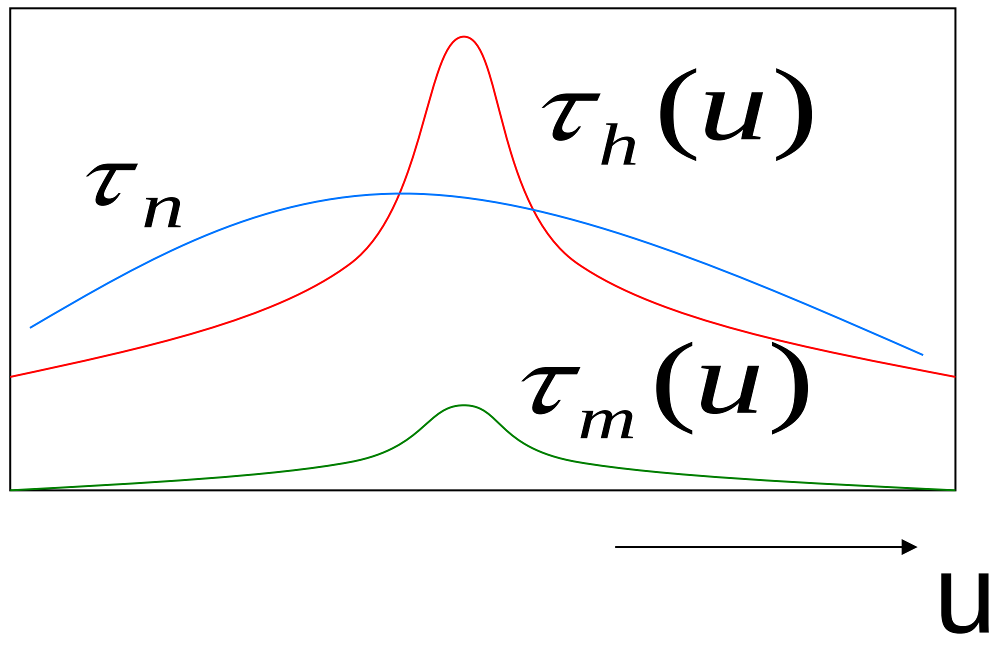

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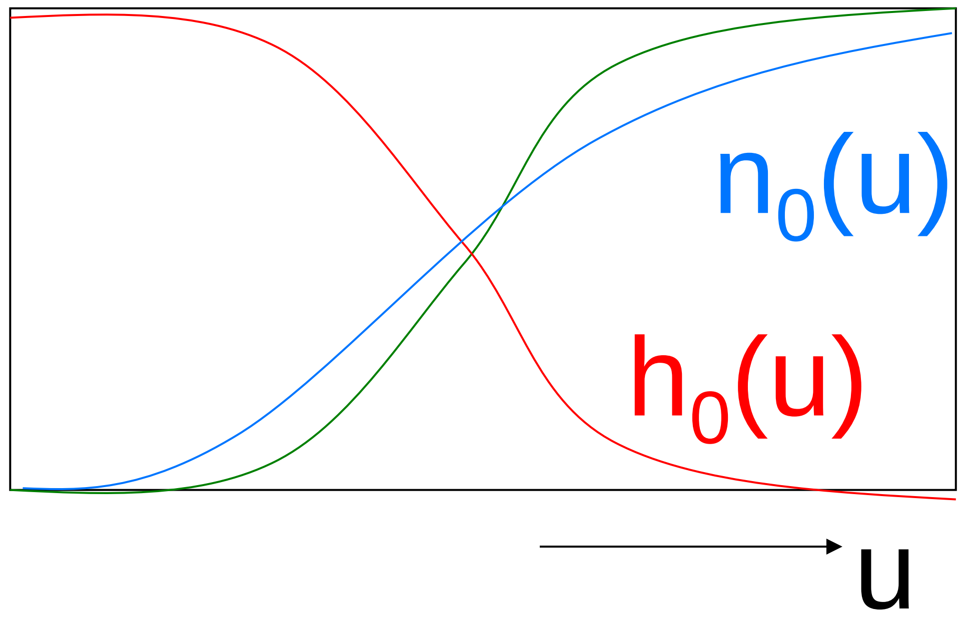

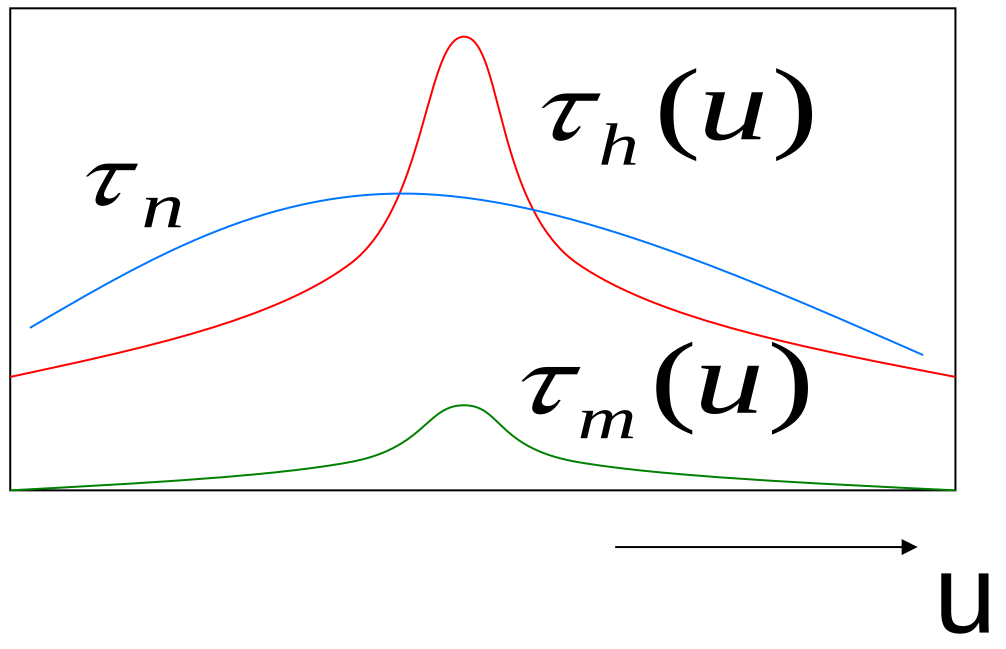

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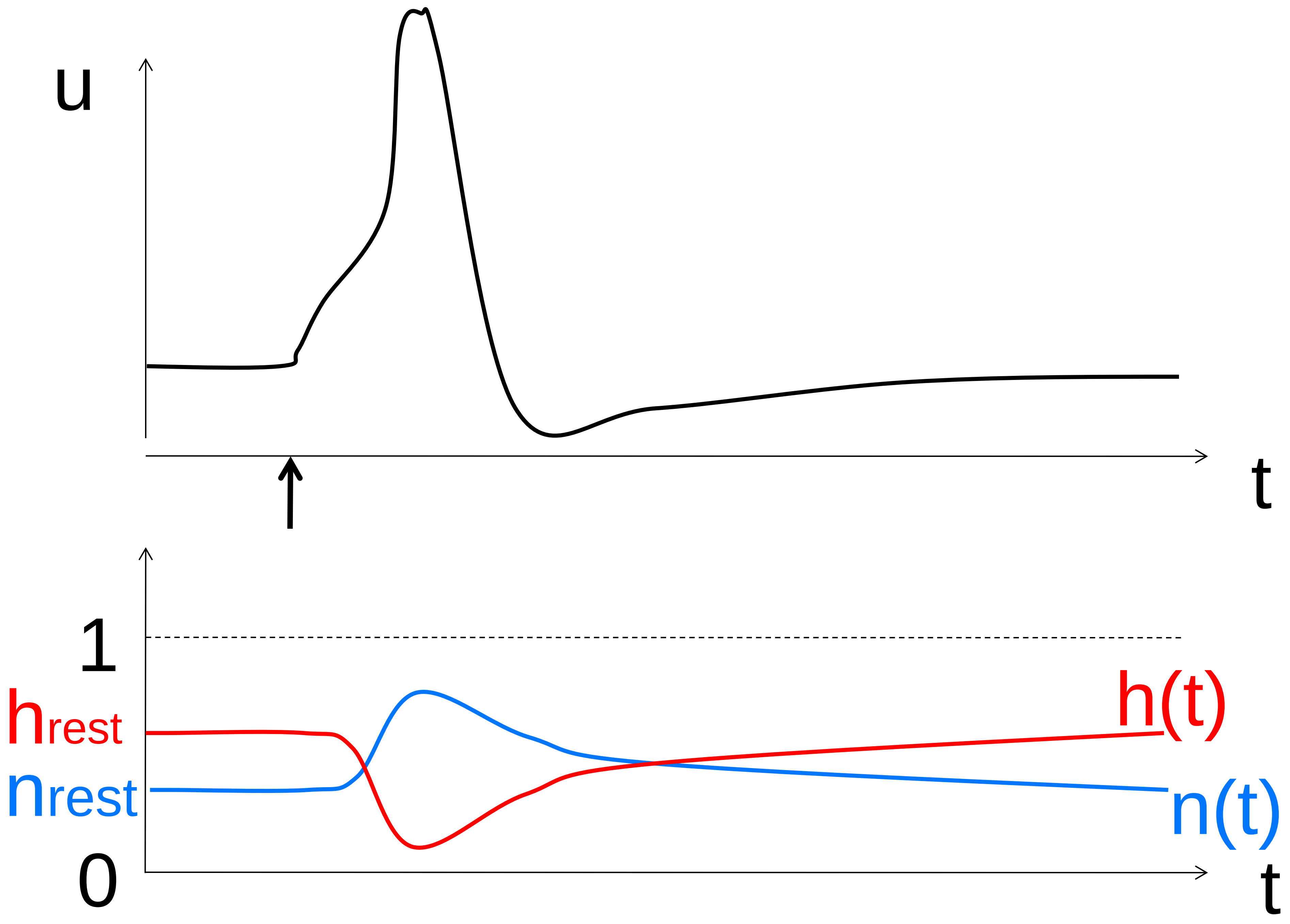

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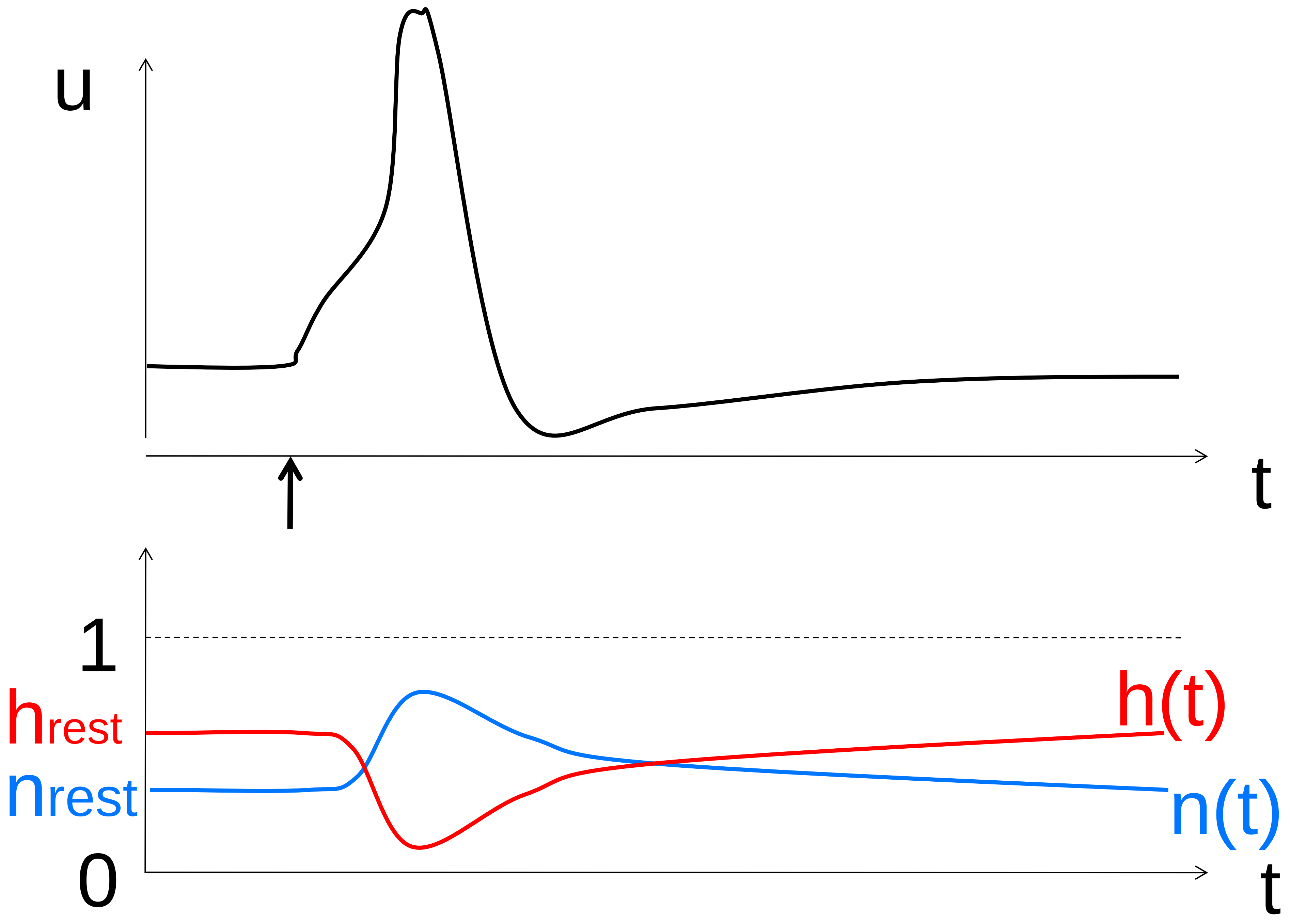

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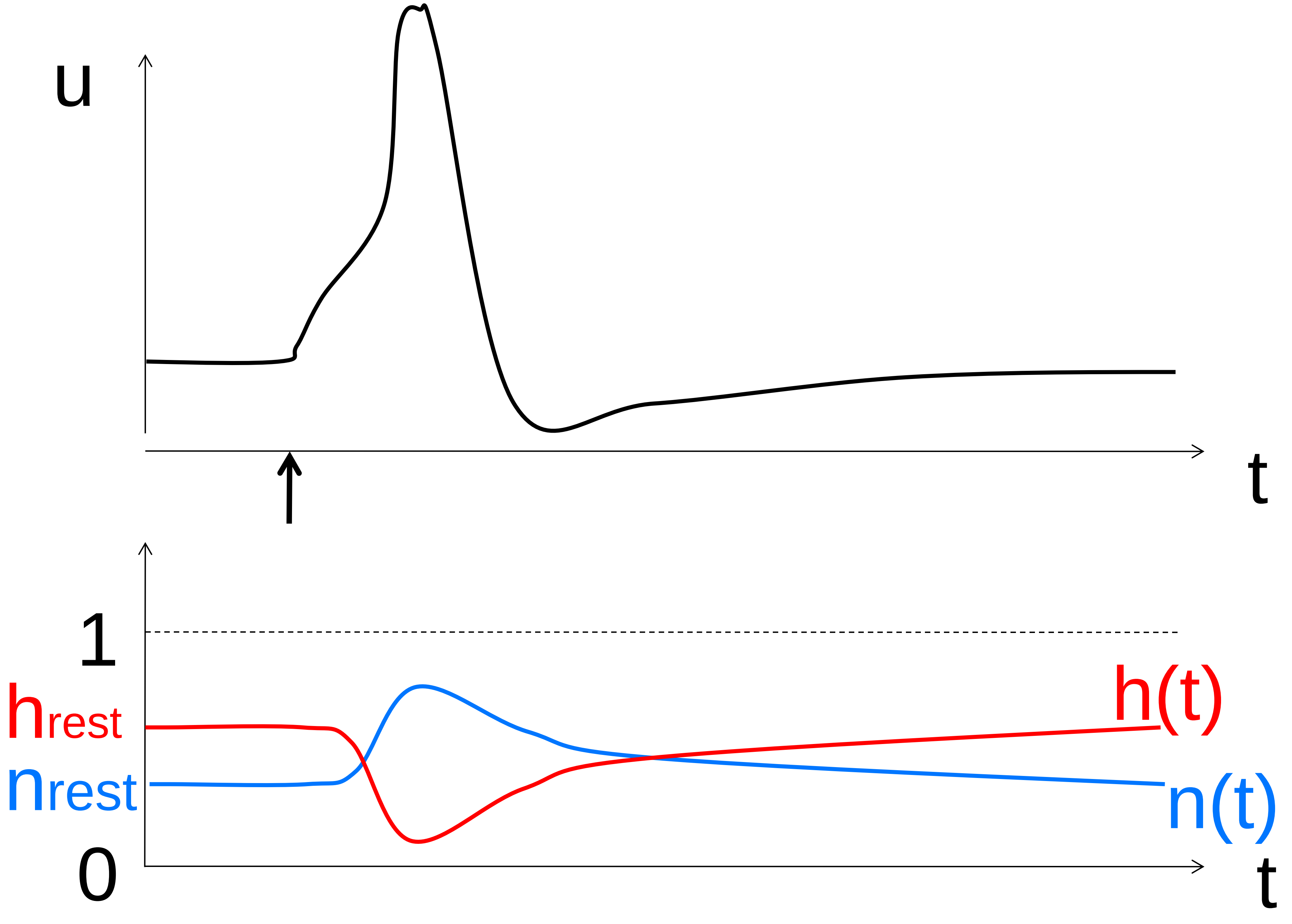

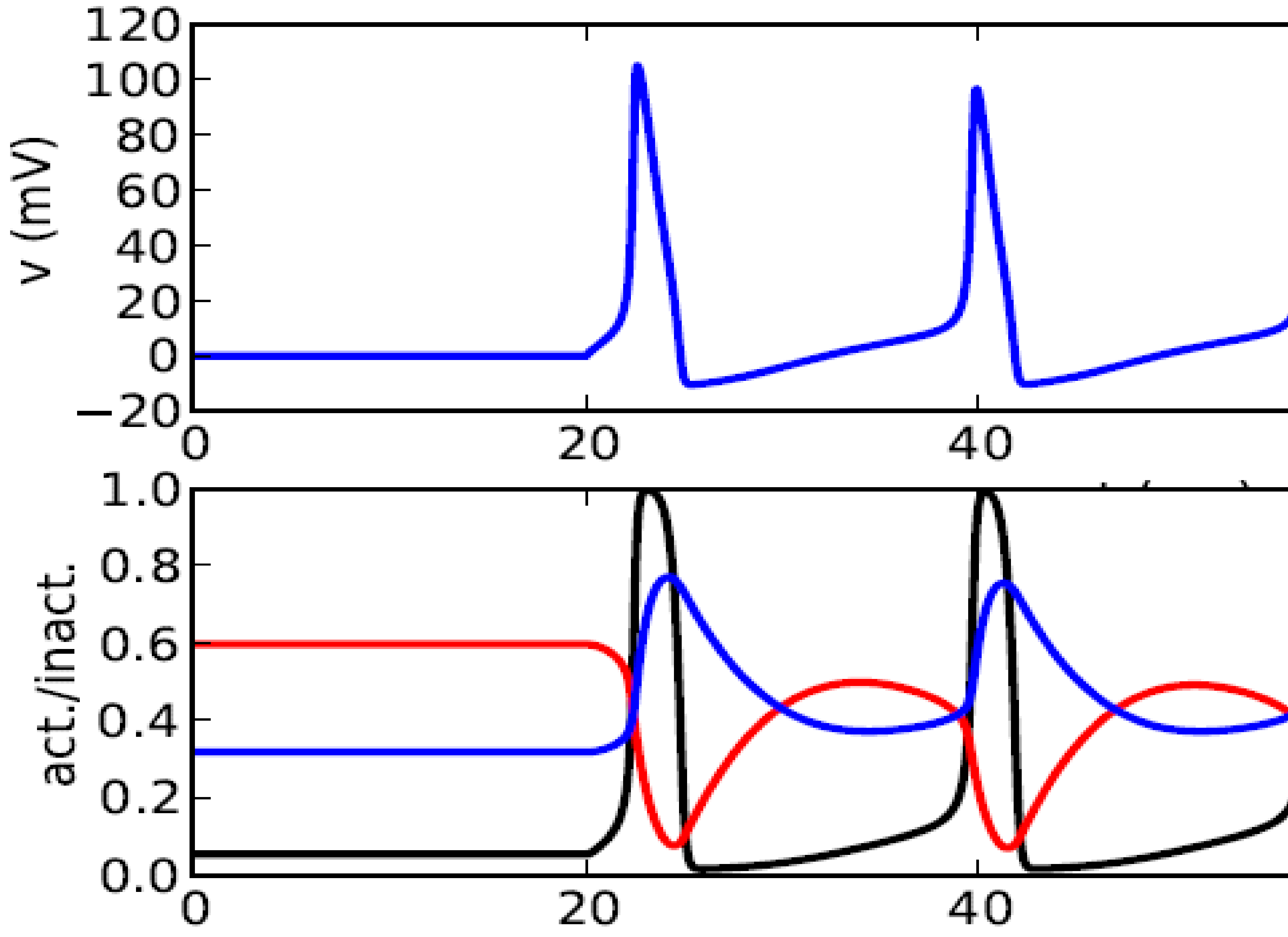

Week 3 – Quiz 3.2-similar dynamics

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)

