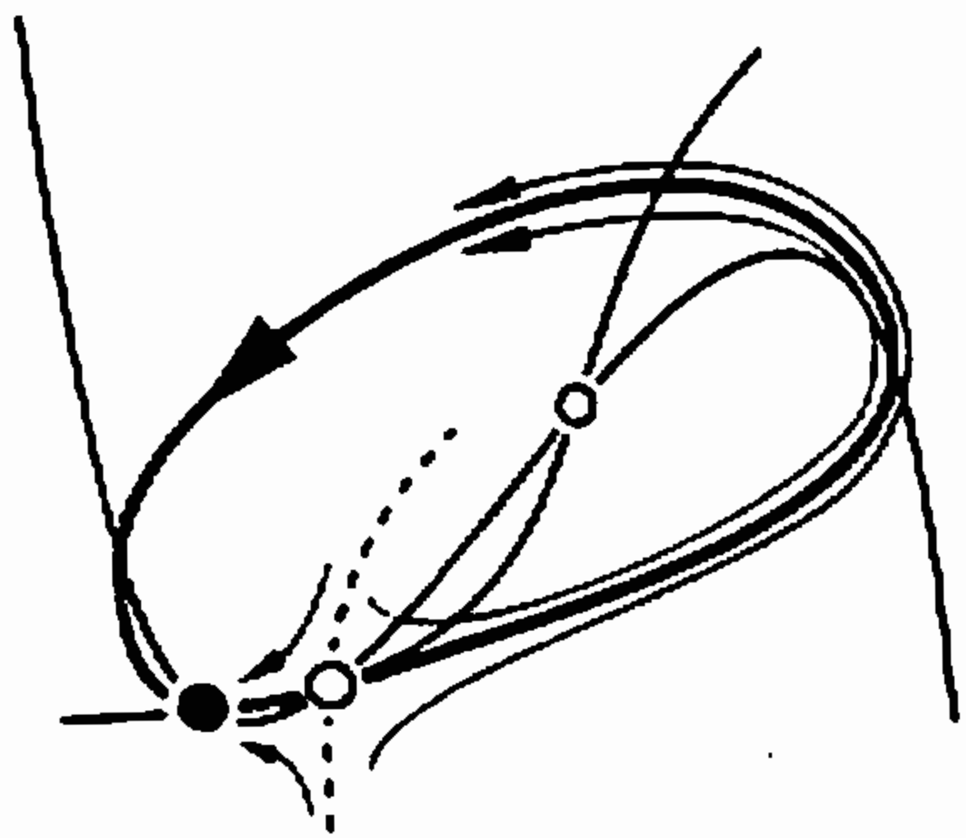
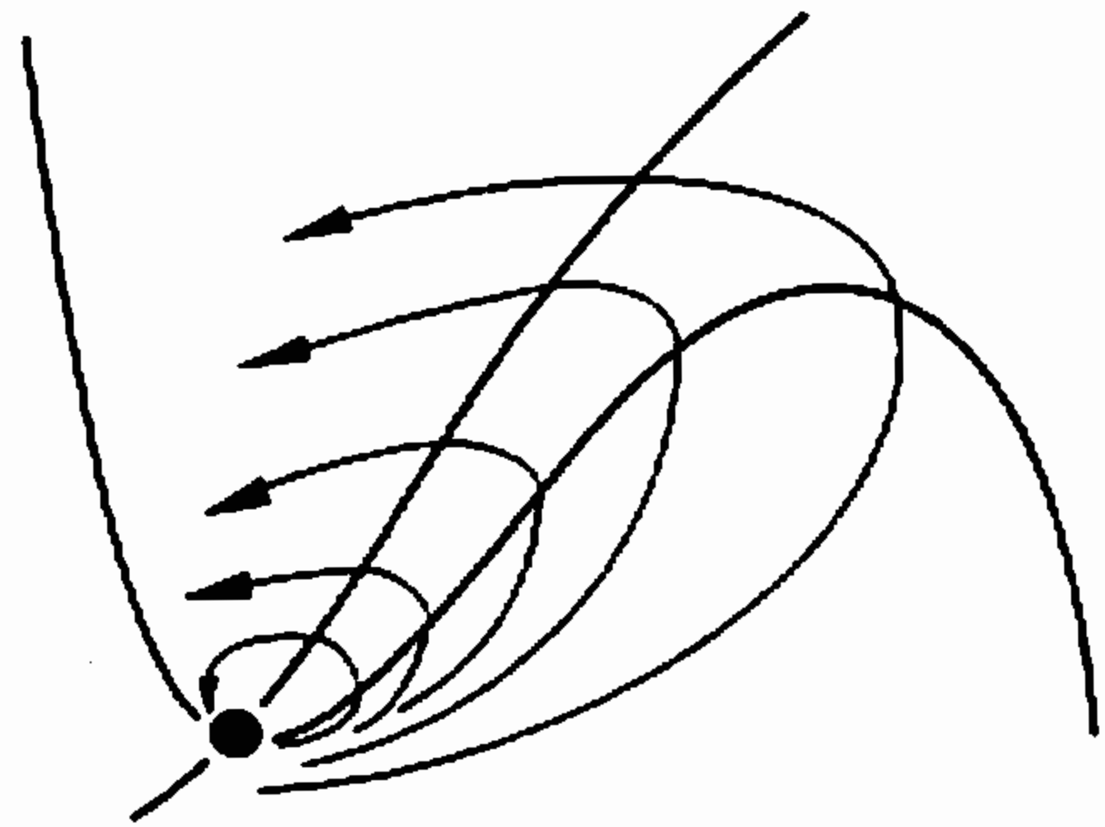
Cellular Biophysics & Modeling

Lecture 13

the Morris-Lecar phase plane
excitability and oscillations



type 1 excitability



type 2 excitability

the Morris-Lecar model

$$C\frac{dV}{dt} = I_{app} - g_L\left(V - E_L\right) - g_{Ca}m_{\infty}(V)\left(V - E_{Ca}\right) - g_K w\left(V - E_K\right)$$

instantaneously equilibrating activation gating variable for the inward Ca^{2+} current

$$\frac{dw}{dt} = -\phi\frac{w - w_{\infty}(V)}{\tau_w(V)}$$

slow activation gating variable for the outward K^+ current

In order to understand behavior of Morris-Lecar,

we look at "nullclines" for this 2D system

the "phase-plane"