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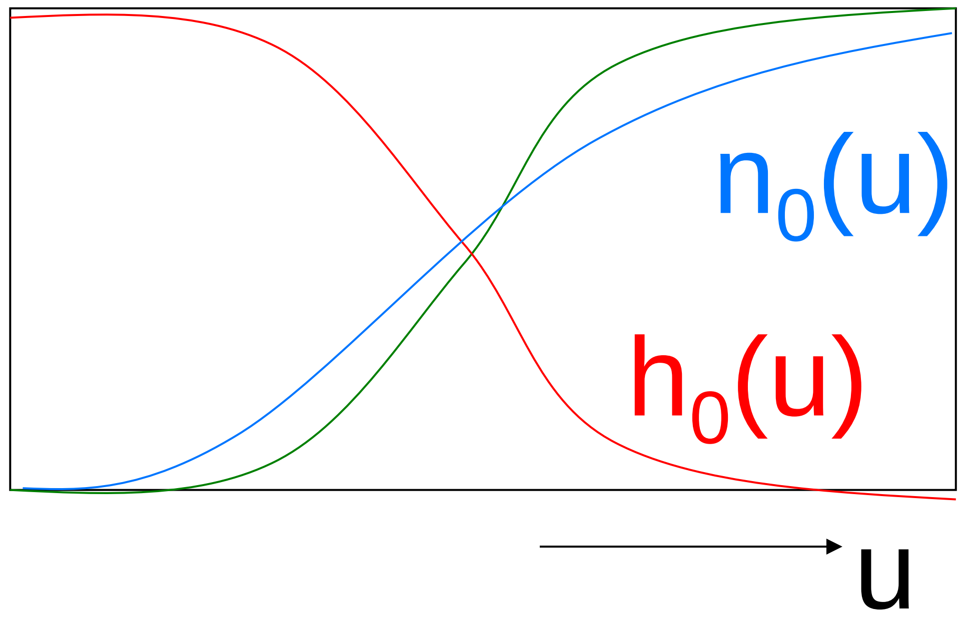

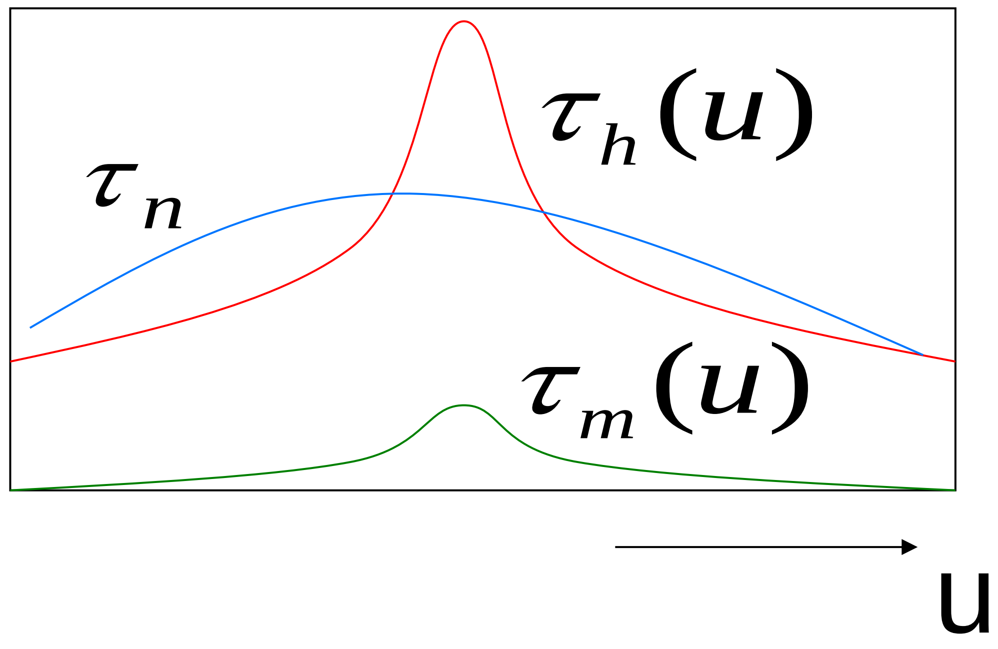

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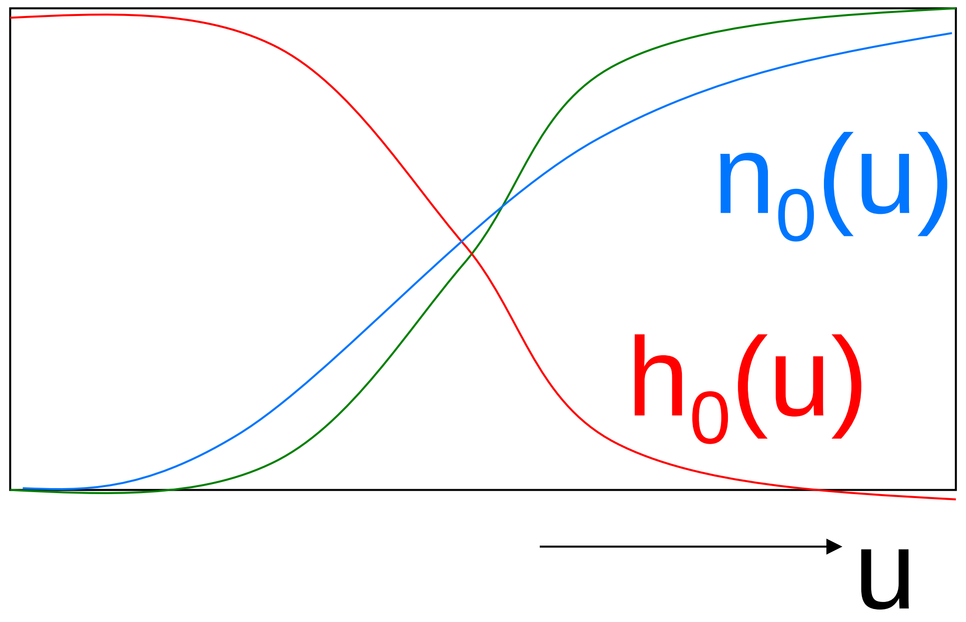

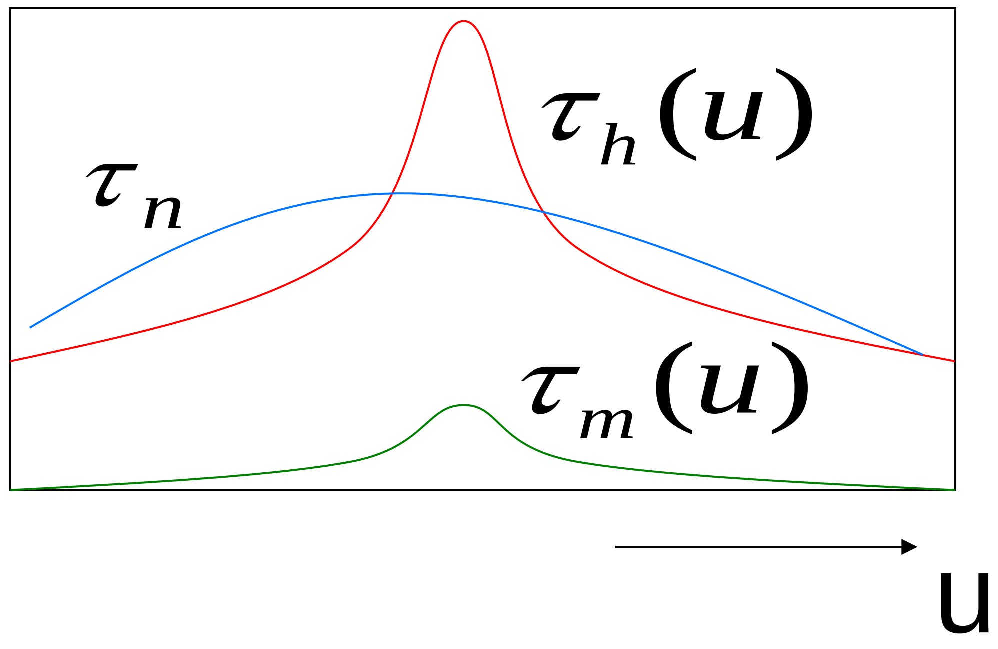

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Fast compared to what?

Question of student:

1. it is possible to approximate m(t) with its asymptotic value if m(t) change is fast enough w.r.t. the others temporal changes and in particular the stimulus change. However it seems to me that very often the stimulus we use is either a pulse or a step (hence instantaneous) current. Wouldn't this mean this approximation is too bad most of the time to be useful ?

Answer: Good question that needs a longer answer:

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A- Separation of time scales:

We start with two equations

$$\tau_1 \frac{dx}{dt} = -x + y + I(t)$$

$$\tau_2 \frac{dy}{dt} = -y + x^2 + A$$

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First part of answer. consider

$$\tau_1 \frac{dm}{dt} = -m + I(t)$$
$$\tau_2 \frac{du}{dt} = \quad G(m,u) = f_m(u)$$

First part of answer. Consider $\tau_1 \ll \tau_2$

Now divide both sides of the equation by a factor of 10

$$\tau_1 \frac{dm}{dt} = -m + I(t)$$
$$(\tau_2/10)\ \frac{du}{dt} = \quad (1/10)\ f_m(u)$$

We can rewrite the lhs with a new time constant $\tilde{\tau}_2 = \frac{\tau_2}{10}$; and then $\tau_1 \ll \tau_2$ may no longer hold. Hence, if we compare 'speed of change', we have to assume that the rhs is of 'order 1'. Concretely, if $f_m(u)$ has a value of 200 for some u, then the speed is rapid even if formally τ_2 is 'large'.

Second part of answer. Consider $\tau_1 \ll \tau_2$

$$\tau_1 \frac{dm}{dt} = -m + I(t)$$

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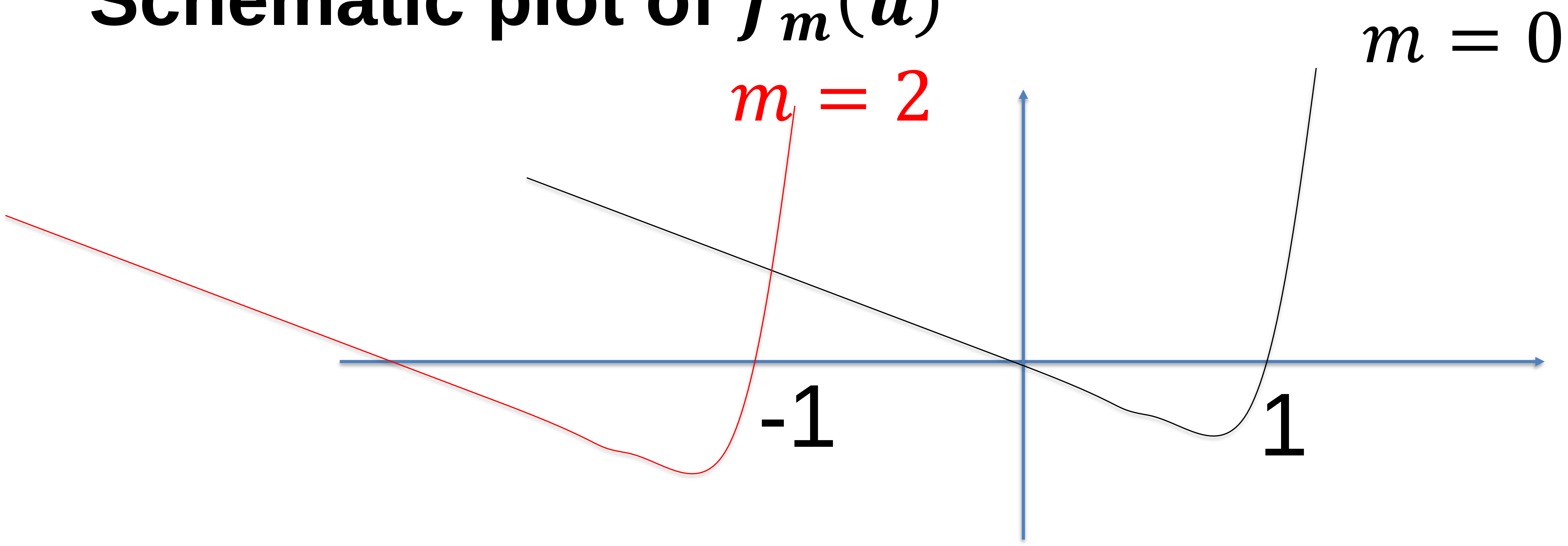
Schematic plot of $f_m(u)$



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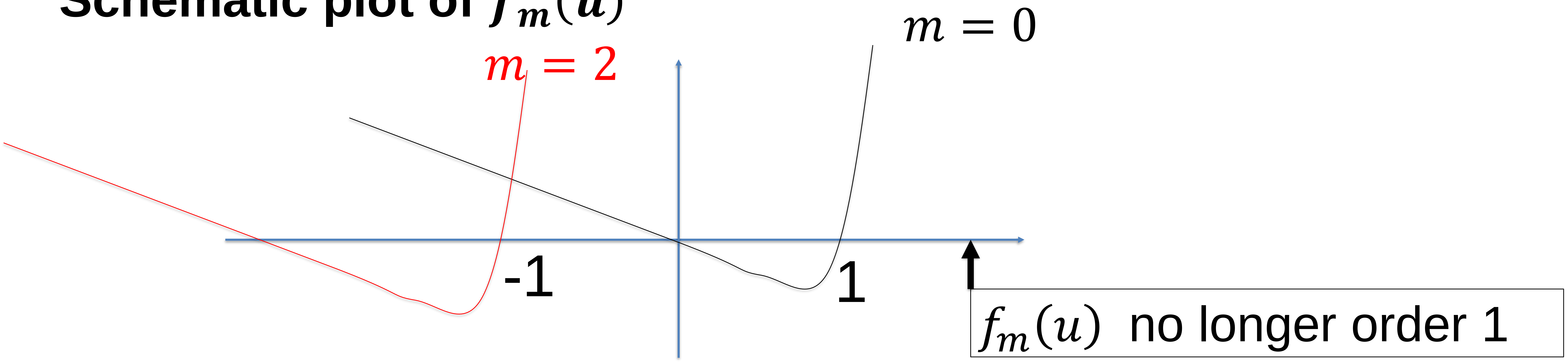

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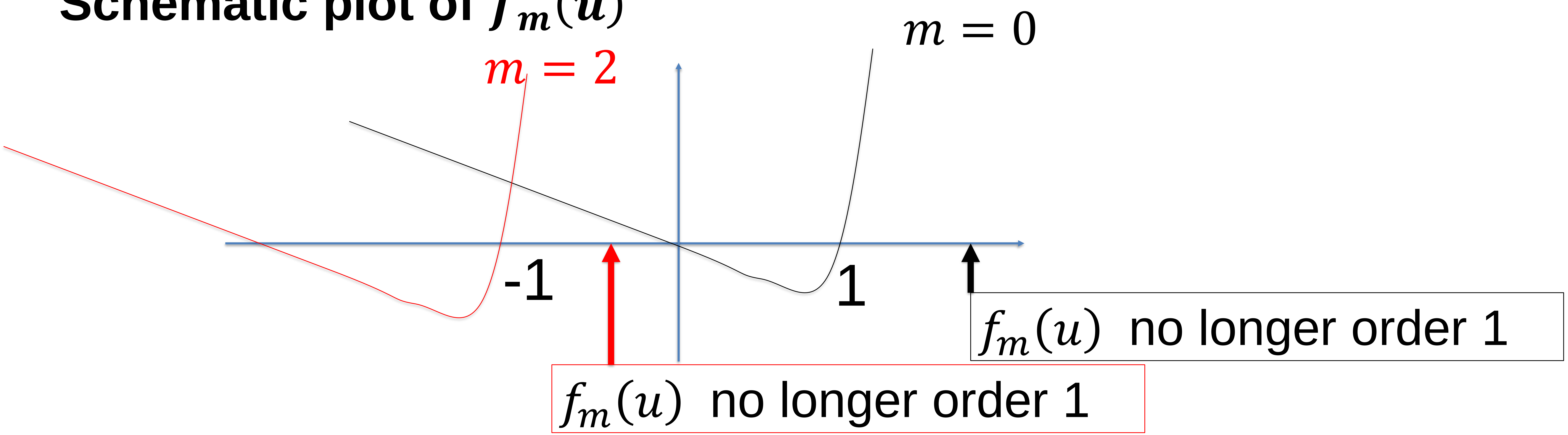

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Second part of answer. Consider $\tau_1 \ll \tau_2$

$$\tau_1 \frac{dm}{dt} = -m + I(t)$$

$$\tau_2 \frac{du}{dt} = \; f_m(u) = -(u+m) + c\exp[(u+m-\vartheta)/\Delta]$$

Assume a short current pulse *I(t)* of amplitude 3.5 and duration $\tau_1/4$.

- A naïve application of the separation of time scales would predict explosion of u(t).
- However, if we consider that during the application of *I(t)* the variable *m* never goes above 7/8, then we conclude that the voltage trajectory will stay in the stable regime and return to zero.

Conclusion: it is wise to consider short current pulses as delta pulse that lead to a new initial condition. In this example, *m* jumps by 7/8.

Week 3 – Summary 3.1

In order to reduce the HH model from 4 to 2 equations we have to simplify. We use two different mathematical methods.

1. Separation of time scale.

If the time scale of two variables is different by a factor 10 or a hundred, we can assume that the faster one of the two variables has already converged to its ‘momentary stable state’ on the slow time scale. Thus, we can remove the fast variable. We use the separation of time scale to remove the variable m.

2. Exploit similarities.

If two variables evolve on the same time scale, they have, if we are lucky, some similar temporal evolution. We can reduce the two variables to one dimension by turning the coordinate system such that the first dimension is the one where the two variables evolve ‘together’. The simplification consists in suppressing the second variable. This is similar to PCA where you would also only keep the first component. However, we need to do this such that also the DYNAMICS stays approximately correct, after reduction to 1 dimension.
We use this trick to compress h and n into a single variable w.

3.2. Nullclines of reduced HH model

stimulus

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

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

u-nullcline

w-nullcline

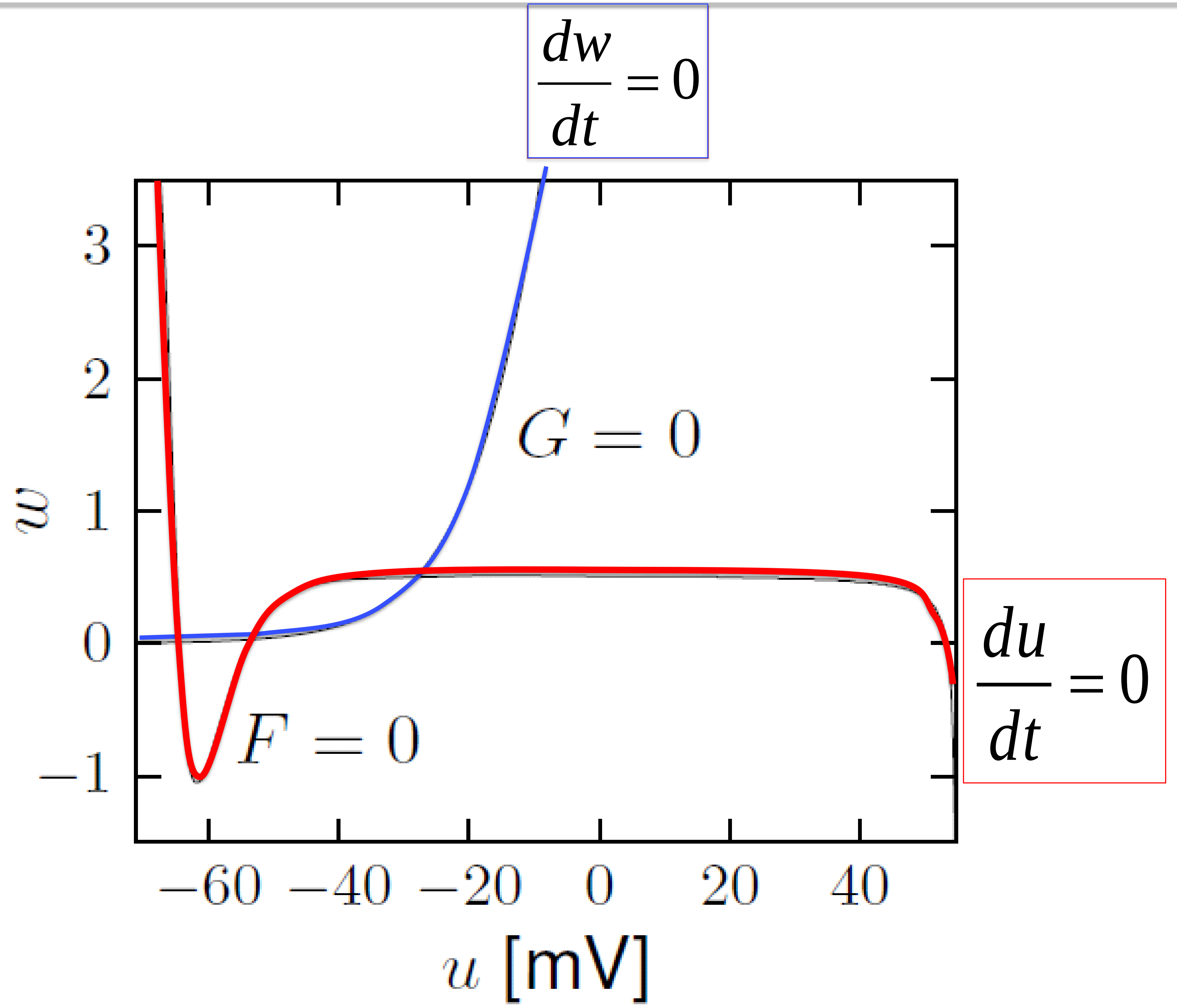

Image: Neuronal Dynamics, Gerstner et al., Cambridge Univ. Press (2014)

3.2. Nullclines of reduced HH model

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

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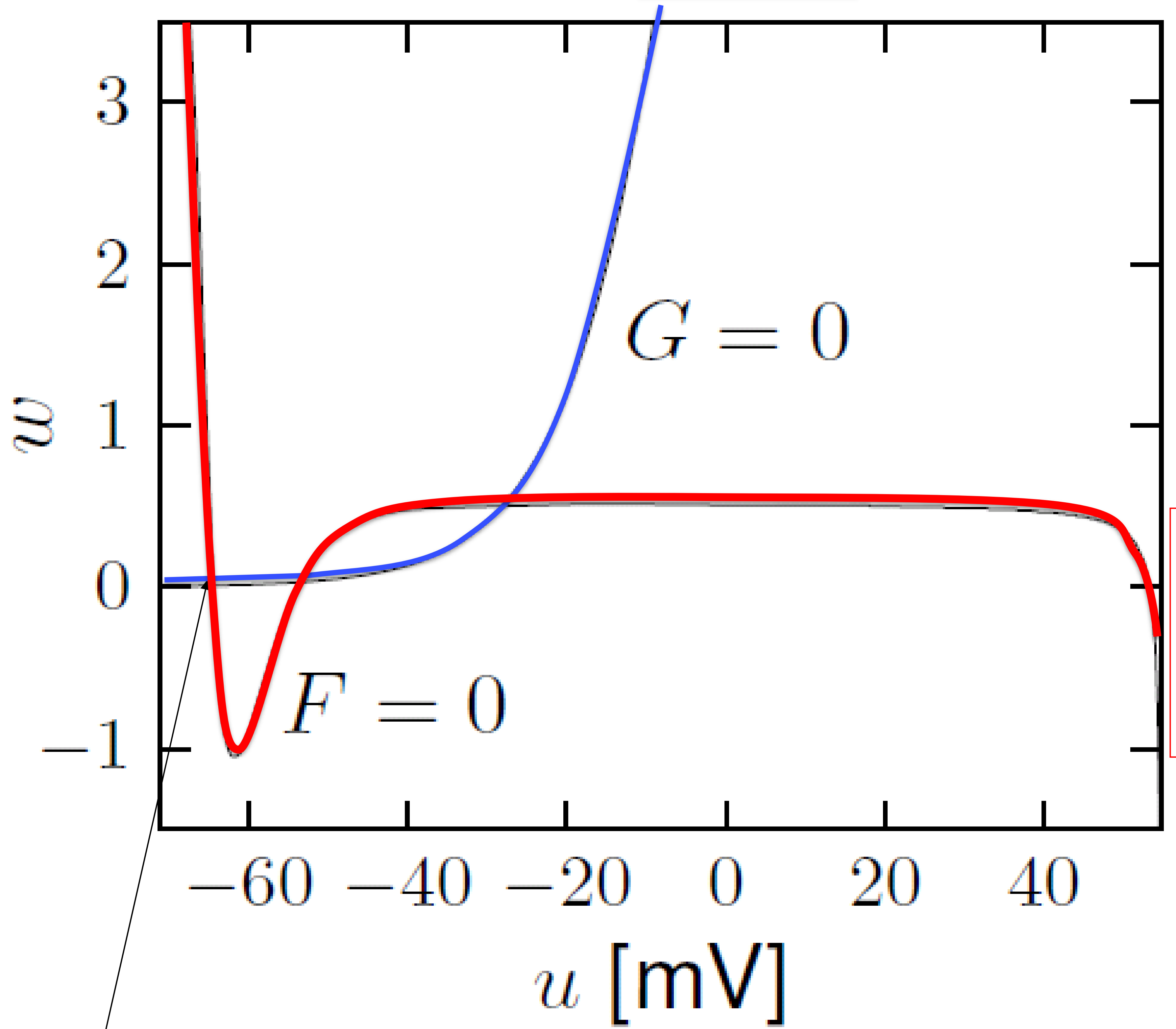
$\frac{dw}{dt} = 0$



$\frac{du}{dt} = 0$

Stable fixed point

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

Week 3 – Quiz 3.4

Take 1 minute

A. u-Nullclines

[ ] On the u-nullcline, arrows are always vertical
[ ] On the u-nullcline, arrows point always vertically upward
[ ] On the u-nullcline, arrows are always horizontal

B. w-Nullclines

[ ] On the w-nullcline, arrows are always vertical
[ ] On the w-nullcline, arrows are always horizontal
[ ] On the w-nullcline, arrows point always to the left

stimulus

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

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Week 3 – Quiz 3.4

Take 1 minute

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[x]

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Week 3 – Quiz 3.4

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stimulus

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Week 3 – Quiz 3.4

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Week 3 – Quiz 3.4

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stimulus

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

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

Question of student.

2. I understand how the change at any given point of either of the nullclines has to be orthogonal to its corresponding variable direction. I didn't understand how we can propagate this outside the locality of the nullclines.

Basic answer: the sign of the component of the flow arrow in x-direction can only change at points with $dx/dt = 0$.
The sign of the component of the flow arrow in y-direction can only change at points with $dy/dt = 0$.
But these condition tell us that changes are only possible on the nullclines.

Week 3 – Summary 3.2

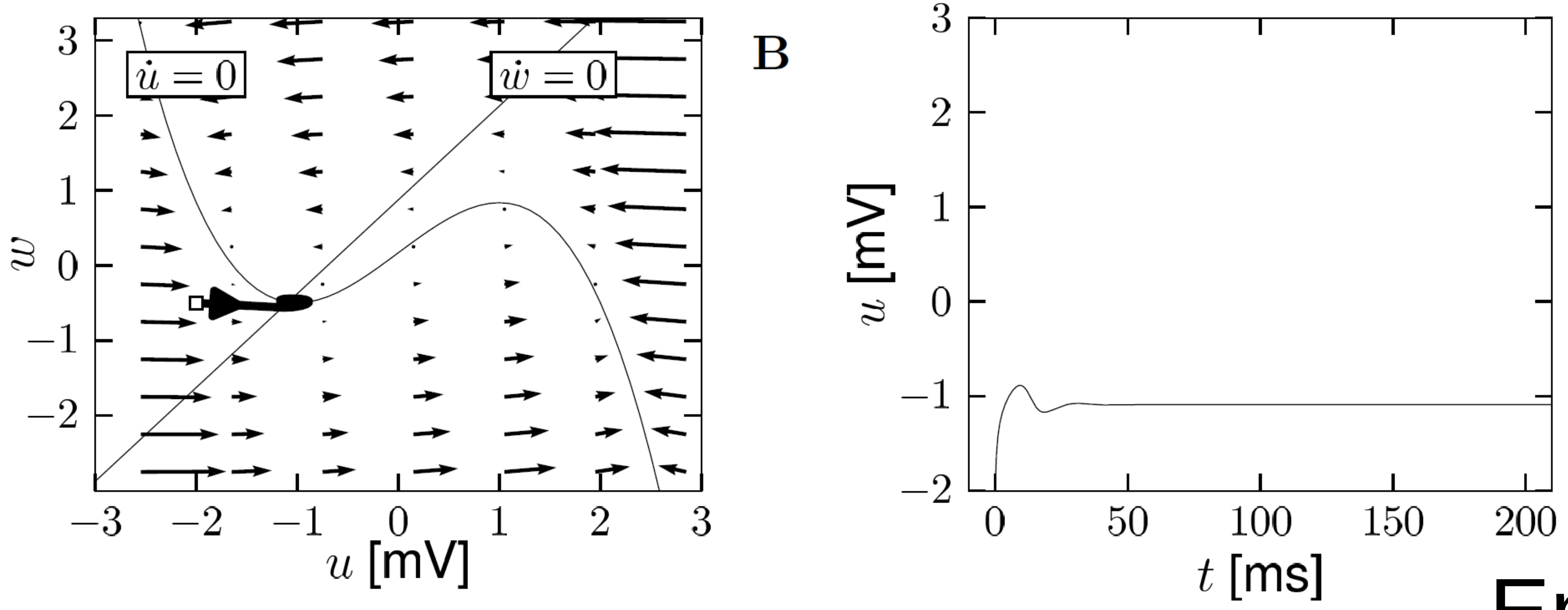
Once we are in two dimensions we can use phase plane analysis. Two important concepts are the ‘nullclines’; and the local direction of the ‘flow’.

Intersections of the two nullclines correspond to fixed points. It is a bit of work to decide whether a fixed point is stable or not. However, in some cases (such as a saddle point) stability is visible directly from the graph.

Stability of a fixed point is determined by linearizing around the fixed point. Since we are in 2 dimensions, linearization yields a 2x2 matrix. The eigenvalues determine the stability (See exercise 2.1).

The FitzHuhg Nagumo model is a particularly simple 2-dimensional model. The reduction of the full Hodgkin-Huxley model yields a more complicated picture in the phase plane.

3.3. Analysis of a 2D neuron model



2-dimensional equation

stimulus

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

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

Enables graphical analysis!

2 important input scenarios

- Pulse input
- Constant input

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 or downward
[ ] By moving the w-nullcline vertically upward or downward
[ ] 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

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Week 3 – Summary 3.3

Phase plane analysis of neuron models is particularly interesting because the input I only enters into the first variable (voltage u).

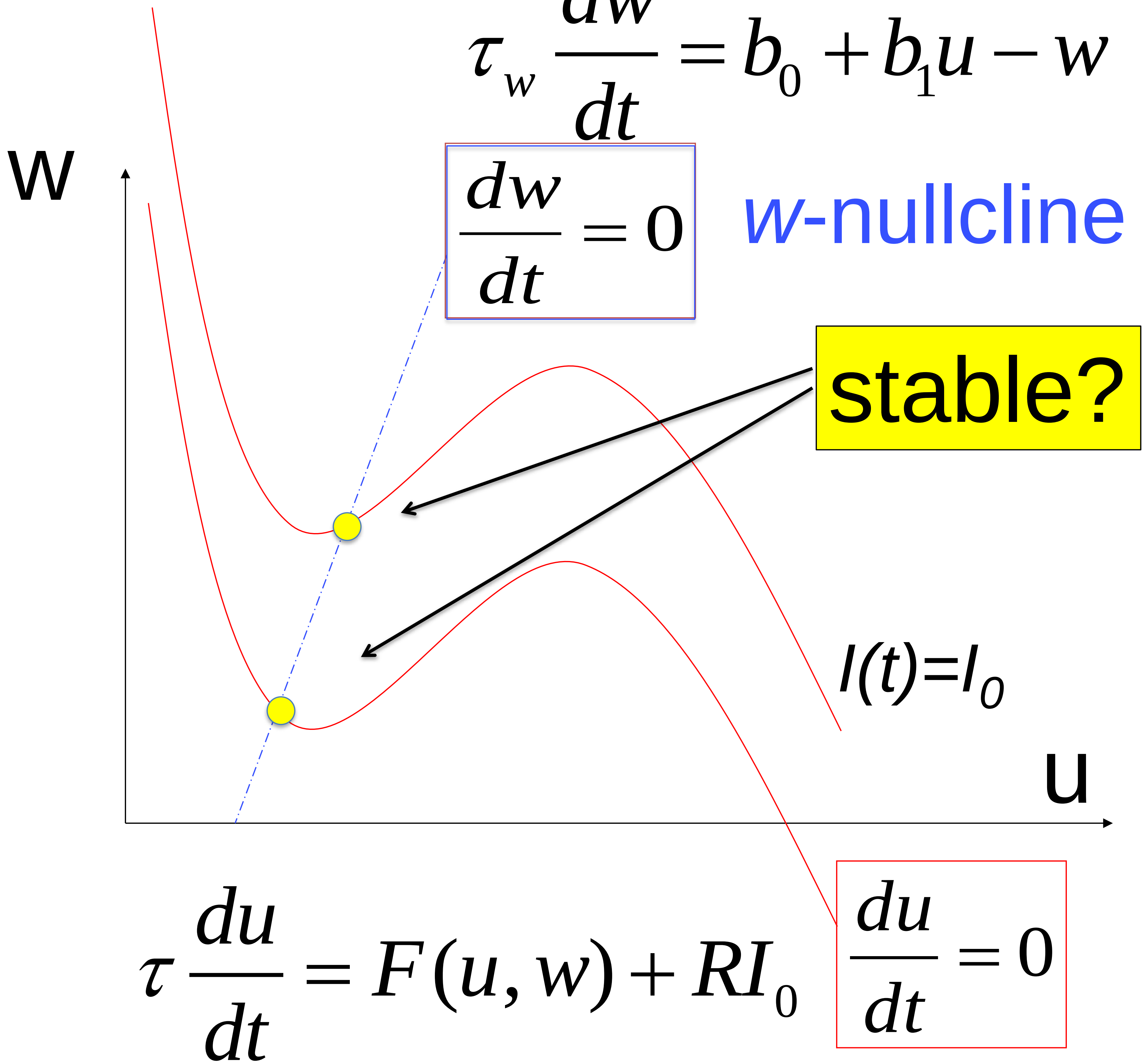
As a consequence of this observation, we can discuss two important input scenarios as follows:

1. Constant input. In this case the u-nullcline is shifted vertically.
2. Pulse input. In this case the u-nullcline is not shifted, but the pulse causes a horizontal shift of the initial condition.

If constant input is applied (or very slowly ramped upward) the number of fixed points or their stability can change.
If we can find a bounding box (with arrows pointing inside) around an unstable fixed point and no other fixed points are inside the box, then there must exist a limit cycle.