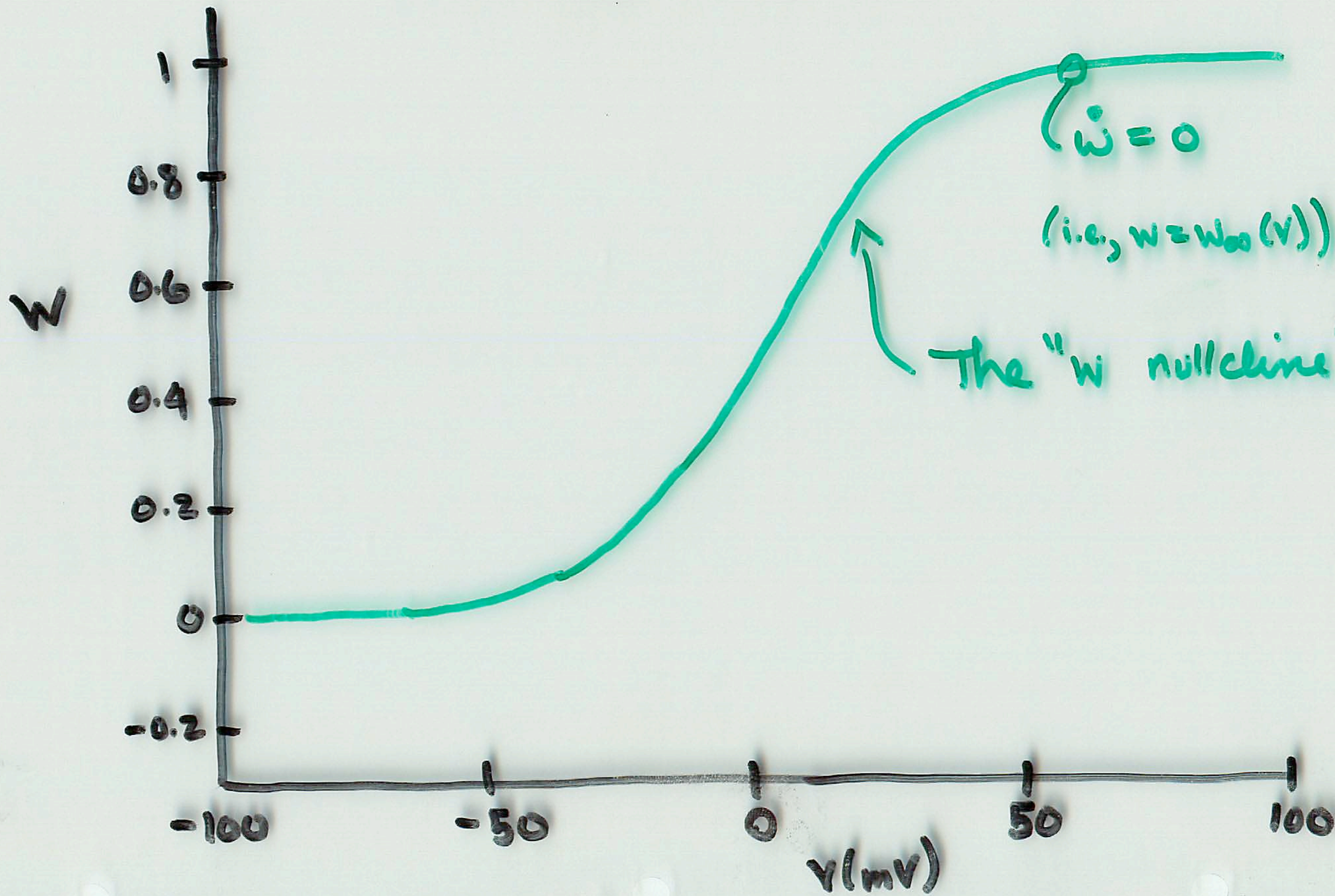
w-nullcline is all points (w, V) for which $\frac{dw}{dt} = 0$

$$0 = \frac{dw}{dt} = \phi \frac{w_\infty(V) - w}{\tau_w(V)}$$

$w = w_\infty(V)$ gives w-nullcline

(doesn't depend on I_{app})

Morris-Lecar "Phase Plane"



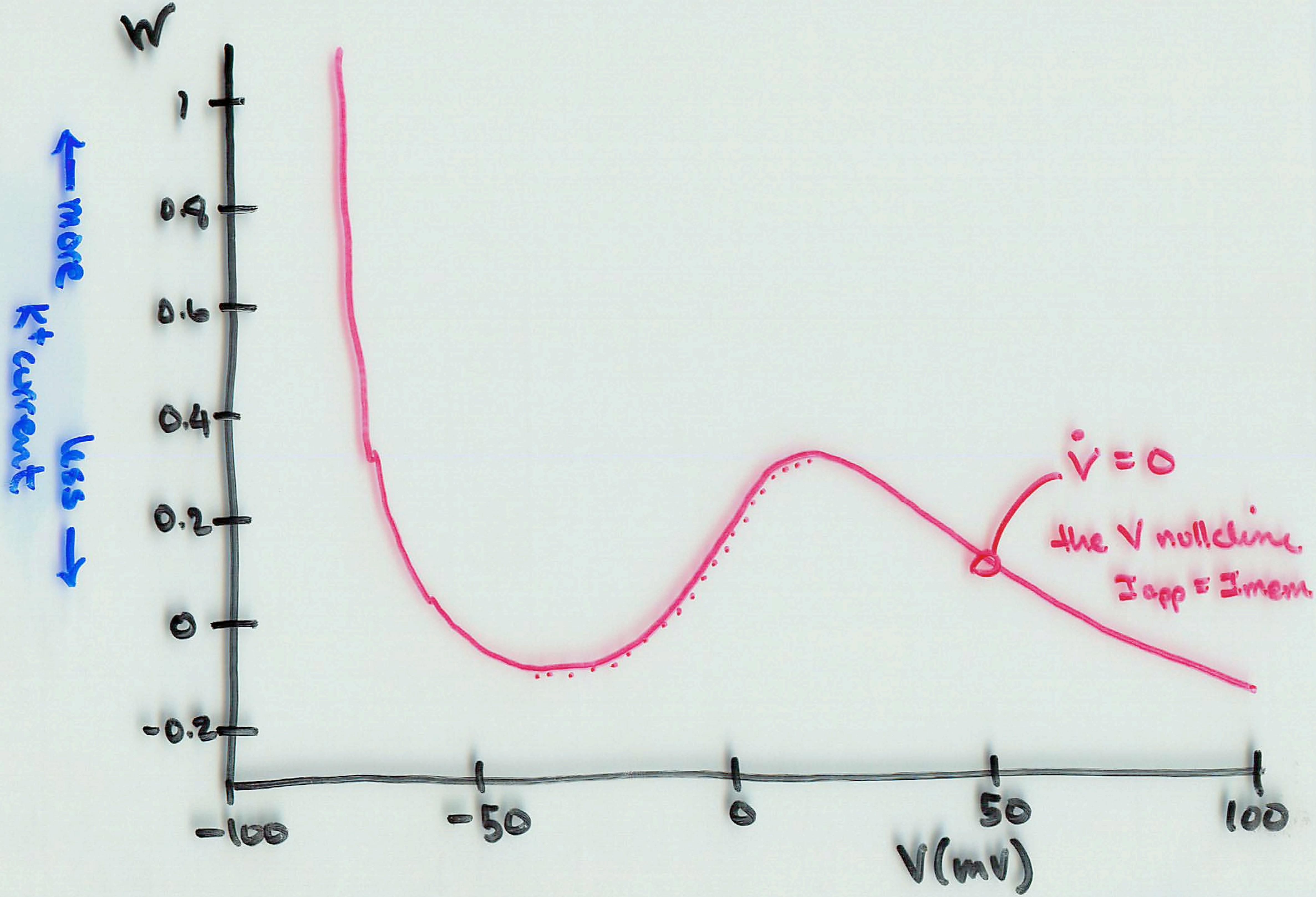
V-nullcline is all points (w, V) for which $\frac{dV}{dt} = 0$

$$0 = C\frac{dV}{dt} = I_{app} - \bar{g}_{Ca} m_\infty(V)(V - V_{Ca}) - \bar{g}_K w (V - V_K) - \bar{g}_L (V - V_L)$$

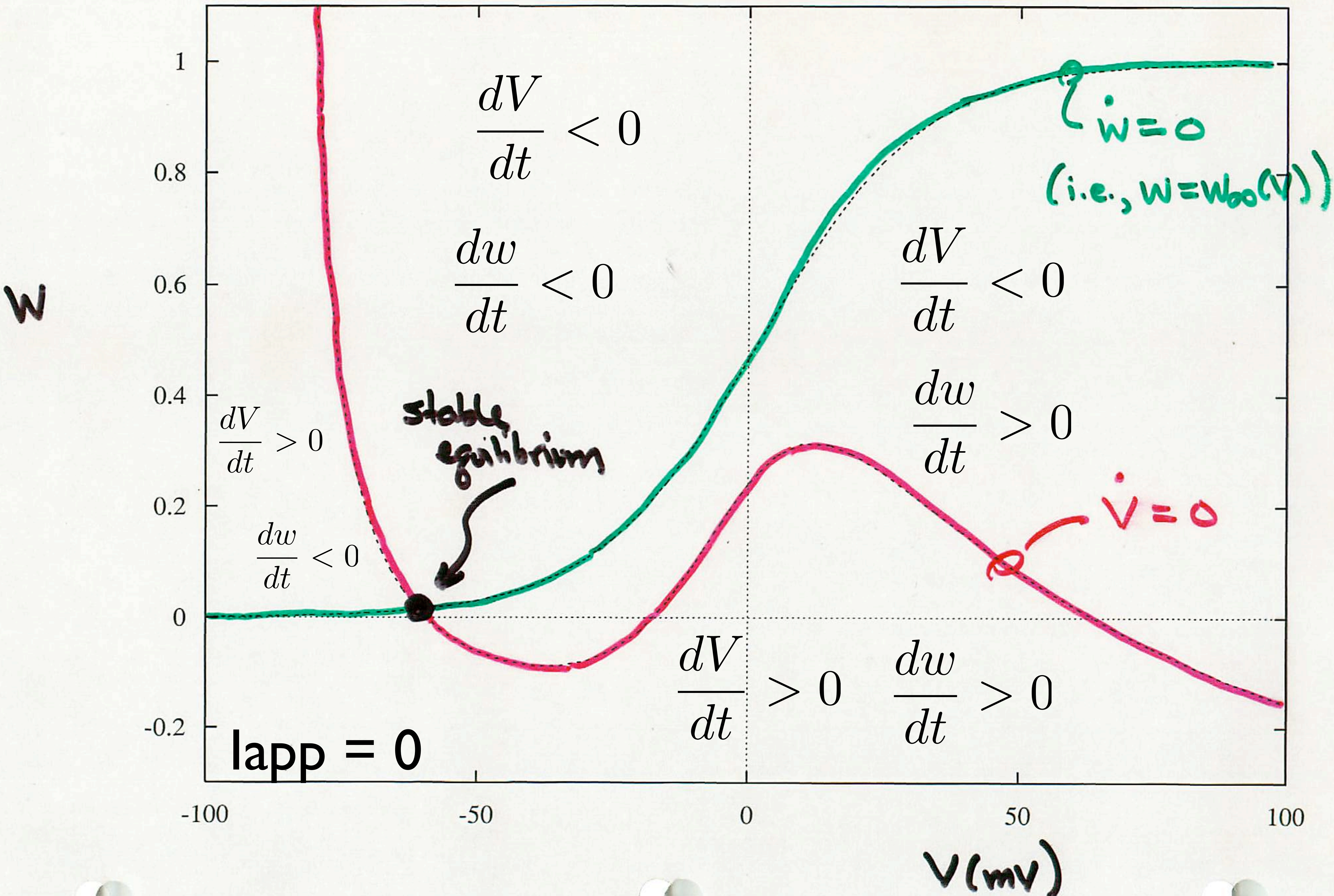
- the V-nullcline depends on I_{app}
- the V-nullcline can be cubic

(show plot)

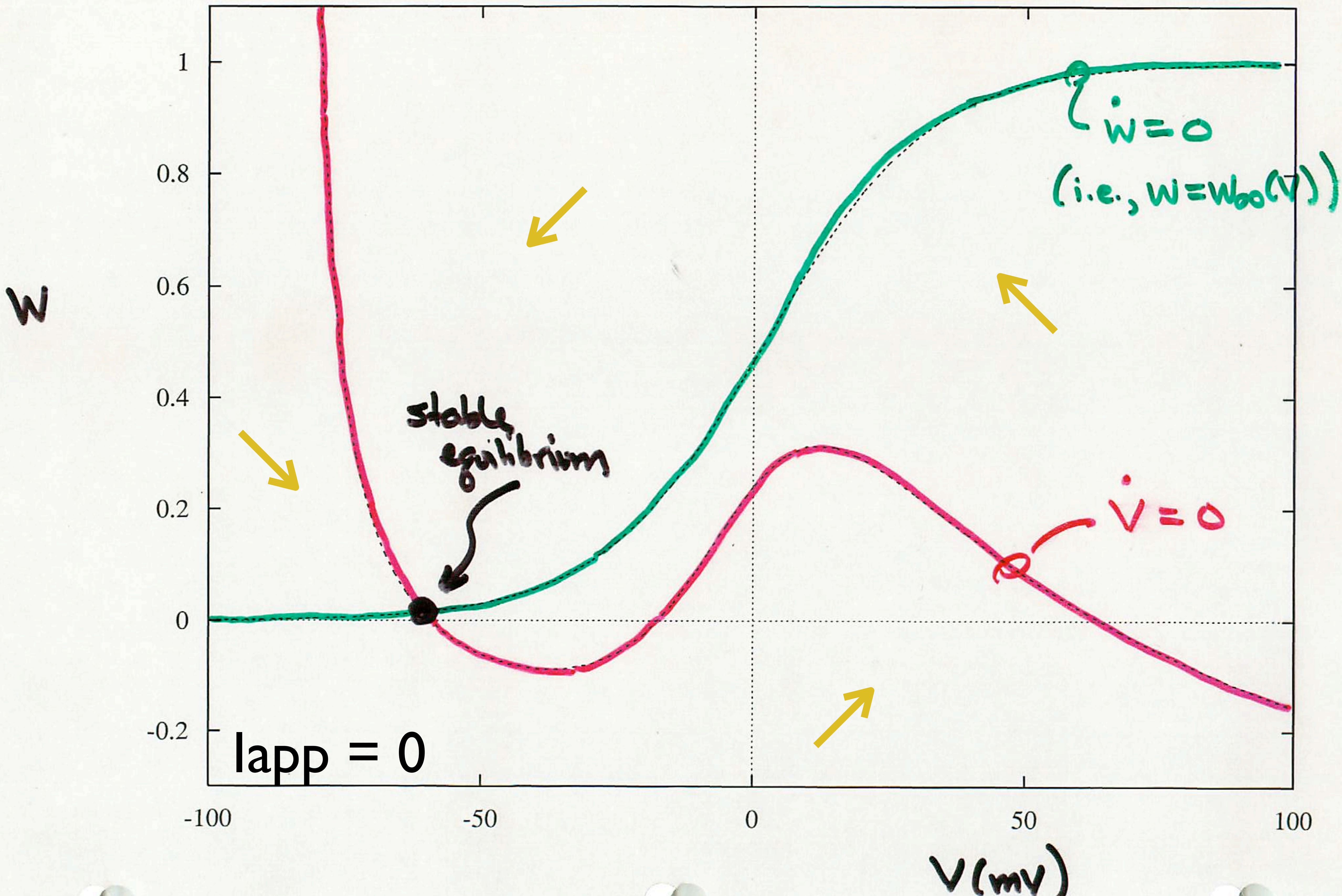
Interpretation: depending on K-current, membrane can be either monostable, bistable, or monostable due to the instantaneously activating Ca^{2+} current.


w
1
0.8
0.6
0.4
0.2
0
-0.2
← more
K+ current
less →
$\dot{V} = 0$
the V nullcline
Iapp = Imem
-100
-50
0
50
100
V(mV)