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

$$\tau_w \frac{dw}{dt} = b_0 + b_1 u - w$$



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

u-nullcline

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

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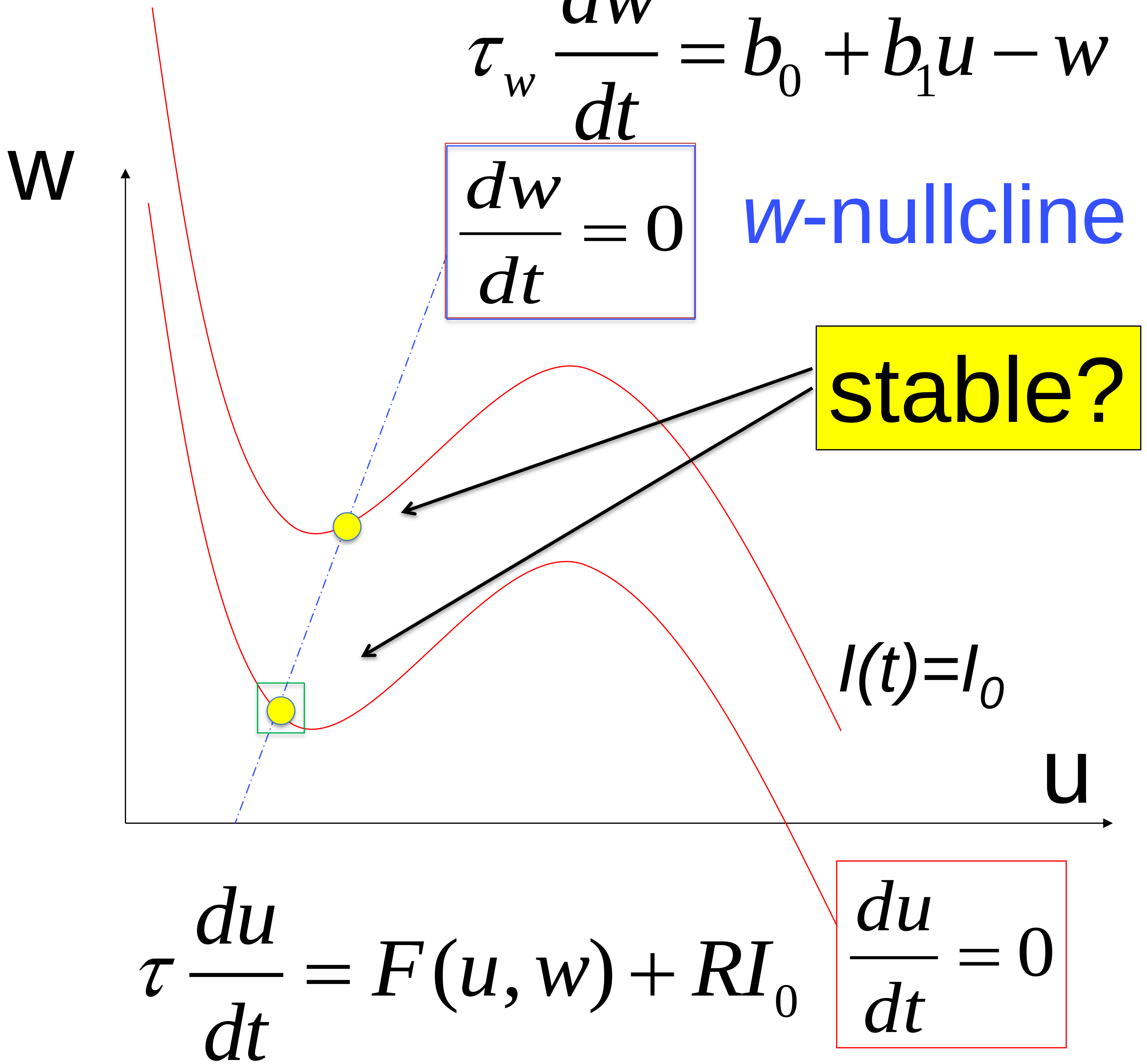

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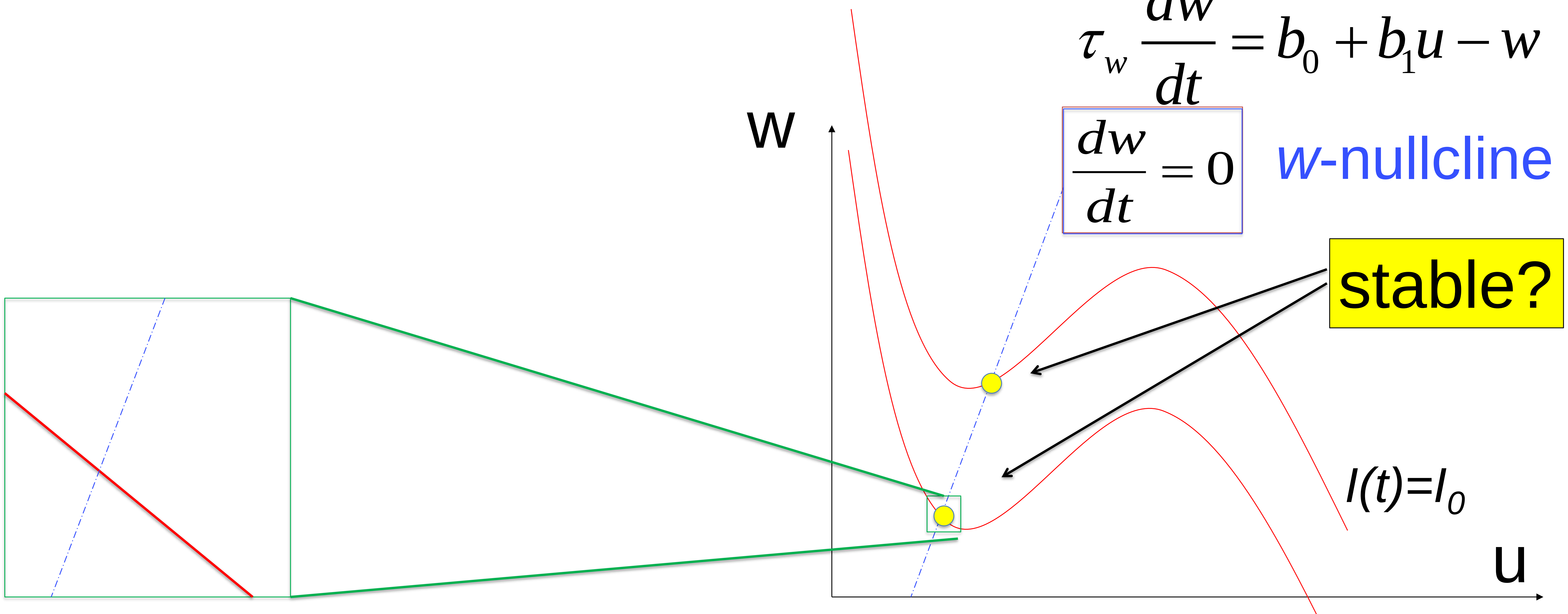
u-nullcline

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

$$\tau_w \frac{dw}{dt} = b_0 + b_1 u - w$$

$$\frac{dw}{dt} = 0$$ *w*-nullcline



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

$$\frac{du}{dt} = 0$$

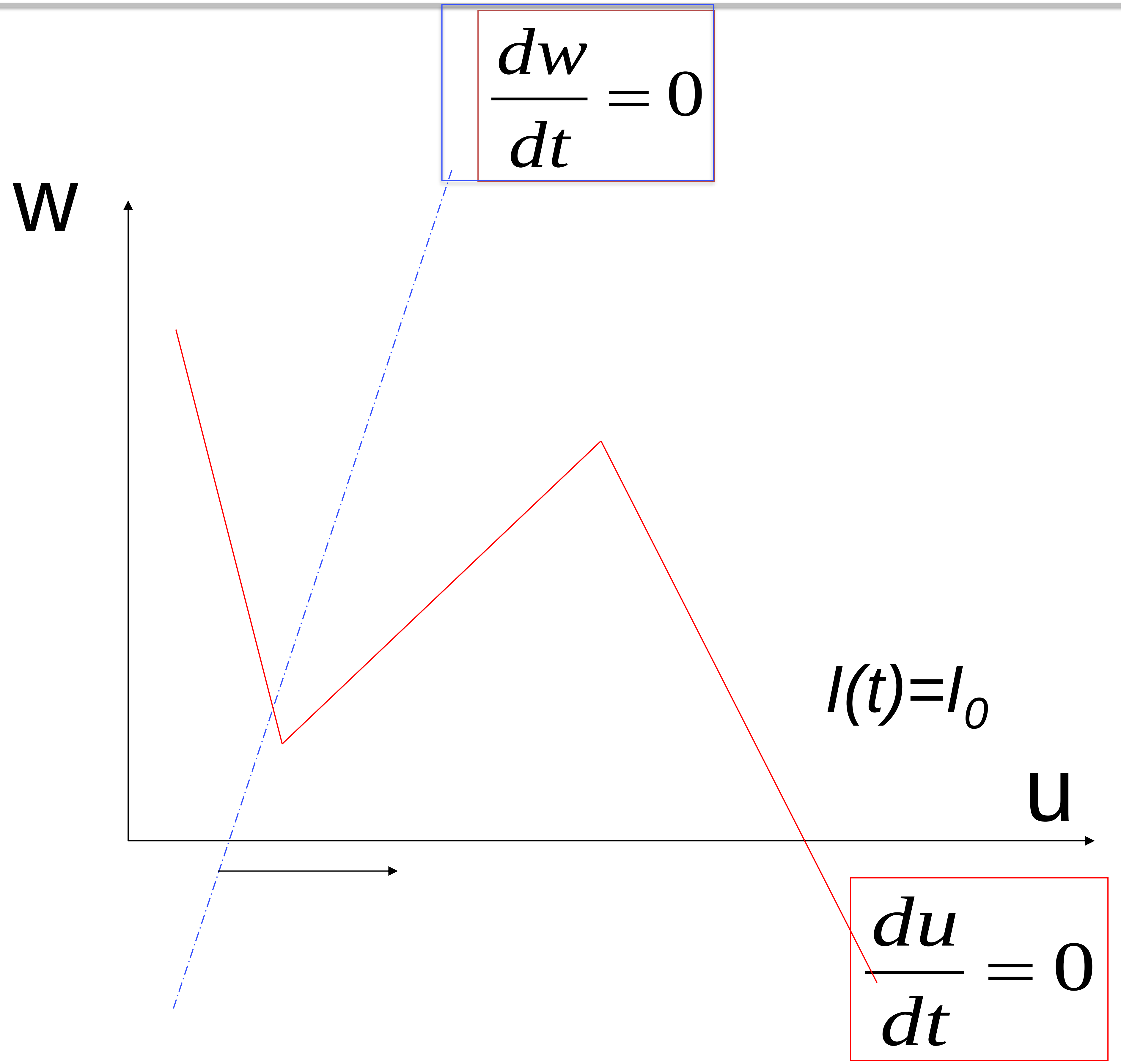
u-nullcline

Preparation of Exercise 2: Detour - Stability of fixed points

stimulus

$$\tau \frac{du}{dt} = au - w + I_0$$

$$\tau_w \frac{dw}{dt} = cu - w$$



Preparation of Exercise 2: Detour - Stability of fixed points

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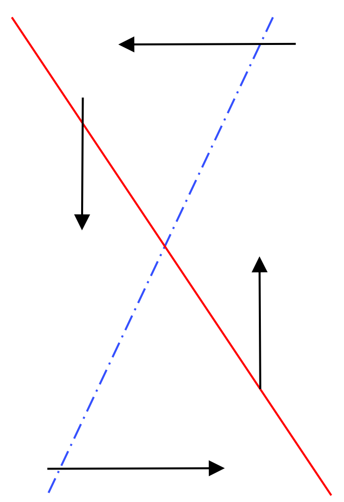

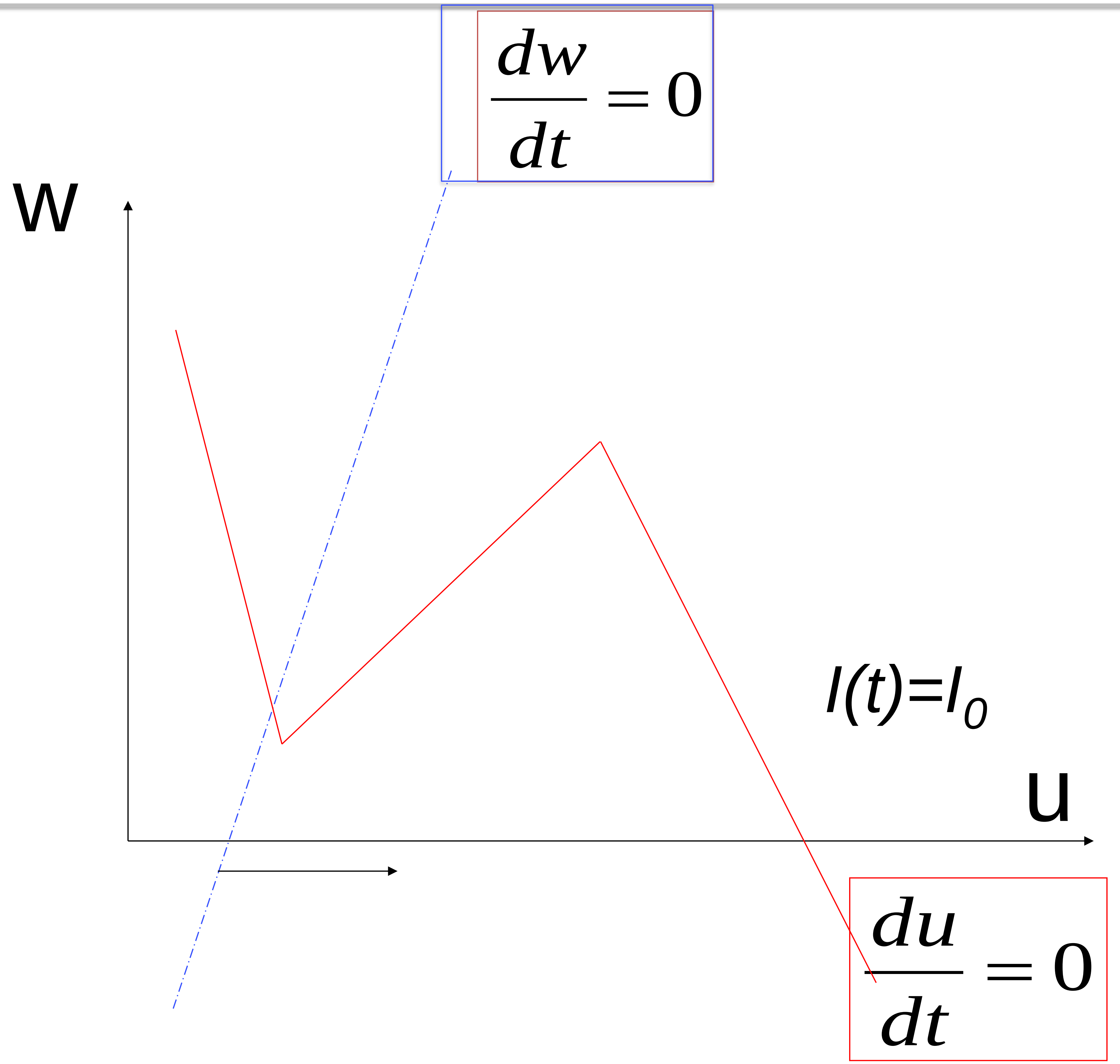

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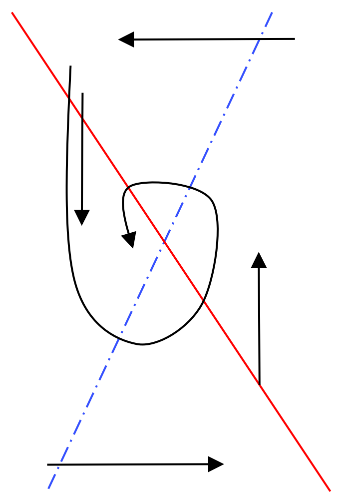

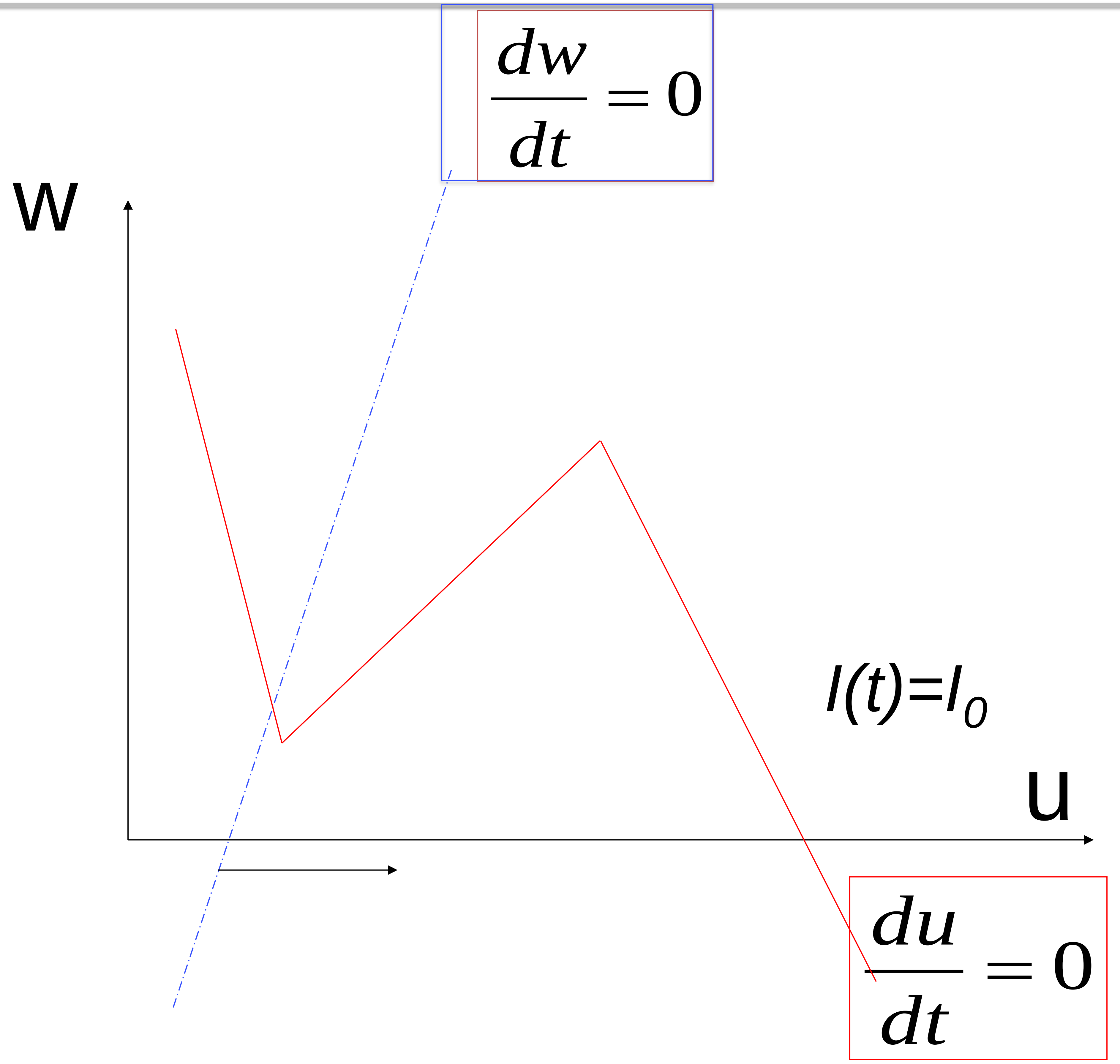

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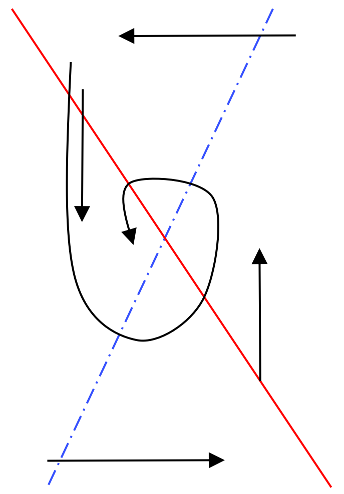