Morris-Lecar nullclines - numerically calculated by XPP

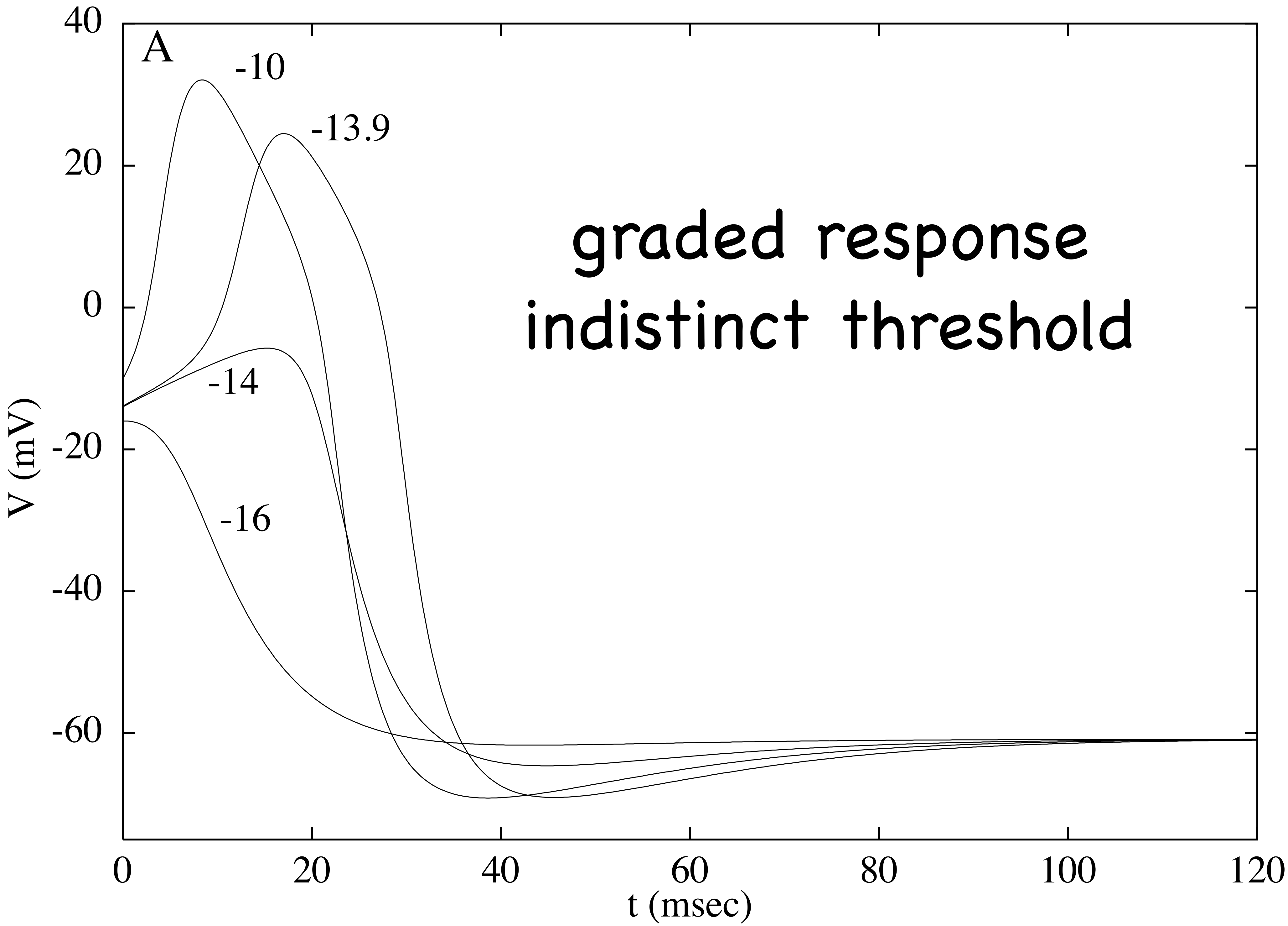


Morris-Lecar nullclines - numerically calculated by XPP



Excitability in the Morris-Lecar Model

Type 2 excitability in the Morris-Lecar model



graded response
indistinct threshold

Type 2 excitability in the Morris-Lecar model

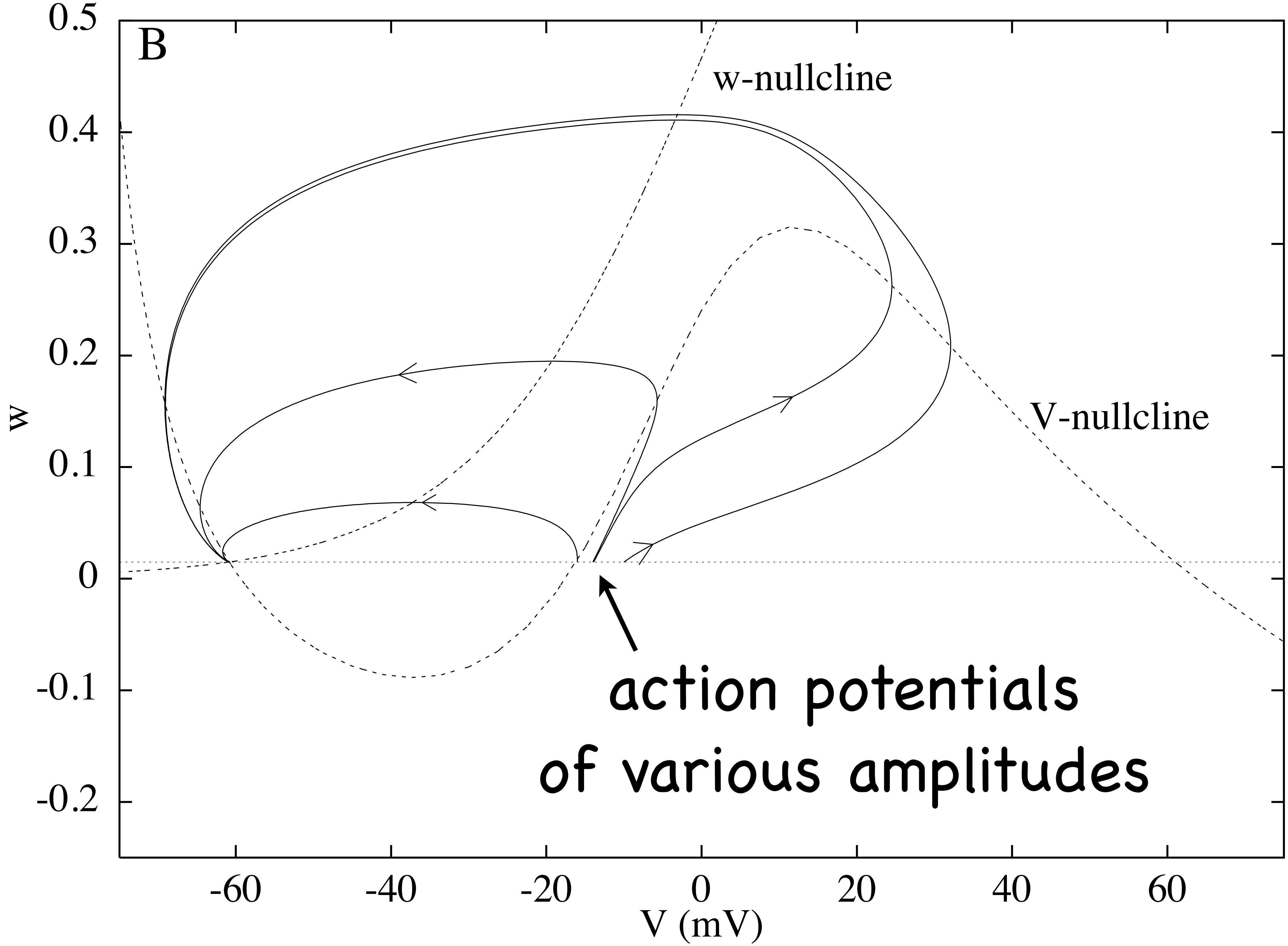
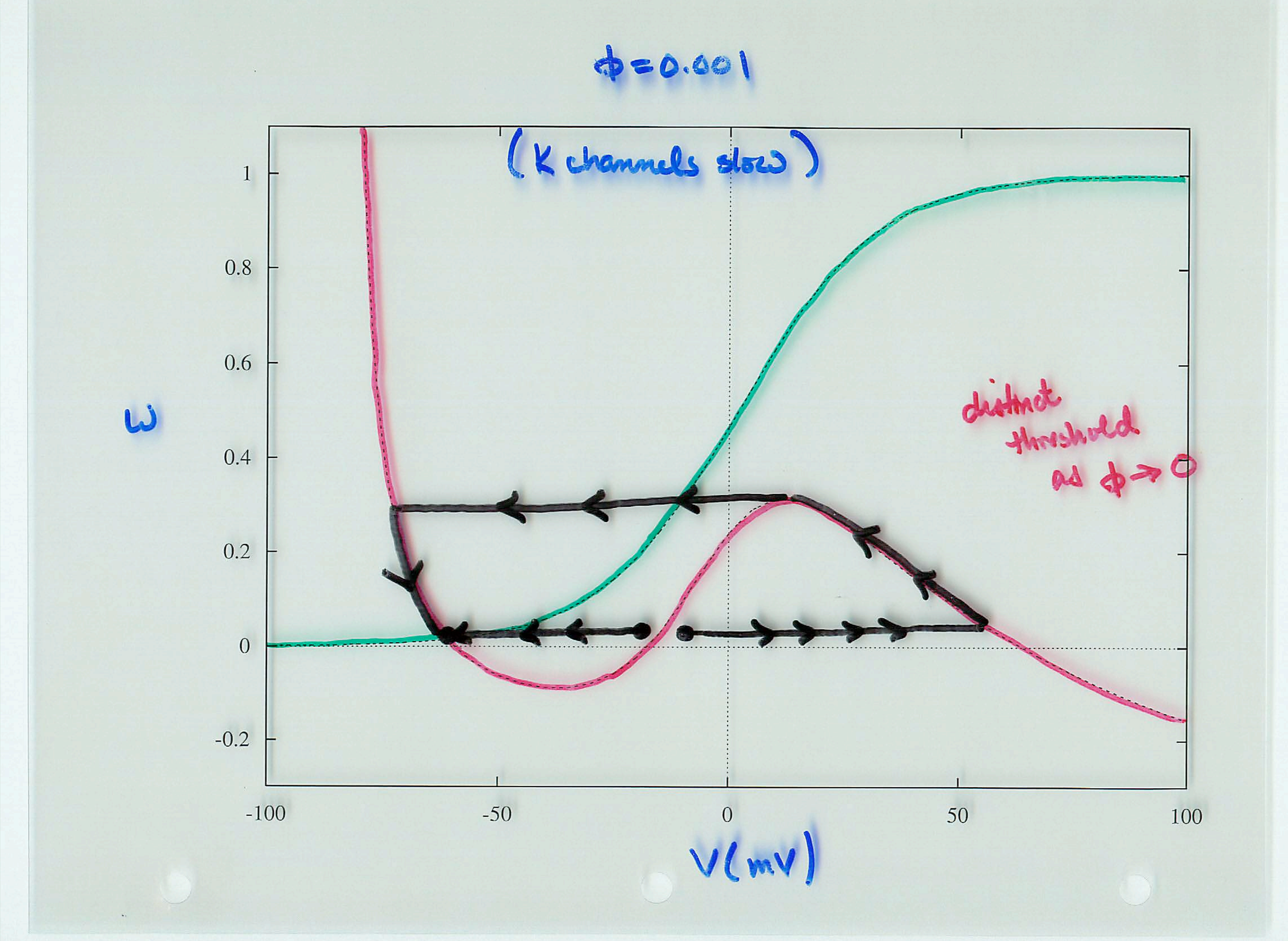


Figure 1: Response of the Morris-Lecar excitable system, equations (4-6), to a brief current pulse. For these parameters (see Appendix A), the system has a unique stable rest state, $\bar{V} = -61$ mV, $\bar{w} = .015$. The line $w = \bar{w}$ is shown lightly dashed. Four different stimuli lead to an instantaneous displacement of V from $\bar{V}$ to V_0 (values of V_0 are shown alongside the curves in **A**). **A** shows the time course of the voltage. Notice that intermediate responses are possible with some stimuli: the threshold is graded; firing occurs with finite latency. **B** shows trajectories in the $V - w$ phase plane; nullclines are shown dashed and intersect only once. The effect of a stimulus is to displace the initial condition horizontally from rest.

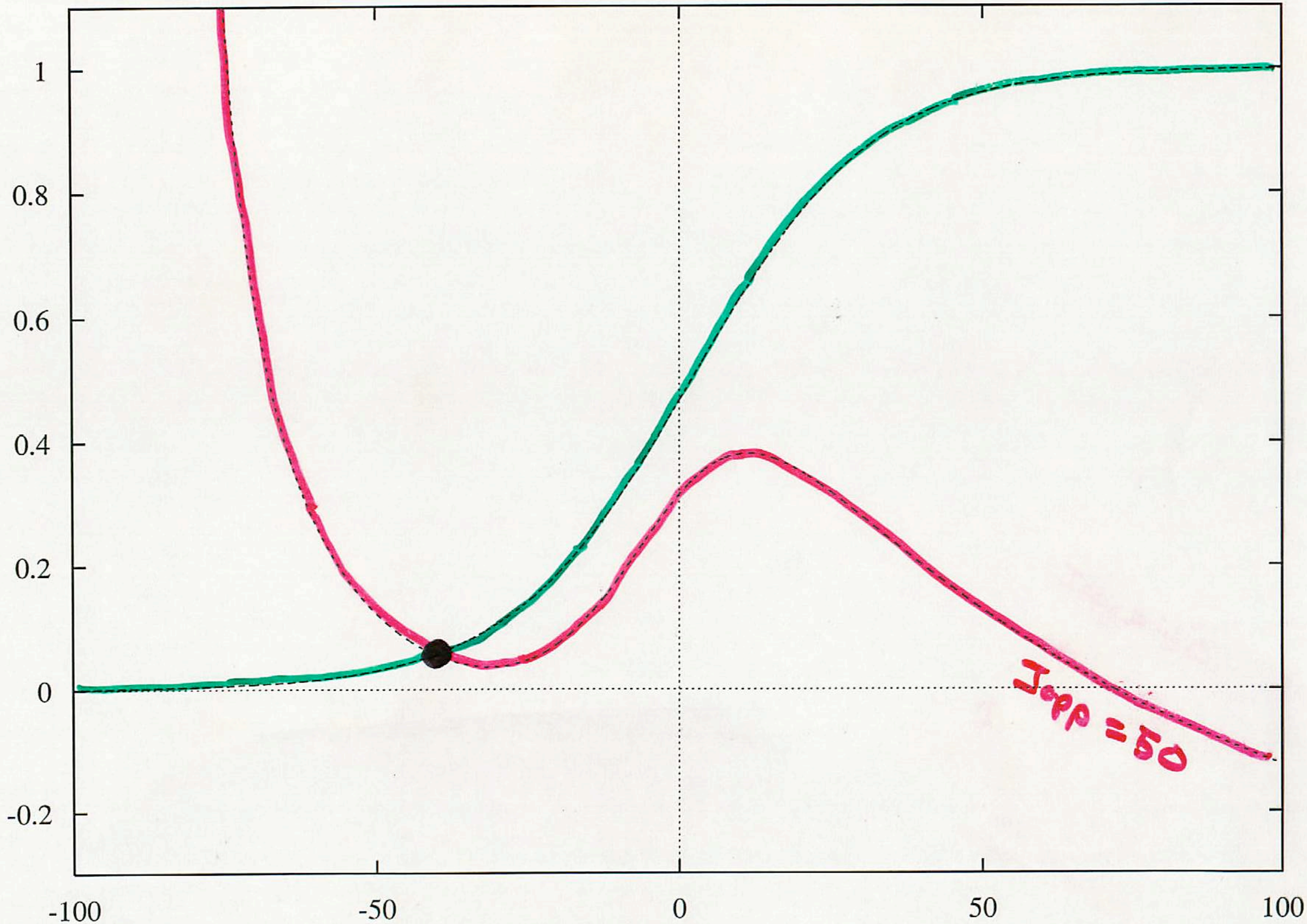
Excitability in the Morris-Lecar Model with separated time scales for voltage (fast) and K channel gating (slow)