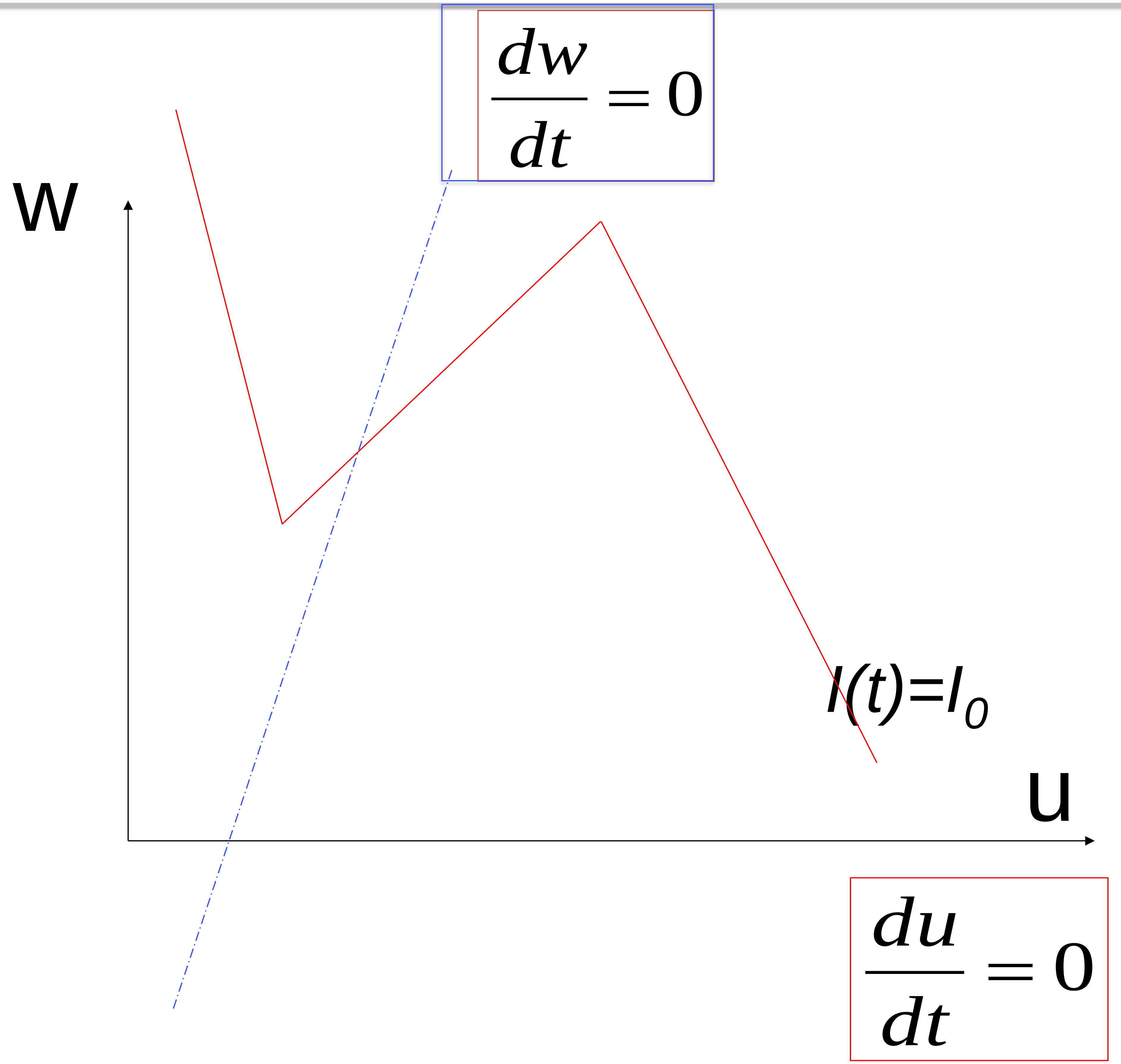

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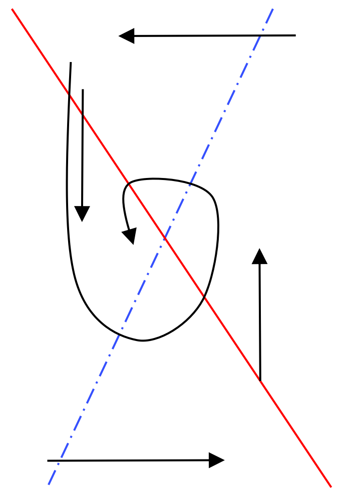

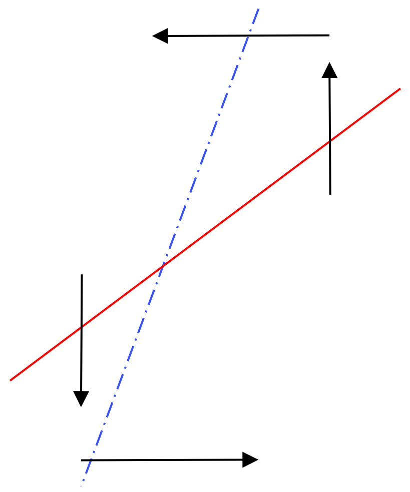

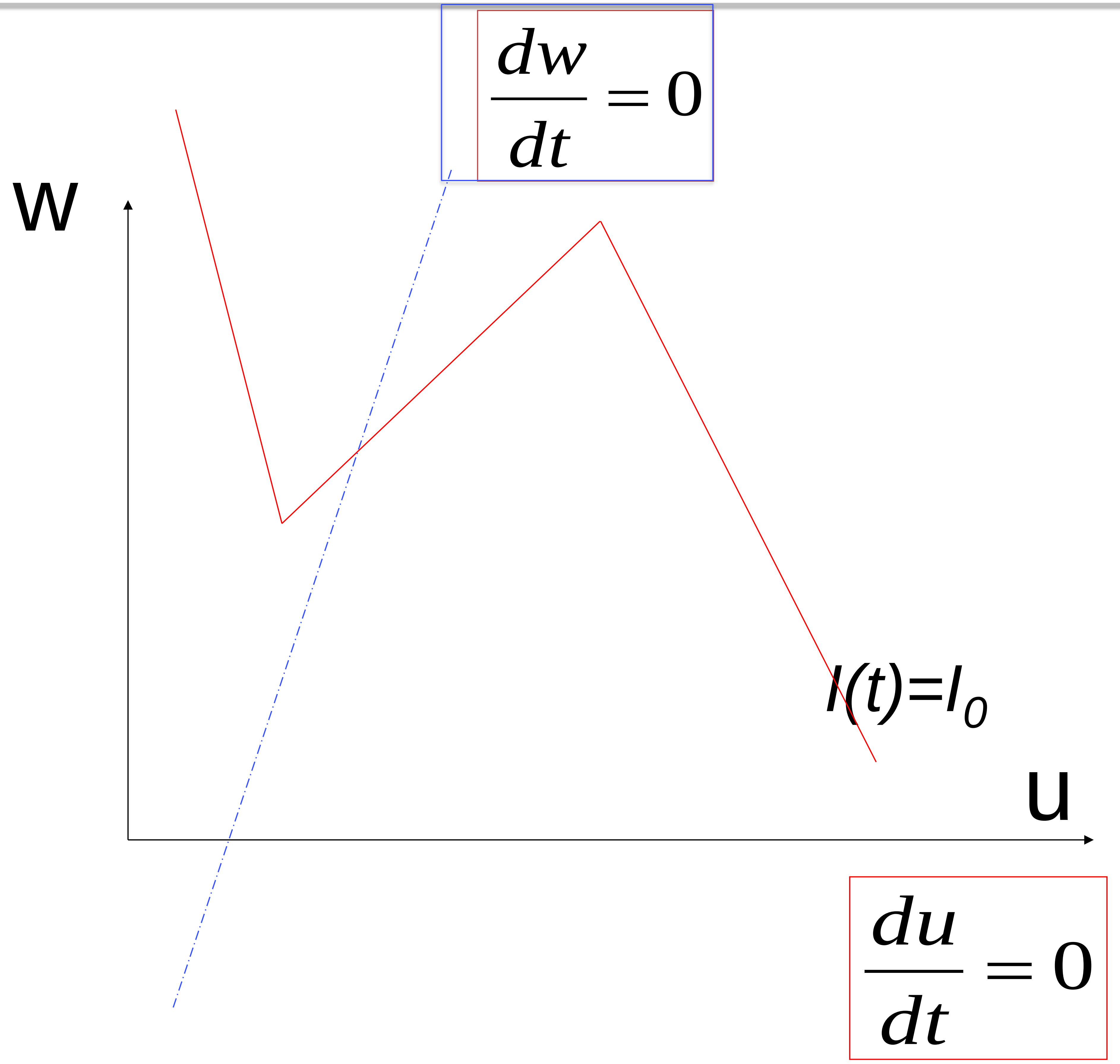

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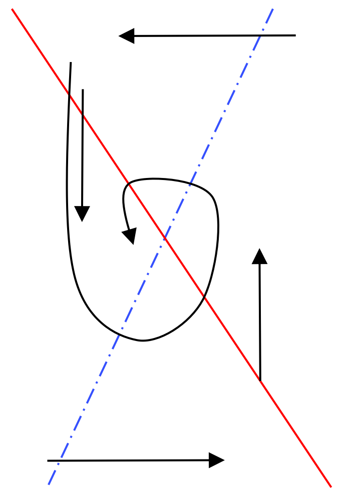

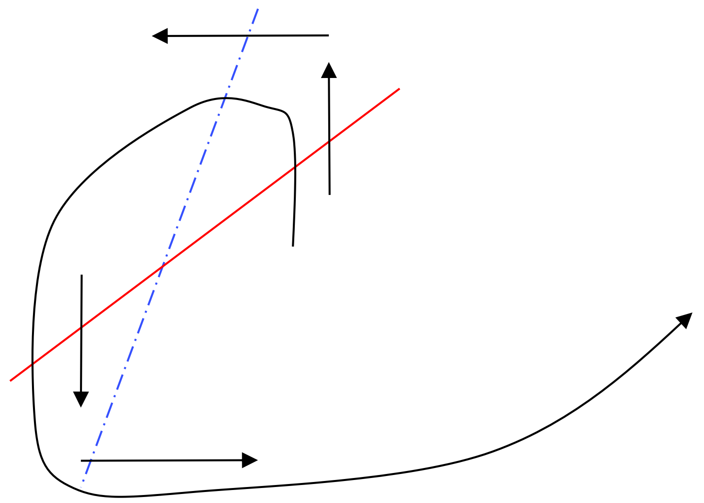

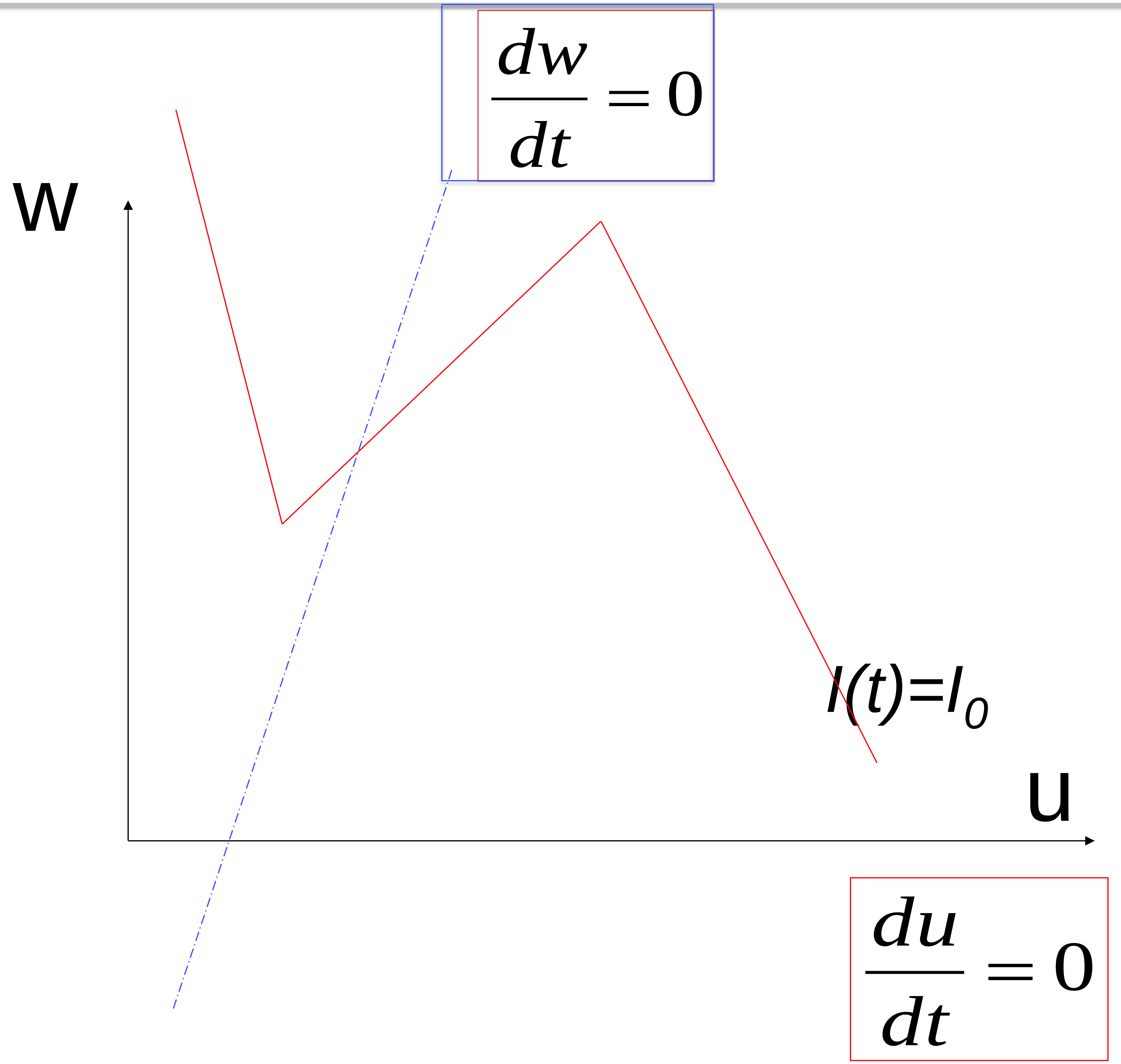

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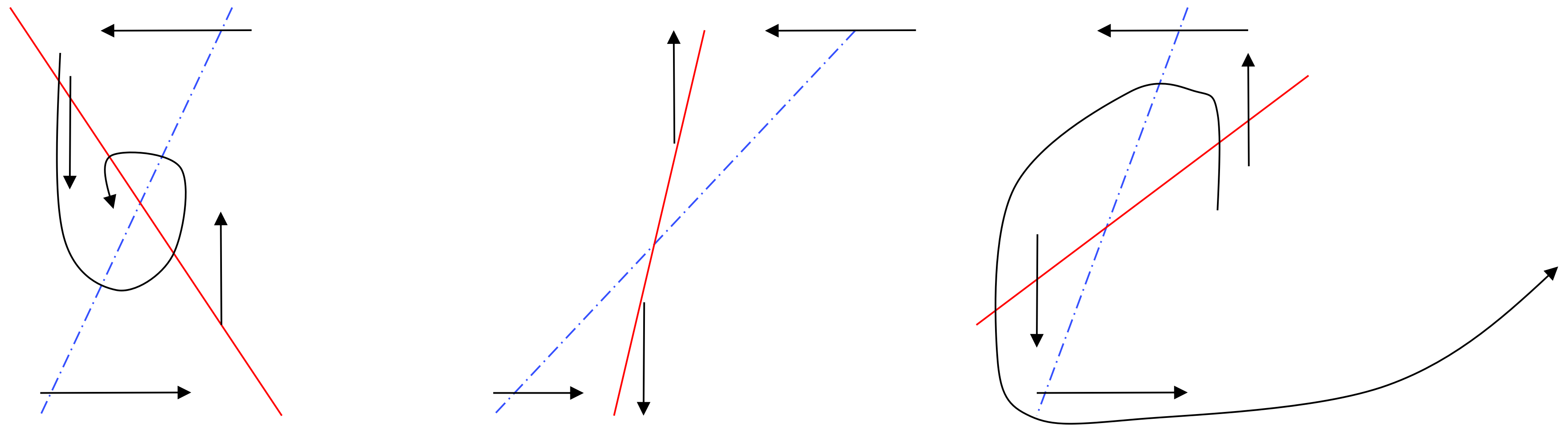