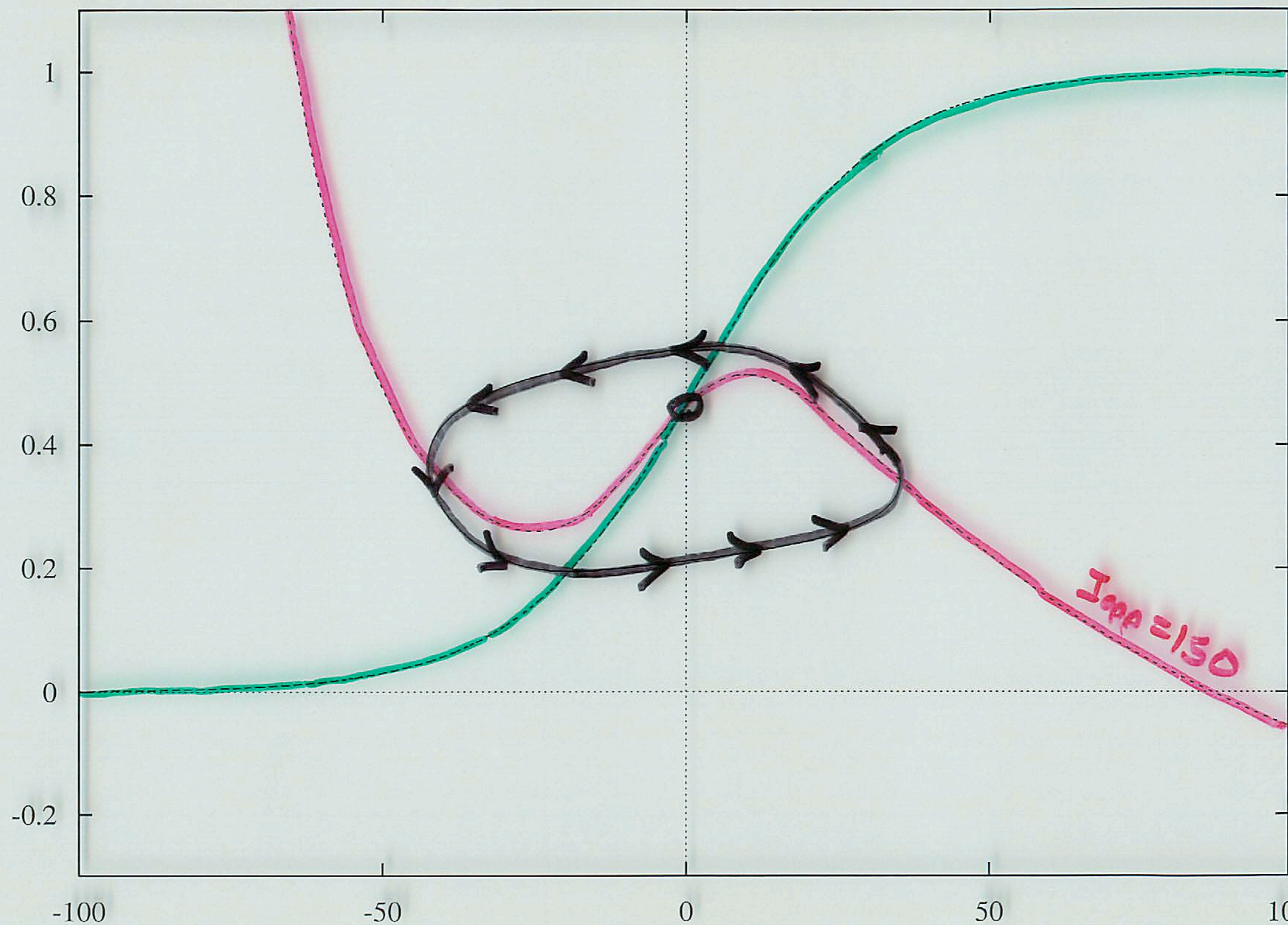
Changing parameters so that K channels are very slow



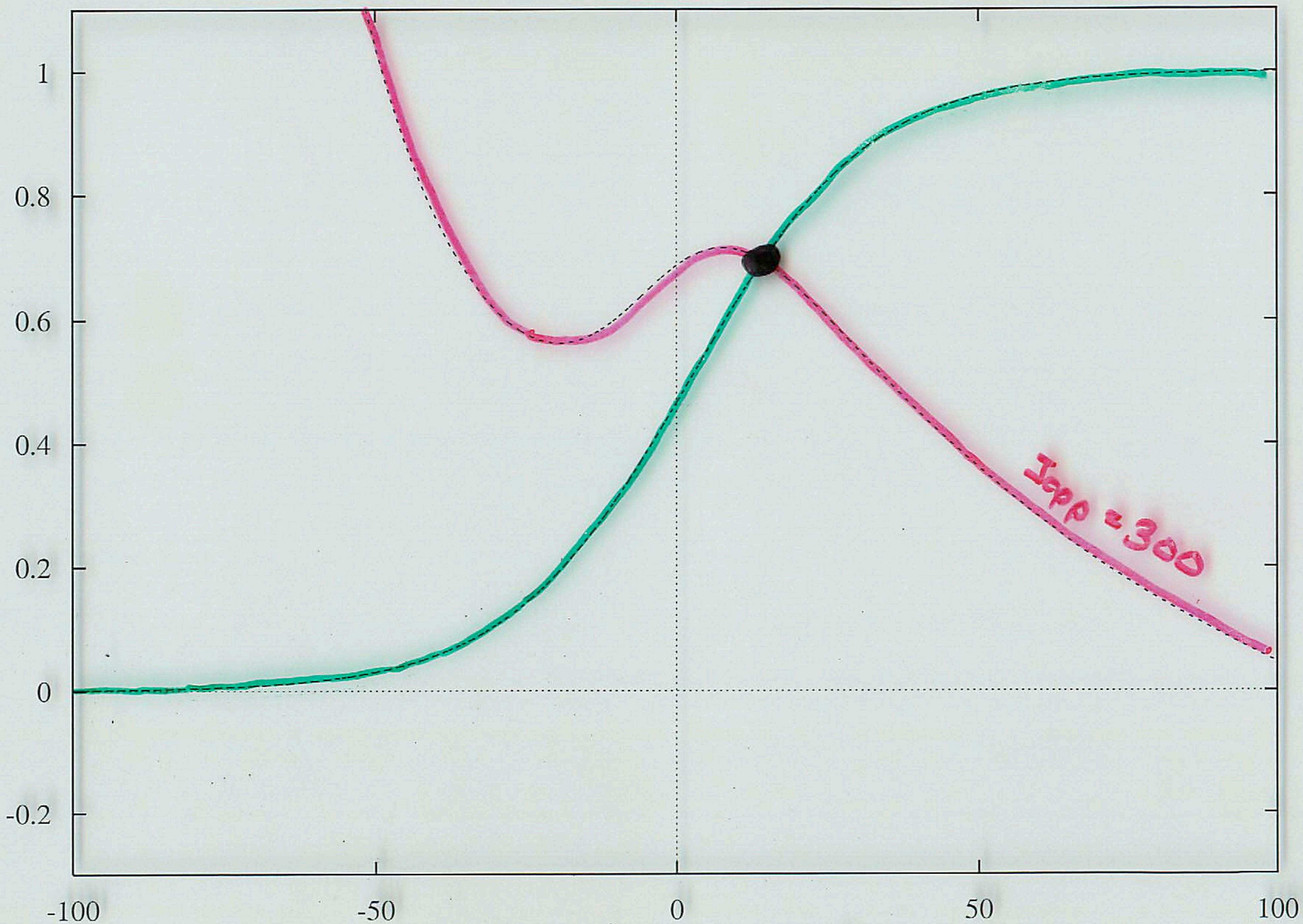
Type 2 Oscillations in the Morris-Lecar Model