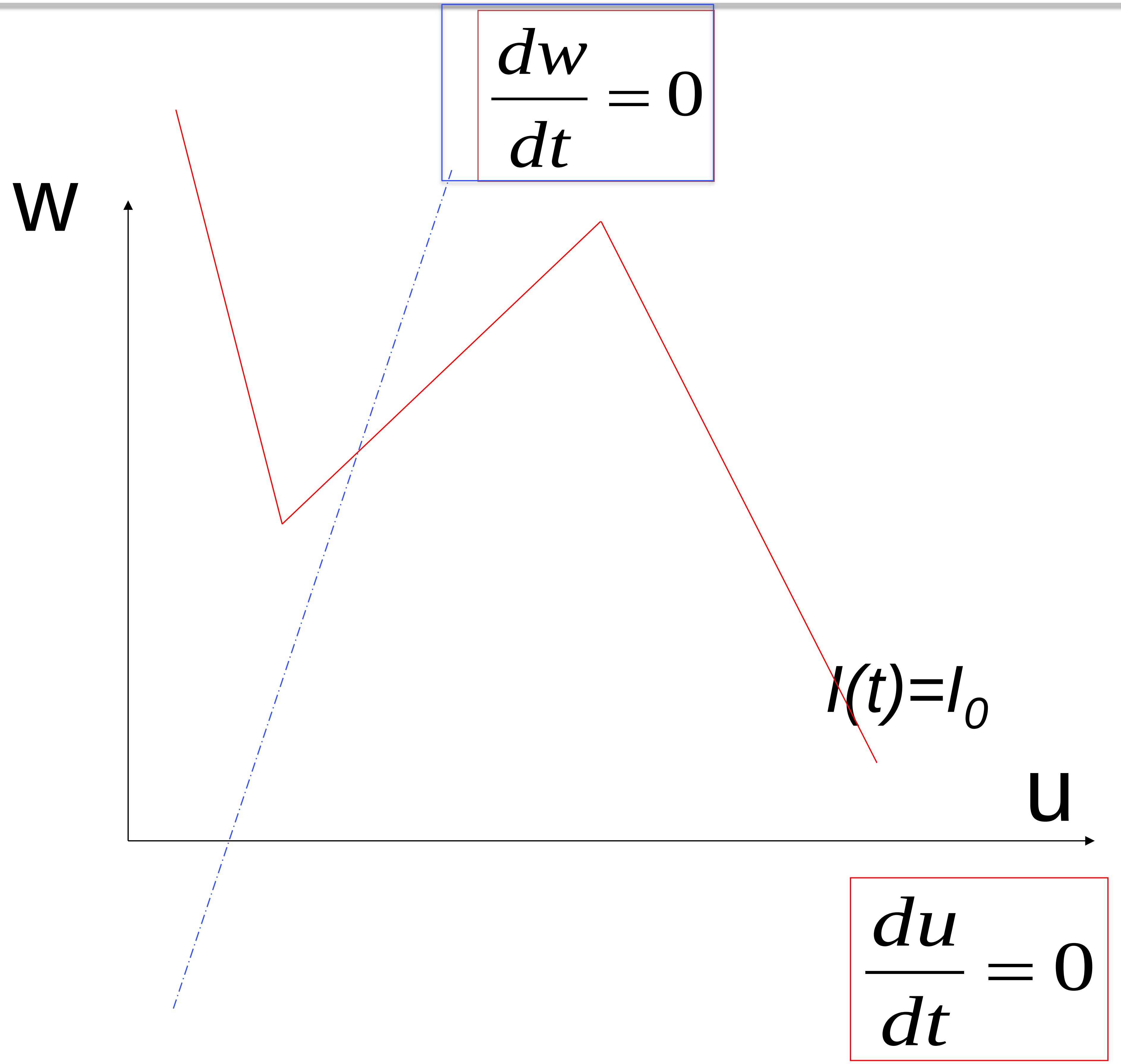

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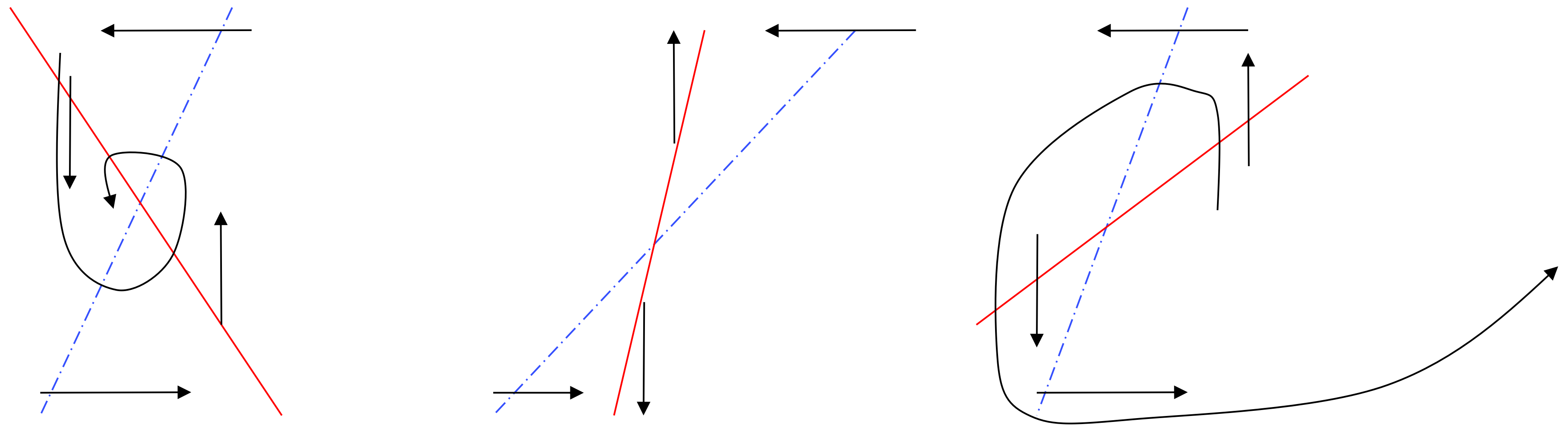
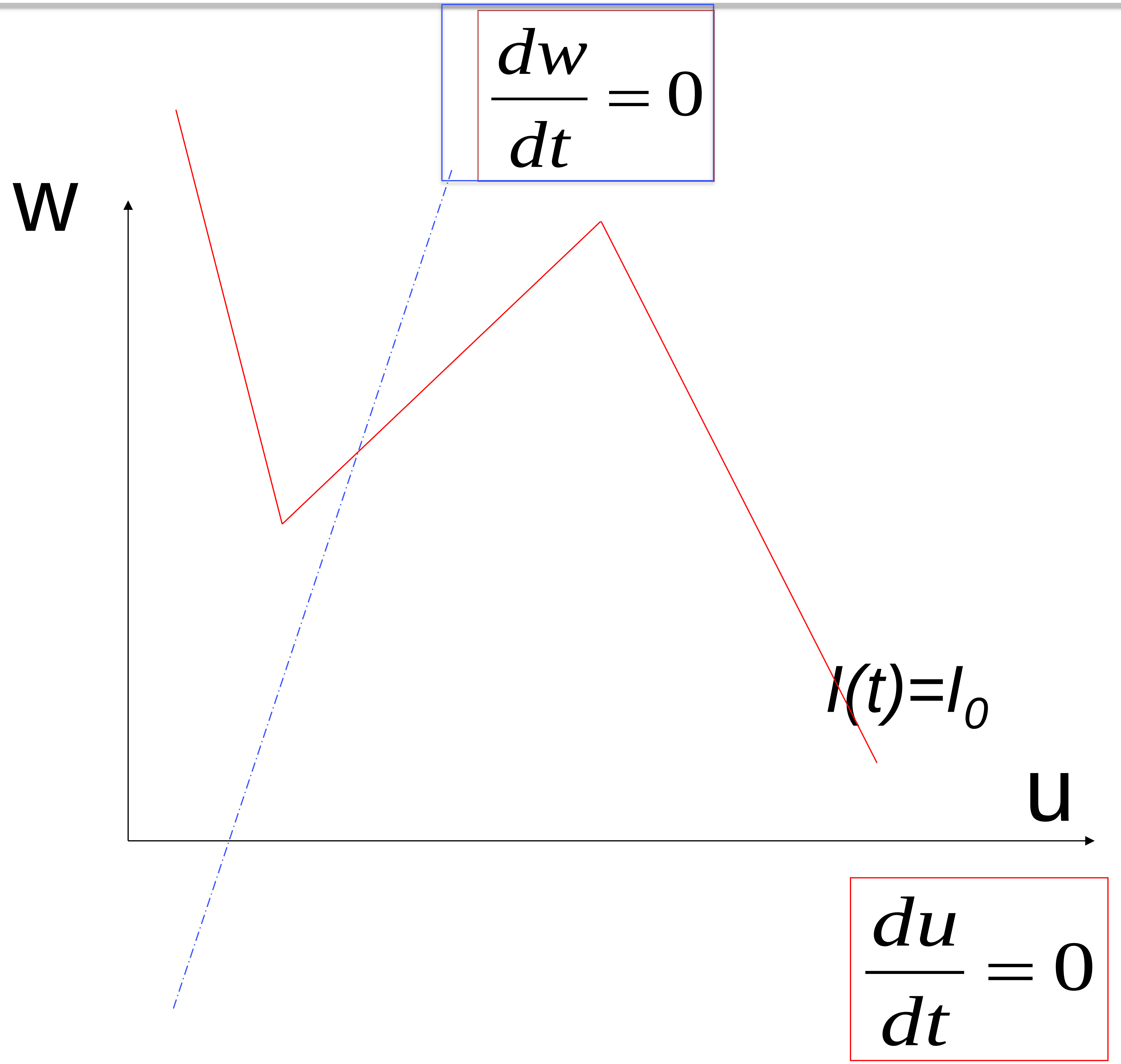


stable saddle unstable

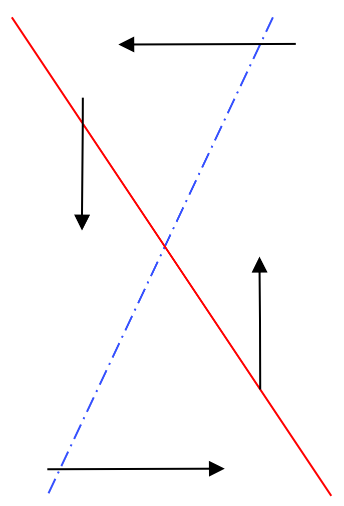


Preparation of Exercise 2: Detour. Stability of fixed points

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

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

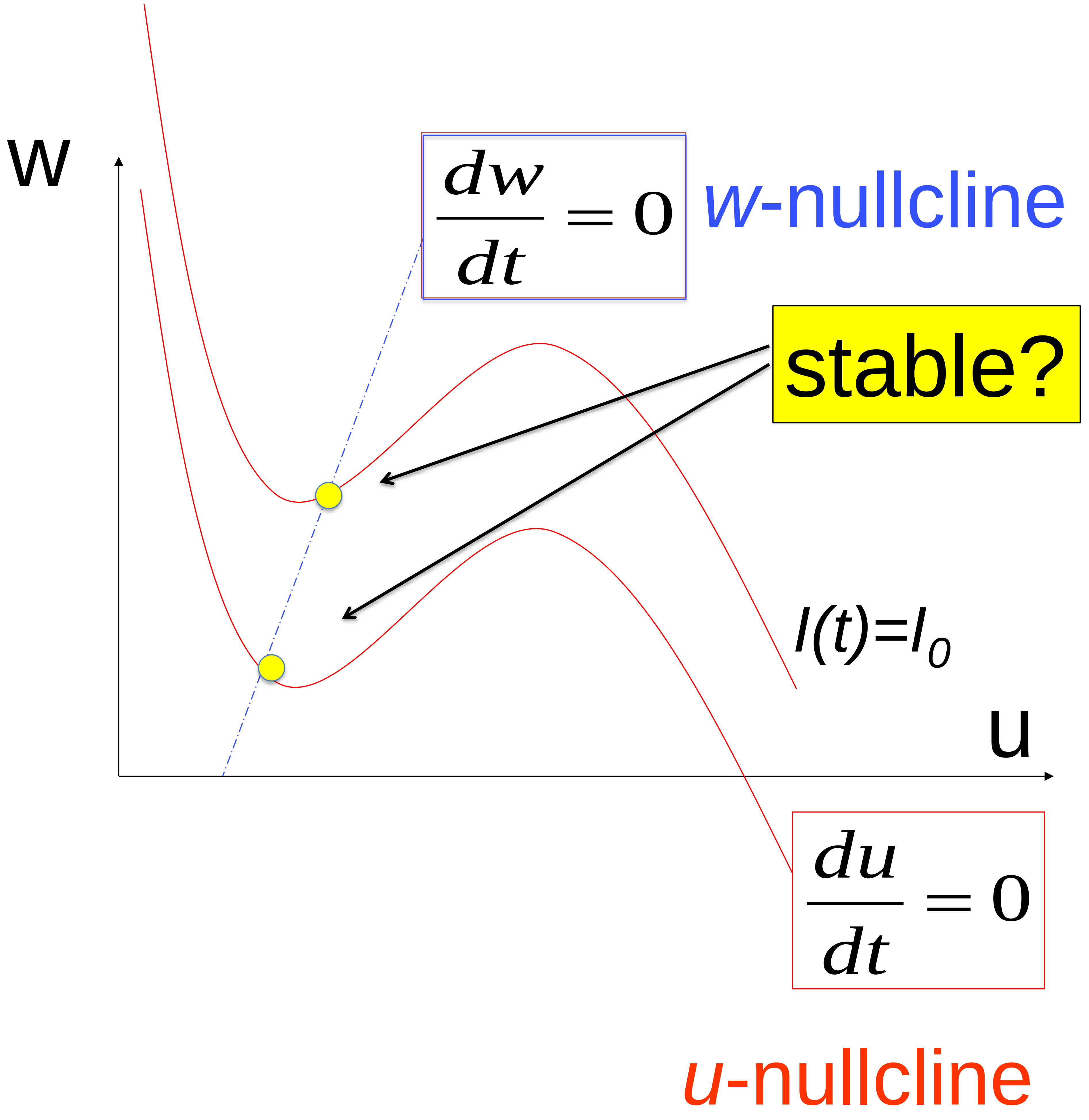
zoom in:



stable

saddle

unstable



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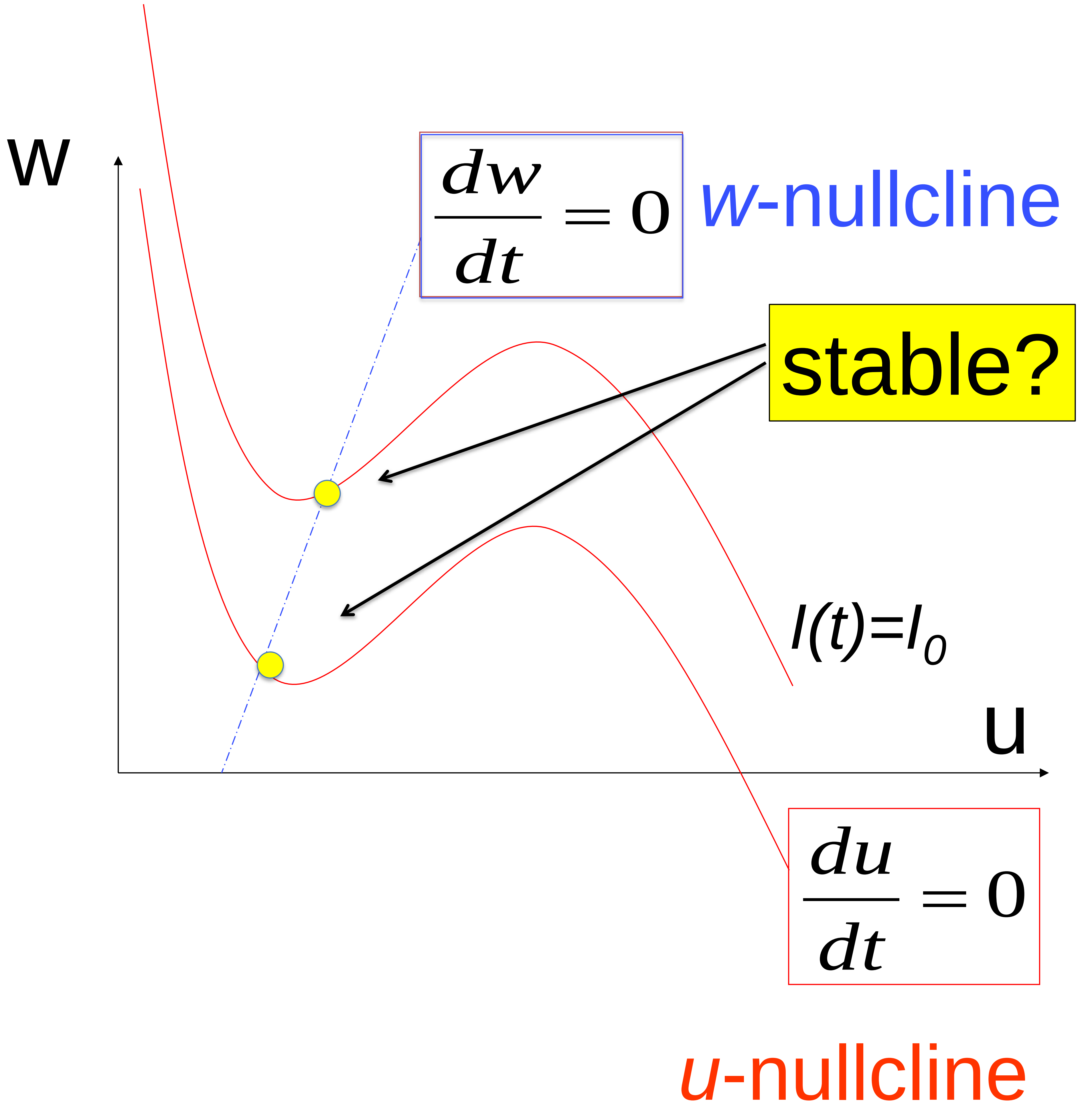

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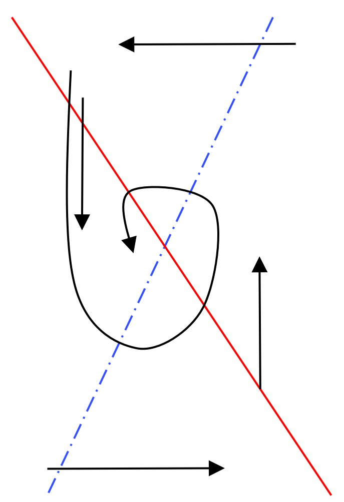

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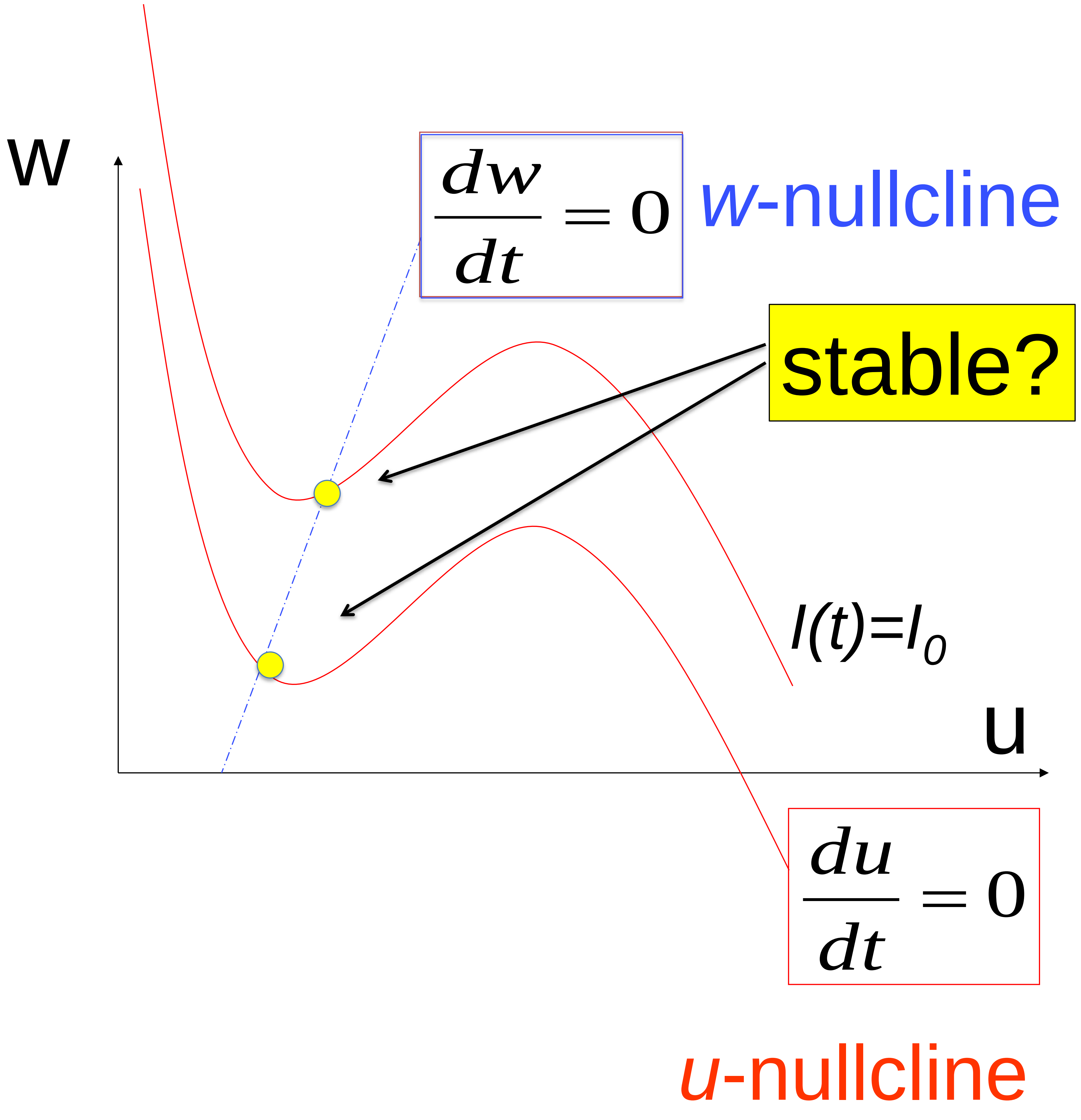

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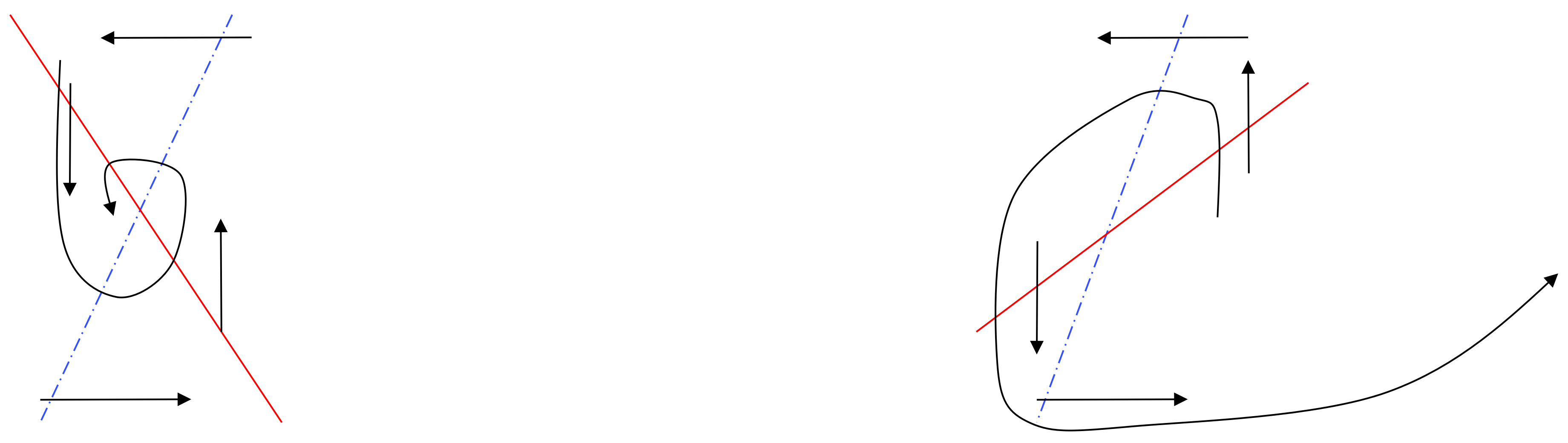

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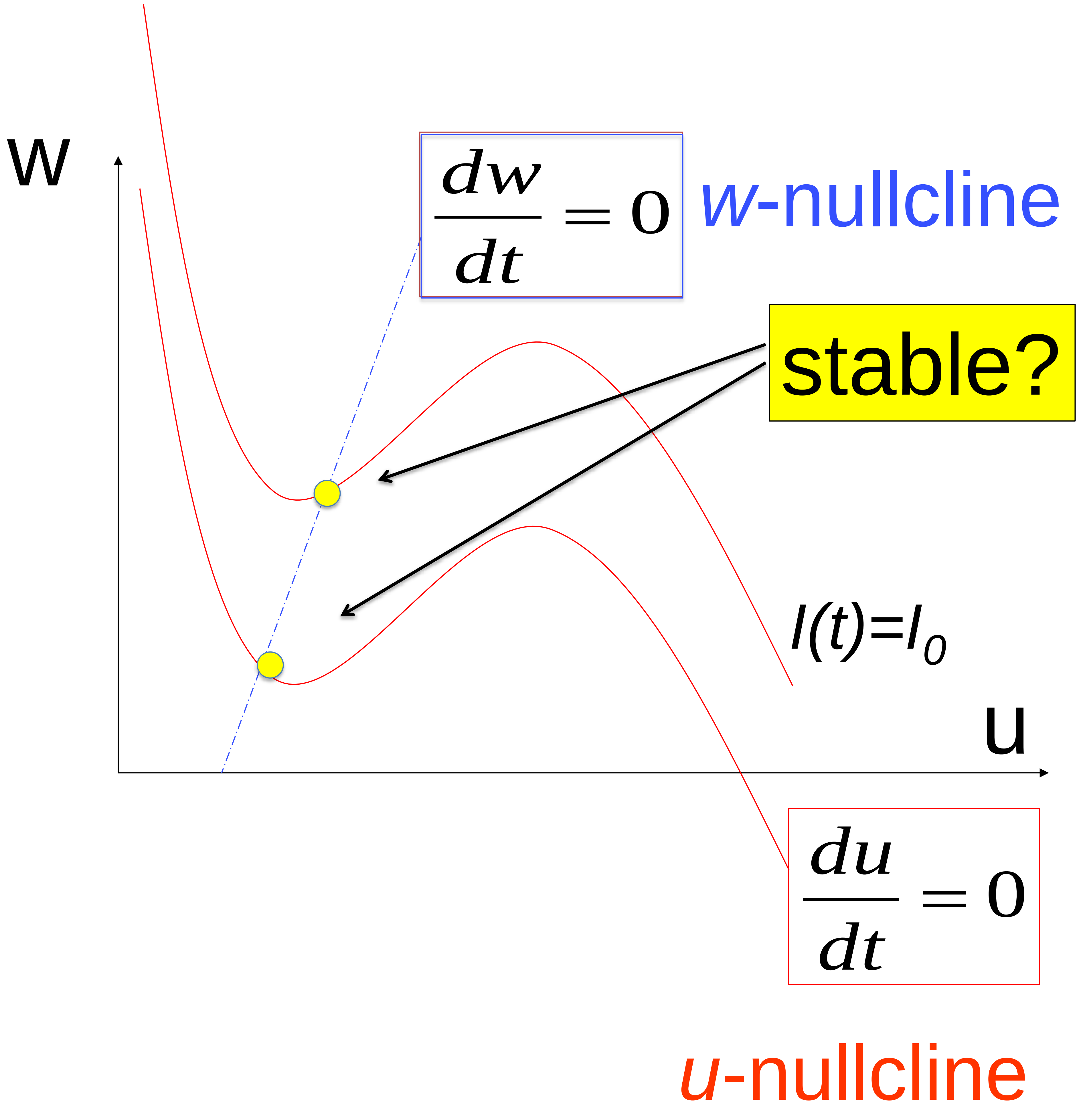

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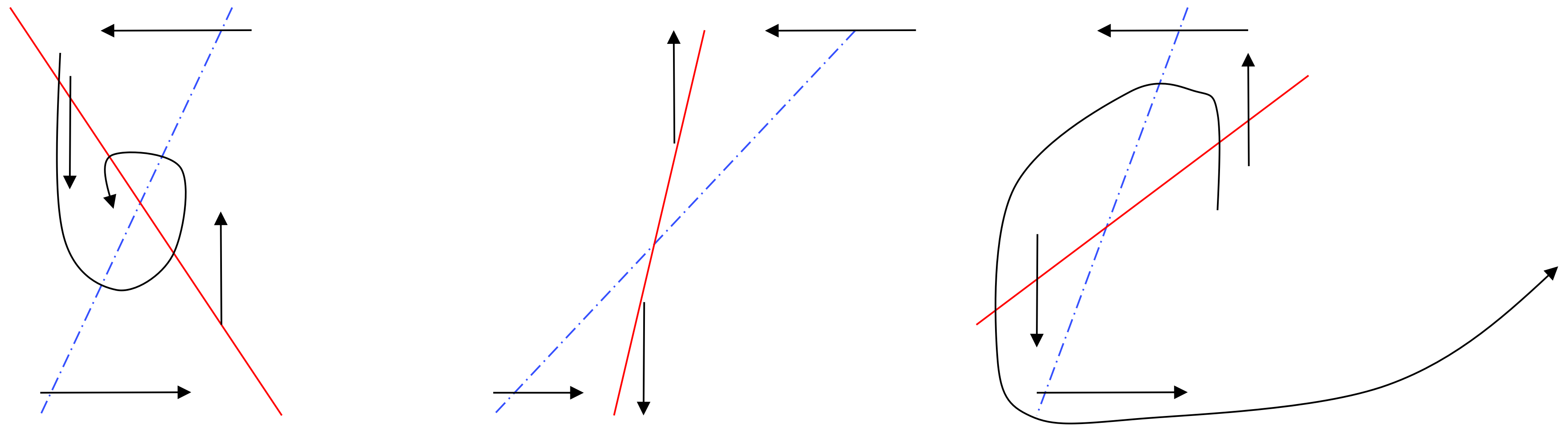

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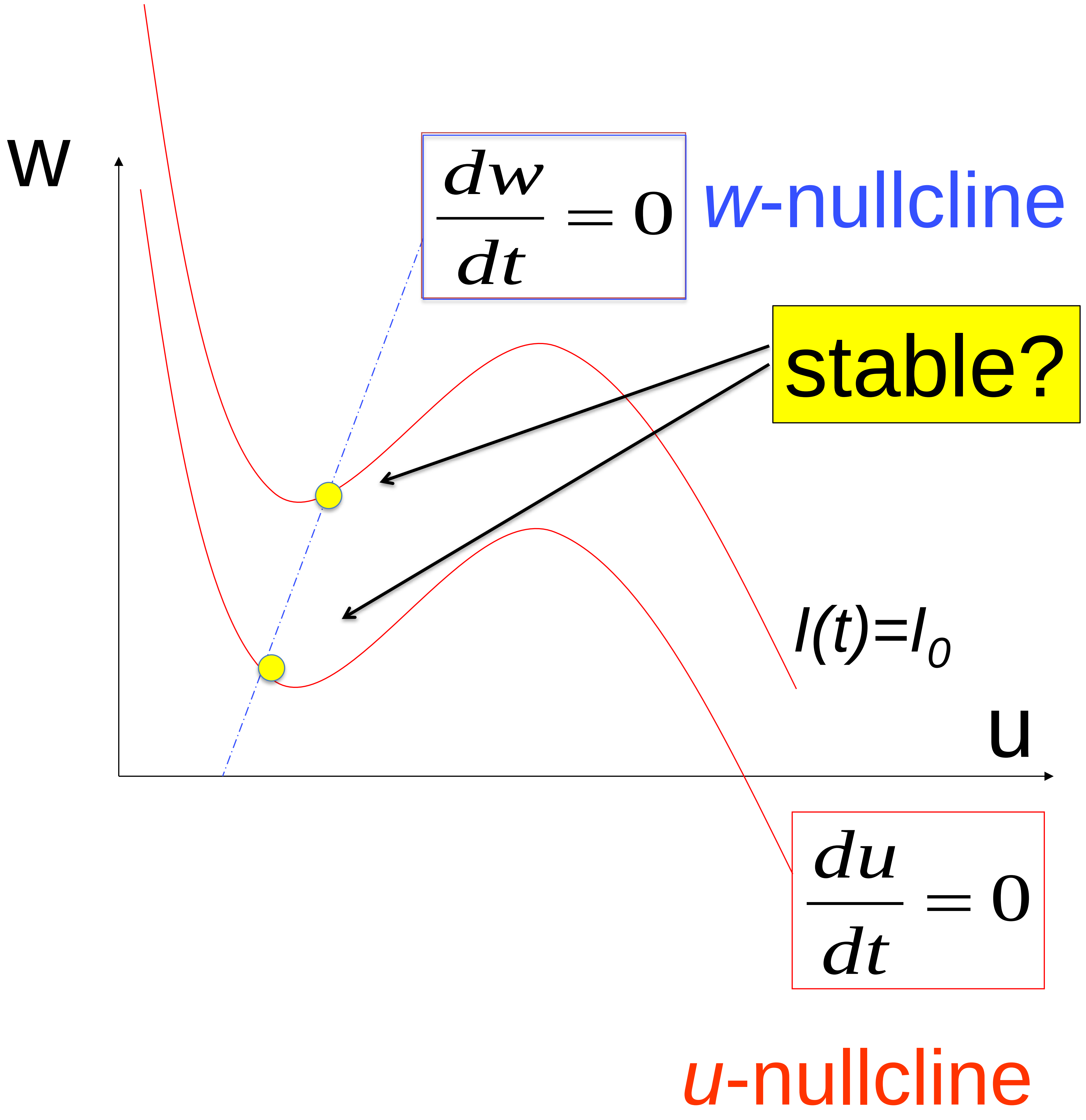
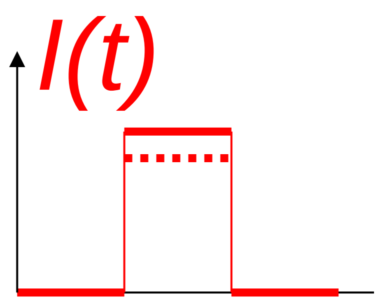
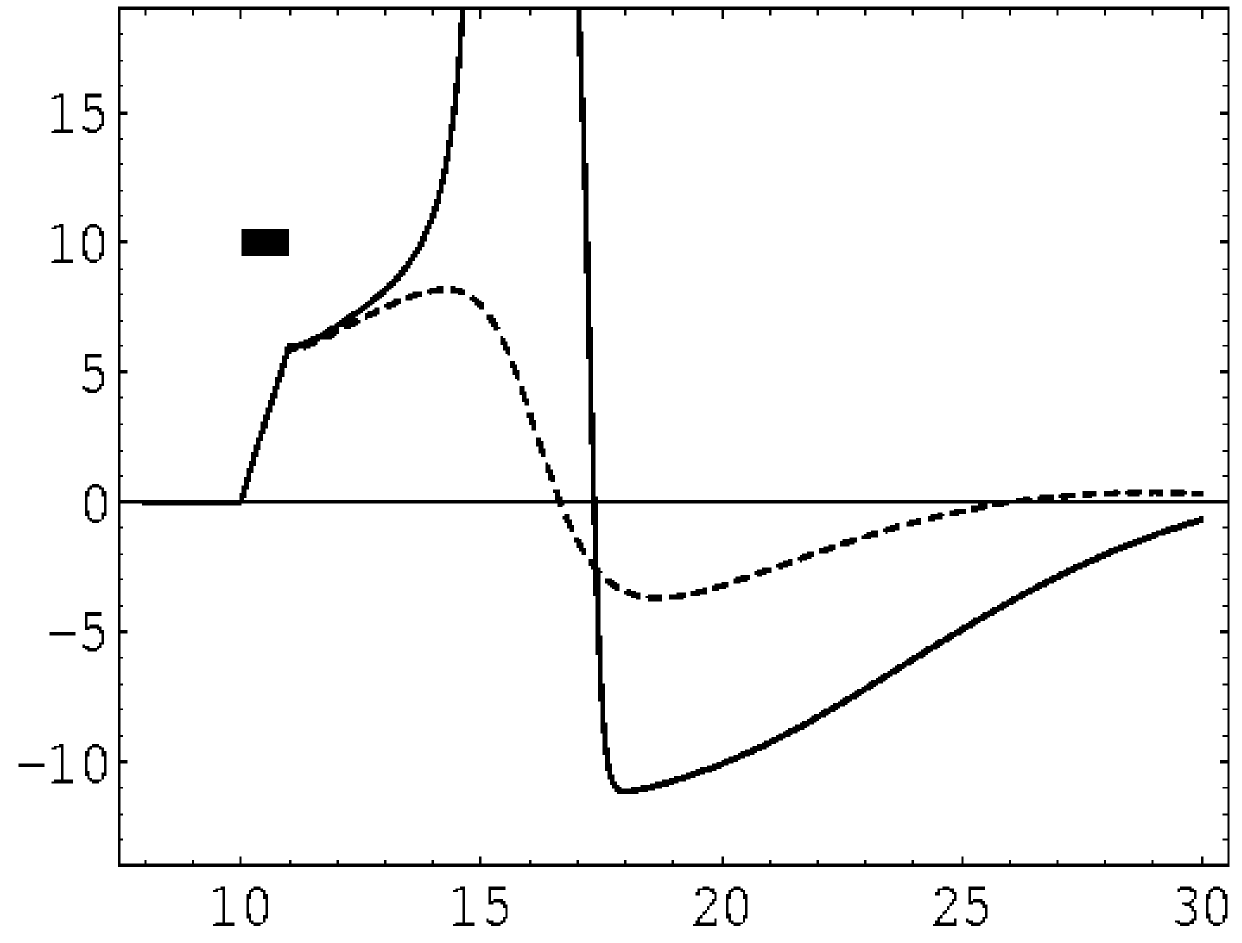
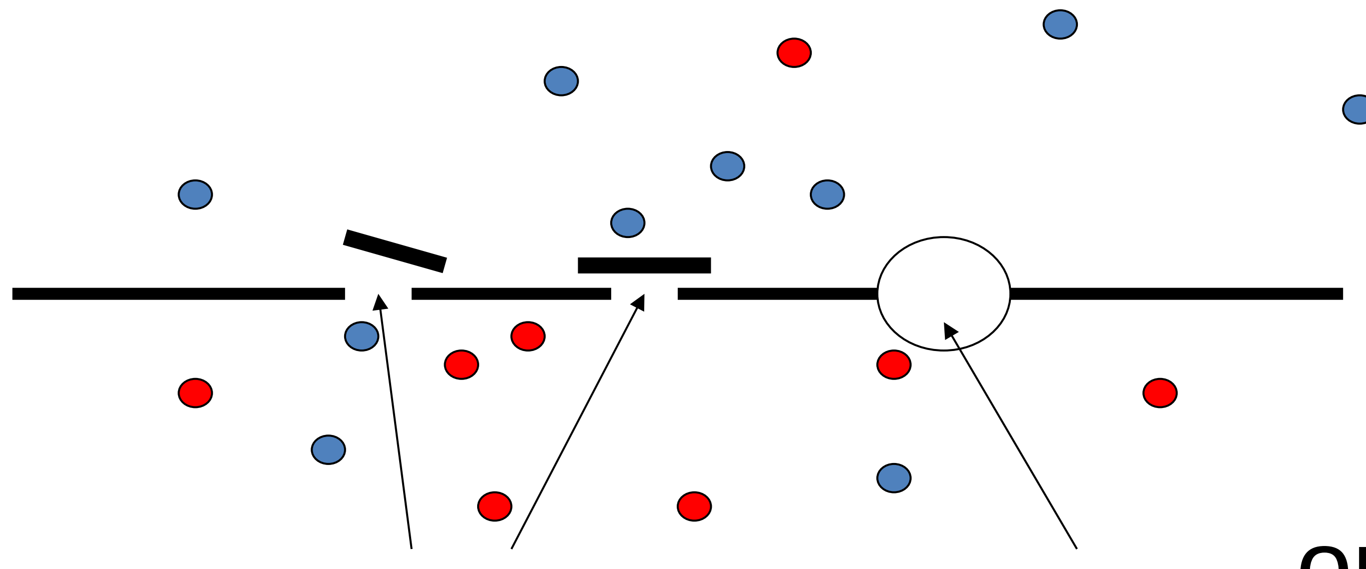


Neuronal Dynamics – 2.4. Threshold in HH model

pulse input







Question of student : 3. Why is the downswing so fast?

-we said upswing is fast because of fast m. More precisely, the dynamics of m leads to an explosion-like instability

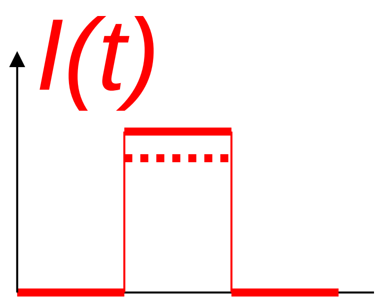
- We said downswing triggered by dynamics of h and n.