Morris-Lecar nullclines - change with Iapp





1
0.8
0.6
0.4
0.2
0
-0.2
-100
-50
0
50
100
Iapp=150

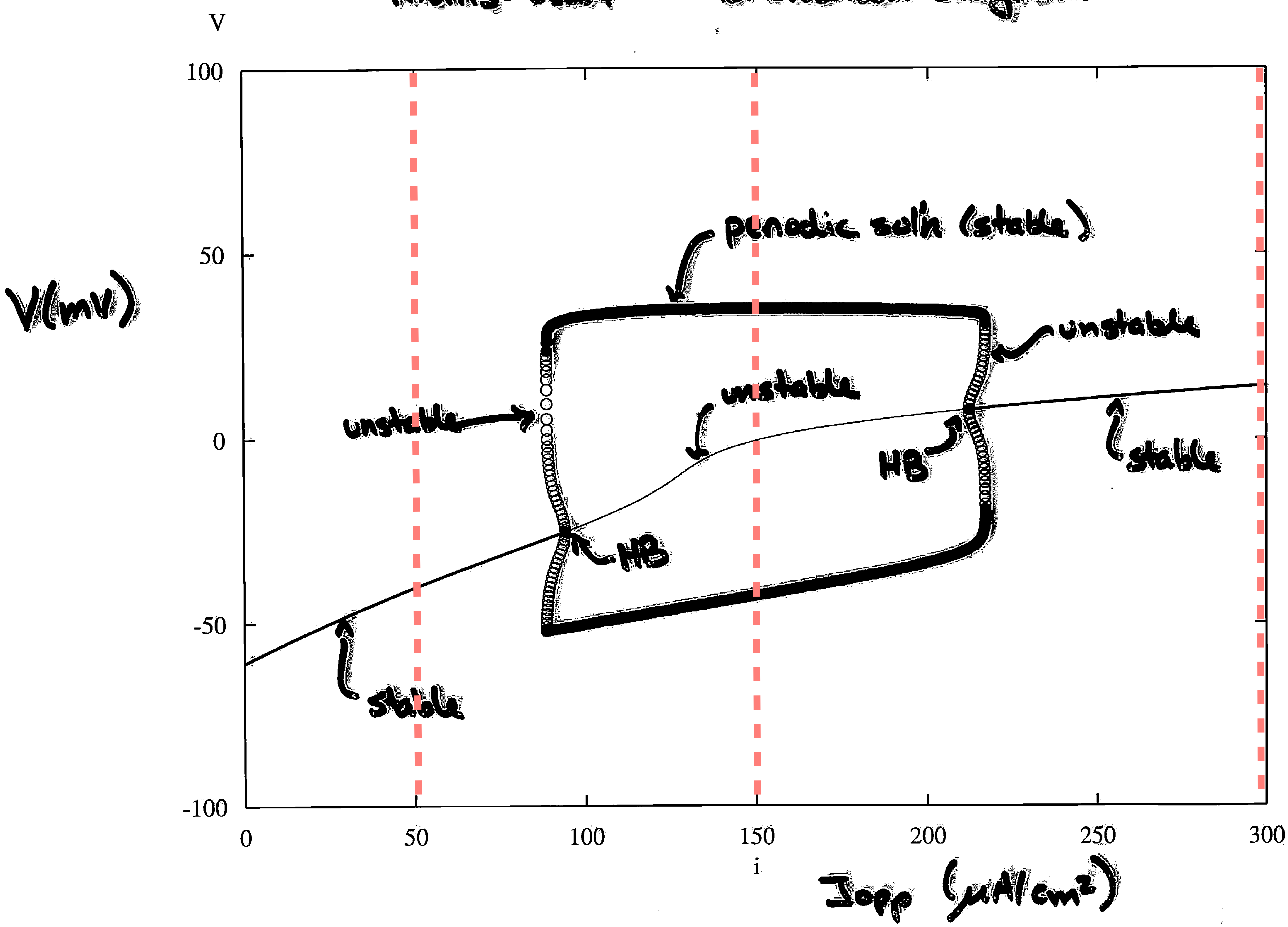


1
0.8
0.6
0.4
0.2
0
-0.2
-100
-50
0
50
100
Iopp = 300

...when the equilibrium occurs outside the "knees" of the voltage nullcline, the equilibrium is stable.

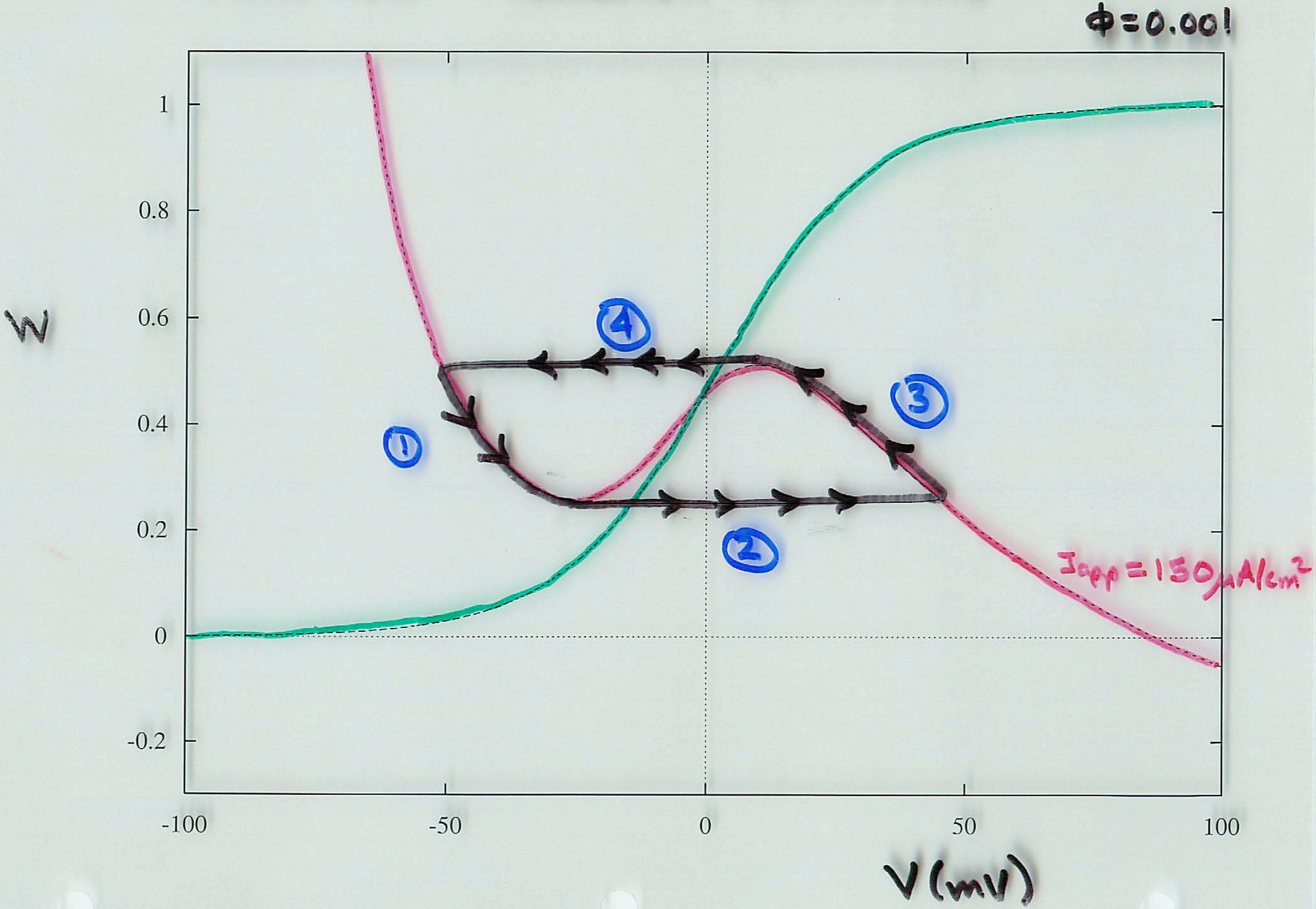
...when the equilibrium occurs inside the "knees" of the voltage nullcline, the equilibrium can be either stable or unstable.