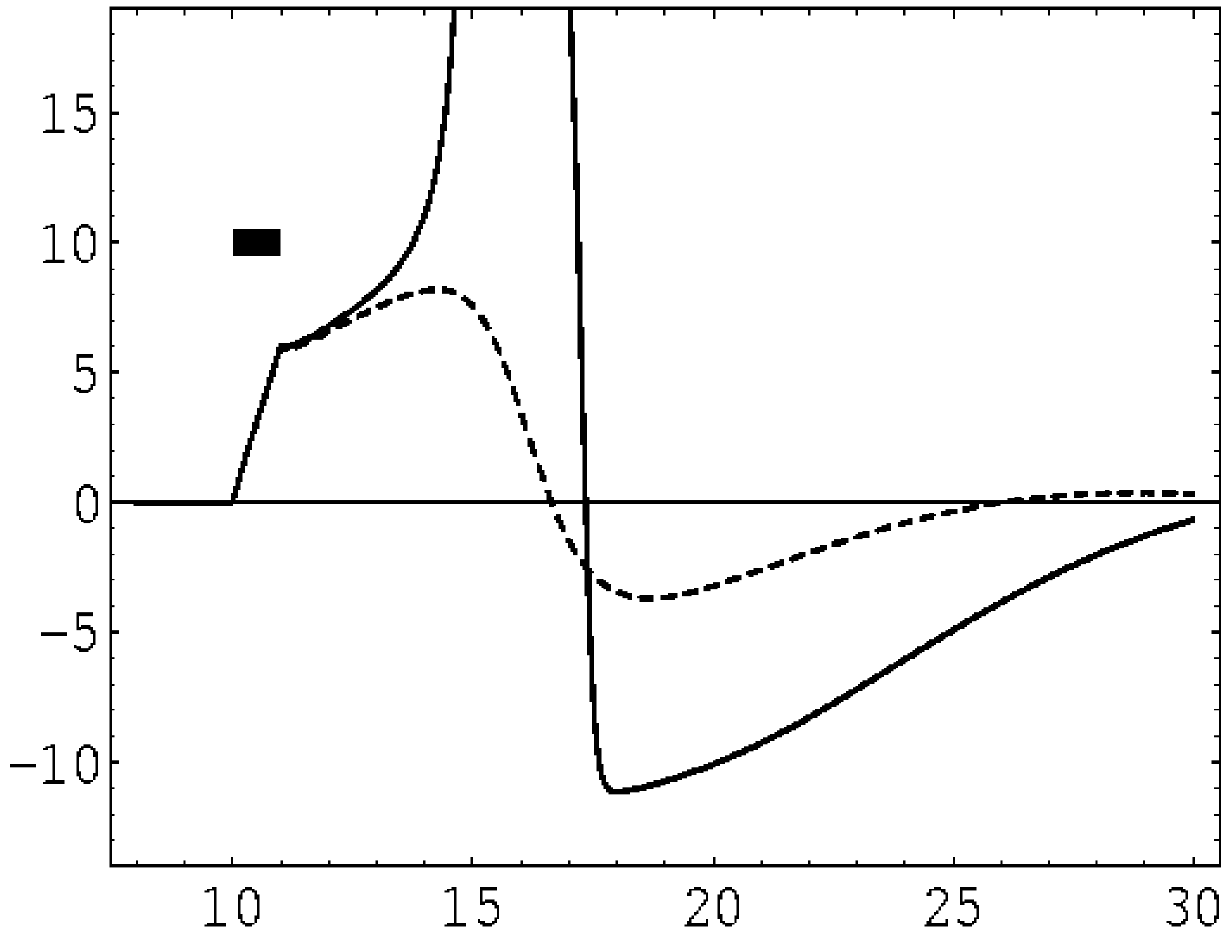
THEN, WHY IS THE DOWNSWING FAST?

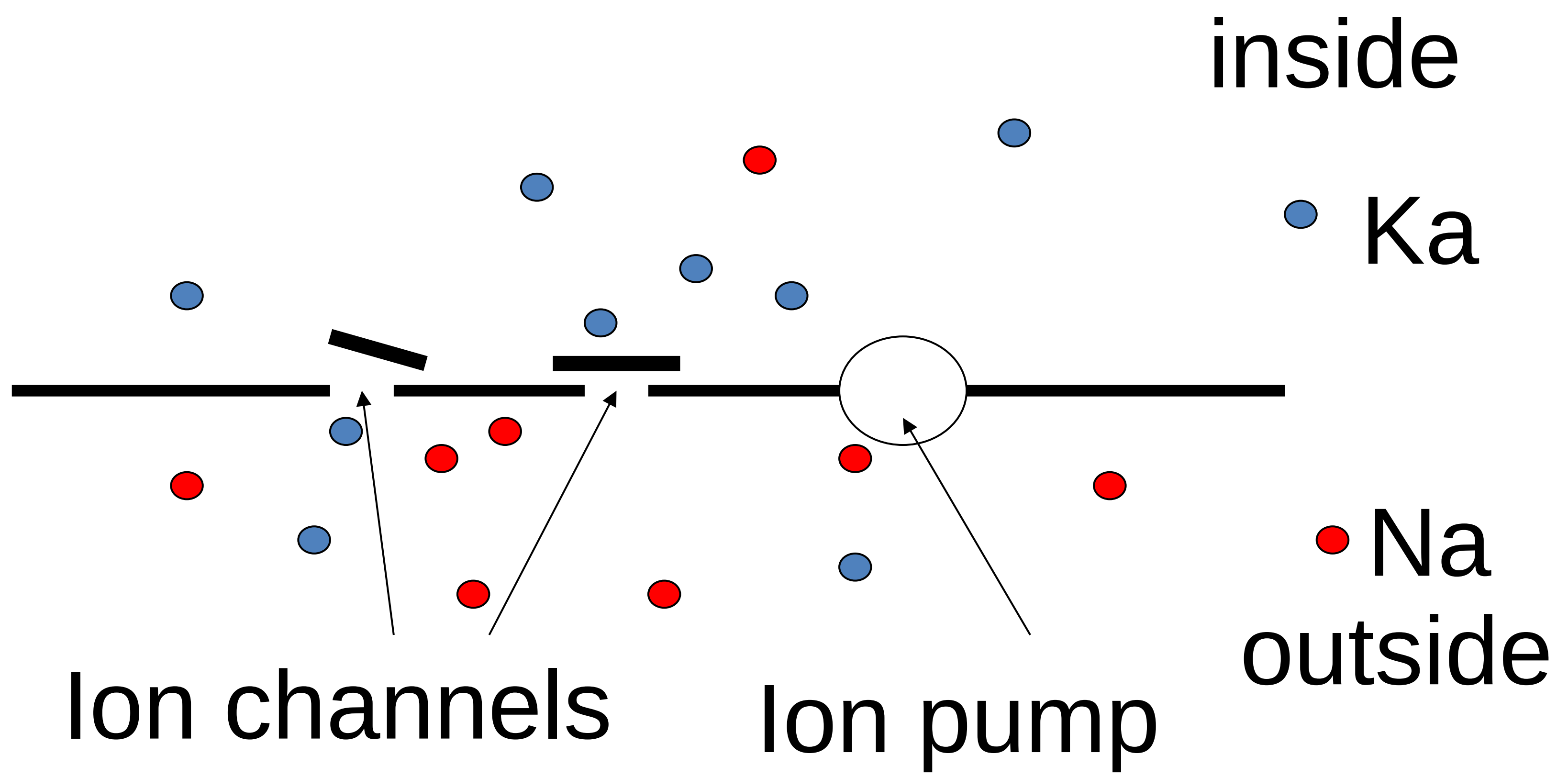
→ Use insights of our 2dim system! Watch videos for next week!

Neuronal Dynamics – 2.4. Threshold in HH model

pulse input







Question of student : 3. Why is the downswing so fast?

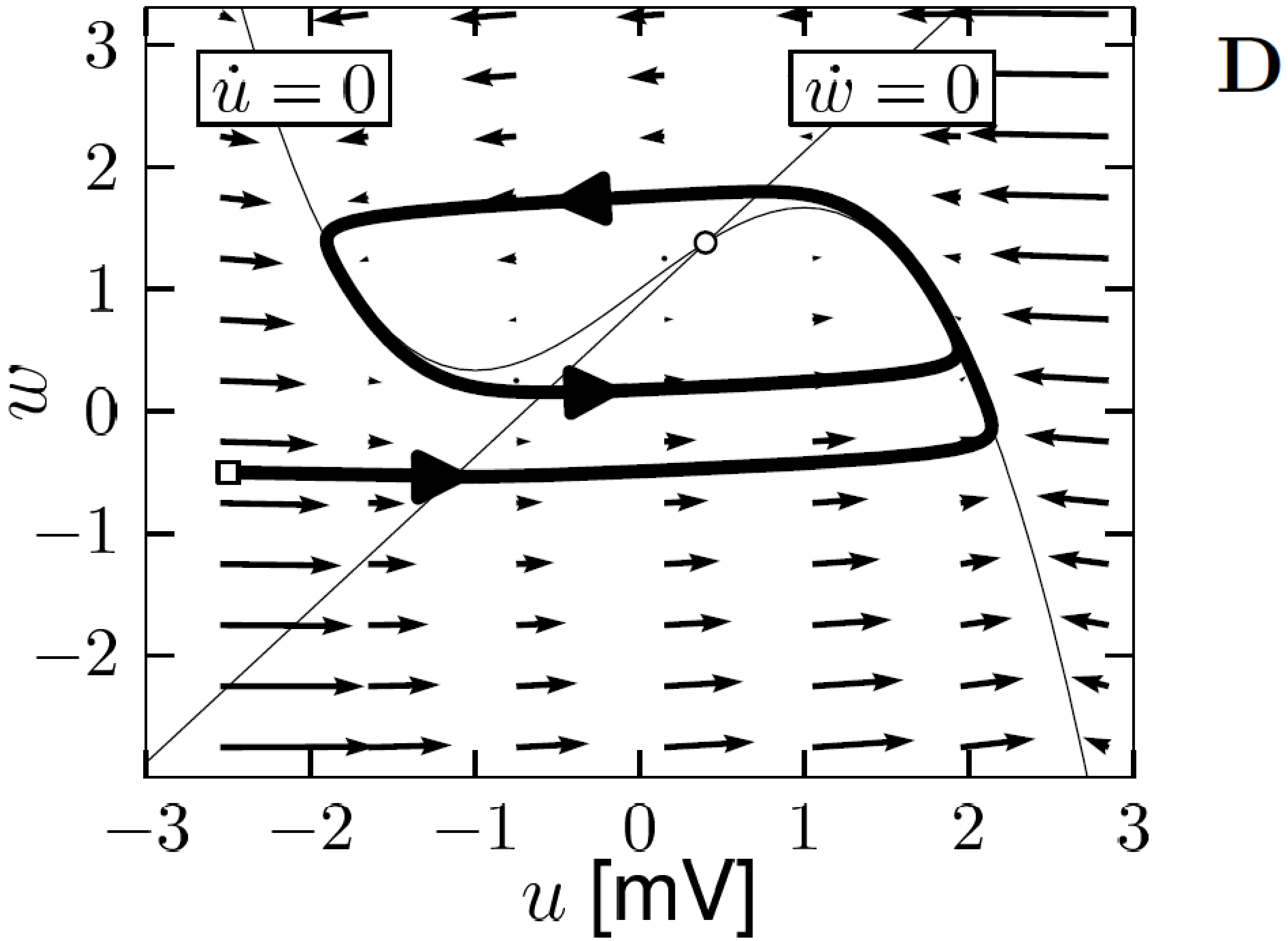
-we said upswing is fast because of fast m. More precisely, the dynamics of m leads to an explosion-like instability

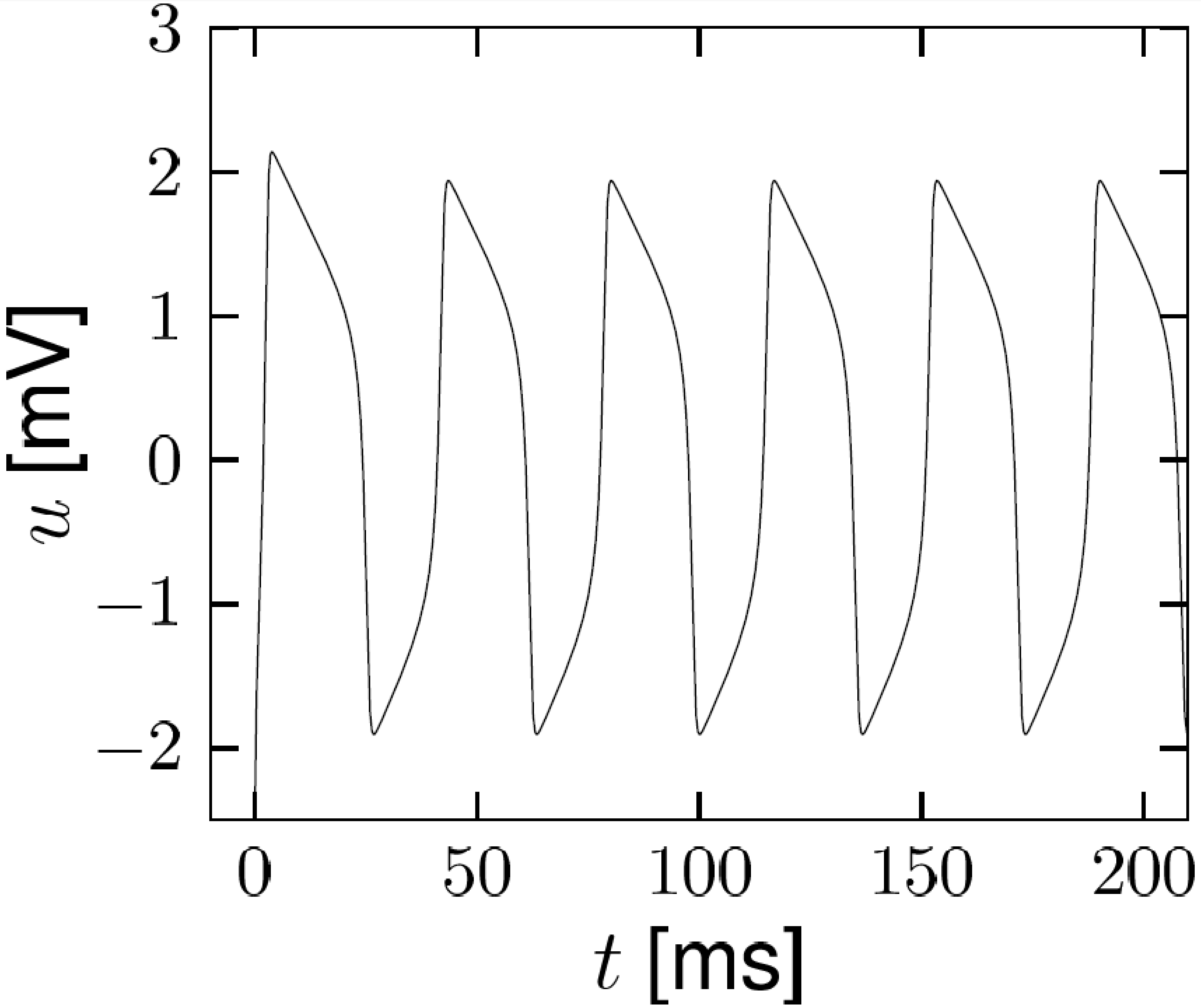
- We said downswing triggered by dynamics of h and n.

THEN, WHY IS THE DOWNSWING FAST?

→ Use insights of our 2dim system! Watch videos for next week!

3.3. FitzHugh-Nagumo Model : Constant input





FN model with $b_0 = 0.9; b_1 = 1.0; RI_0 = 2$

constant input: limit cycle,
fast downswing!

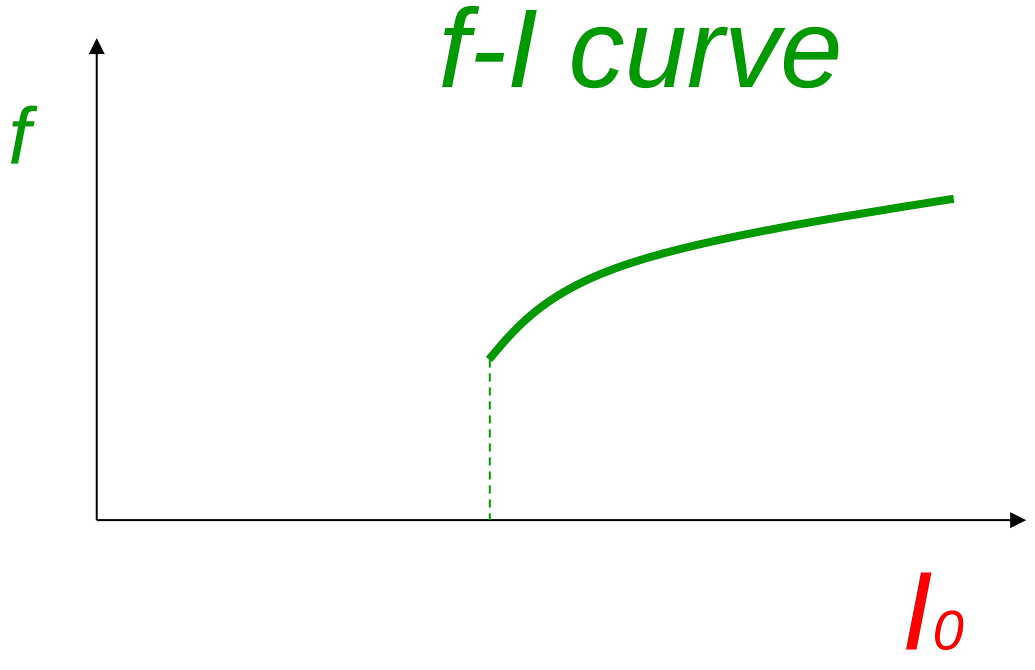
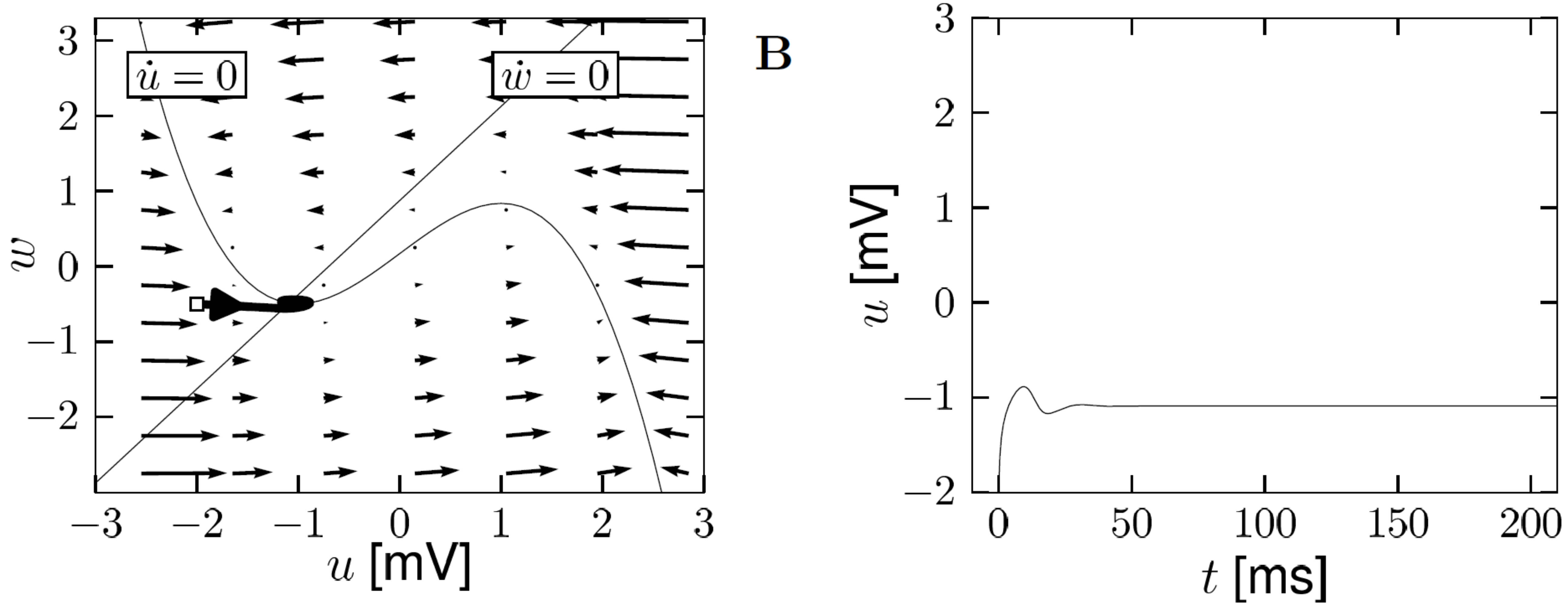


Image: Neuronal Dynamics, Gerstner et al., Cambridge (2014)

3.3. Analysis of a 2D neuron model



2-dimensional equation

stimulus

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

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

Time constants:

- Describe approach to stable fixed point
- Describe exponential growth around unstable fixed point

Week 4:

Suppose $\tau_u \ll \tau_w$

Then arrows nearly horizontal.

(second separation of time scales)