Morris-Lecar Bifurcation Diagram

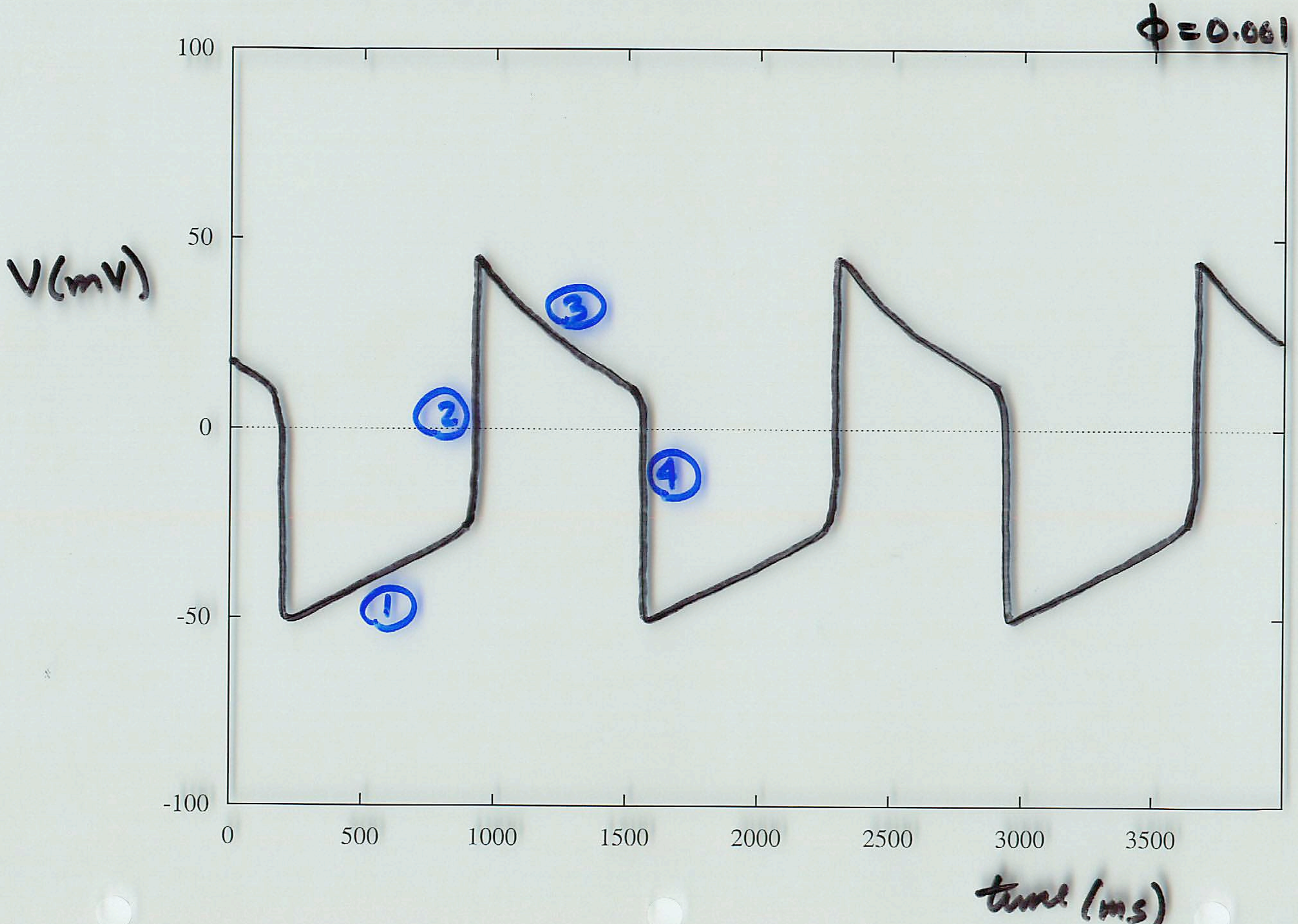


Type 2 Oscillations in the Morris-Lecar Model with separated time scales for voltage (fast) and K channel gating (slow)

Morris-Lecar Relaxation Oscillations



Morris Lecar Relaxation Oscillations



Explanation what is observed in phase plane

(1) at hyper. branch. $w_\infty(V)$ is below so K-channels must de-activate ... membrane depolarizes slightly

(2) Suddenly fold bifurcation is reached. Ca^{2+} channels activate and membrane depolarizes.

(3) at depol branch. $w_\infty(V)$ is above so K-channels must activate ... membrane hyperpolarizes slightly

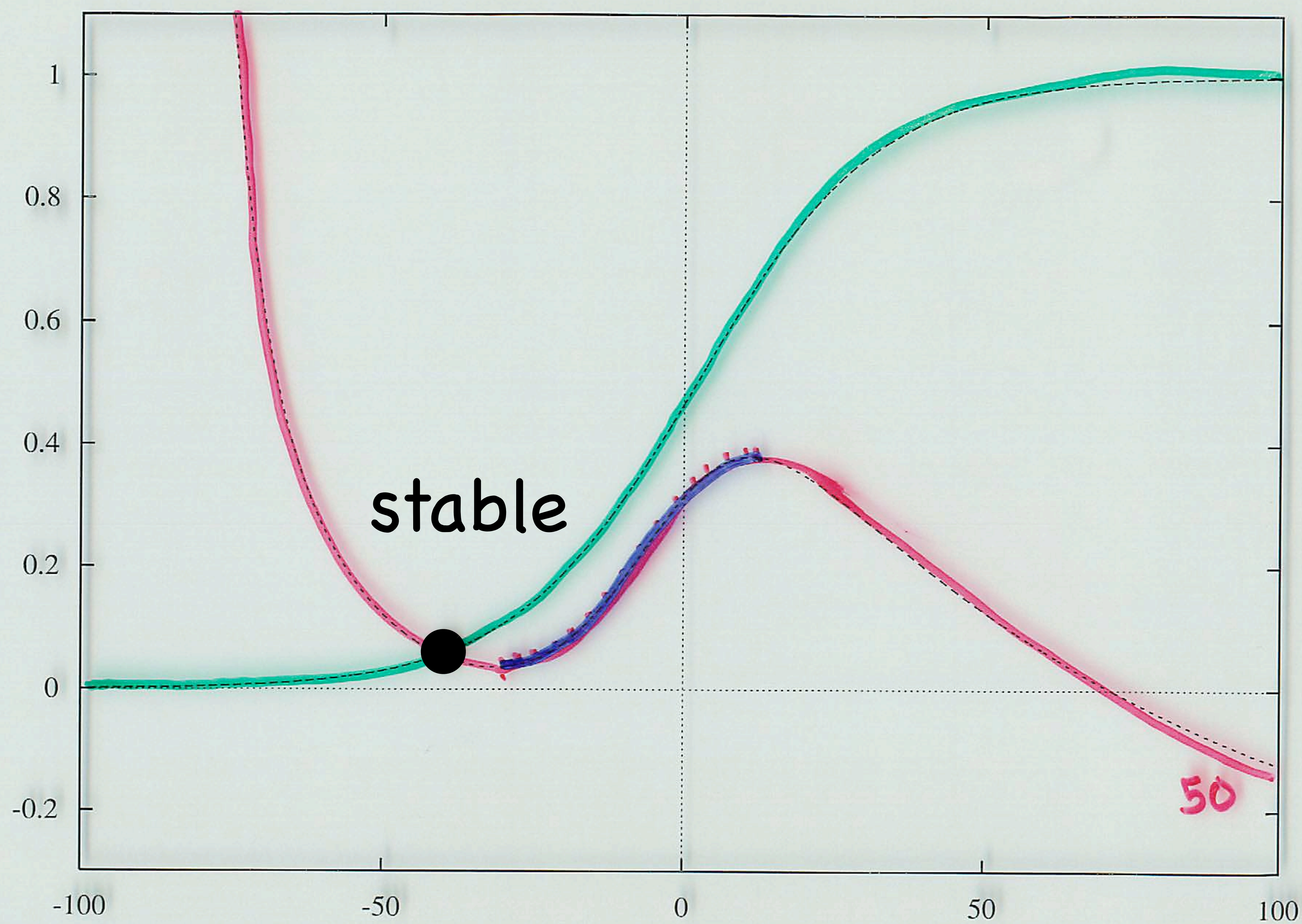
(4) Suddenly fold bifurcation is reached. Ca^{2+} channels de-activate and membrane hyperpolarizes.

When K channels are very slow,

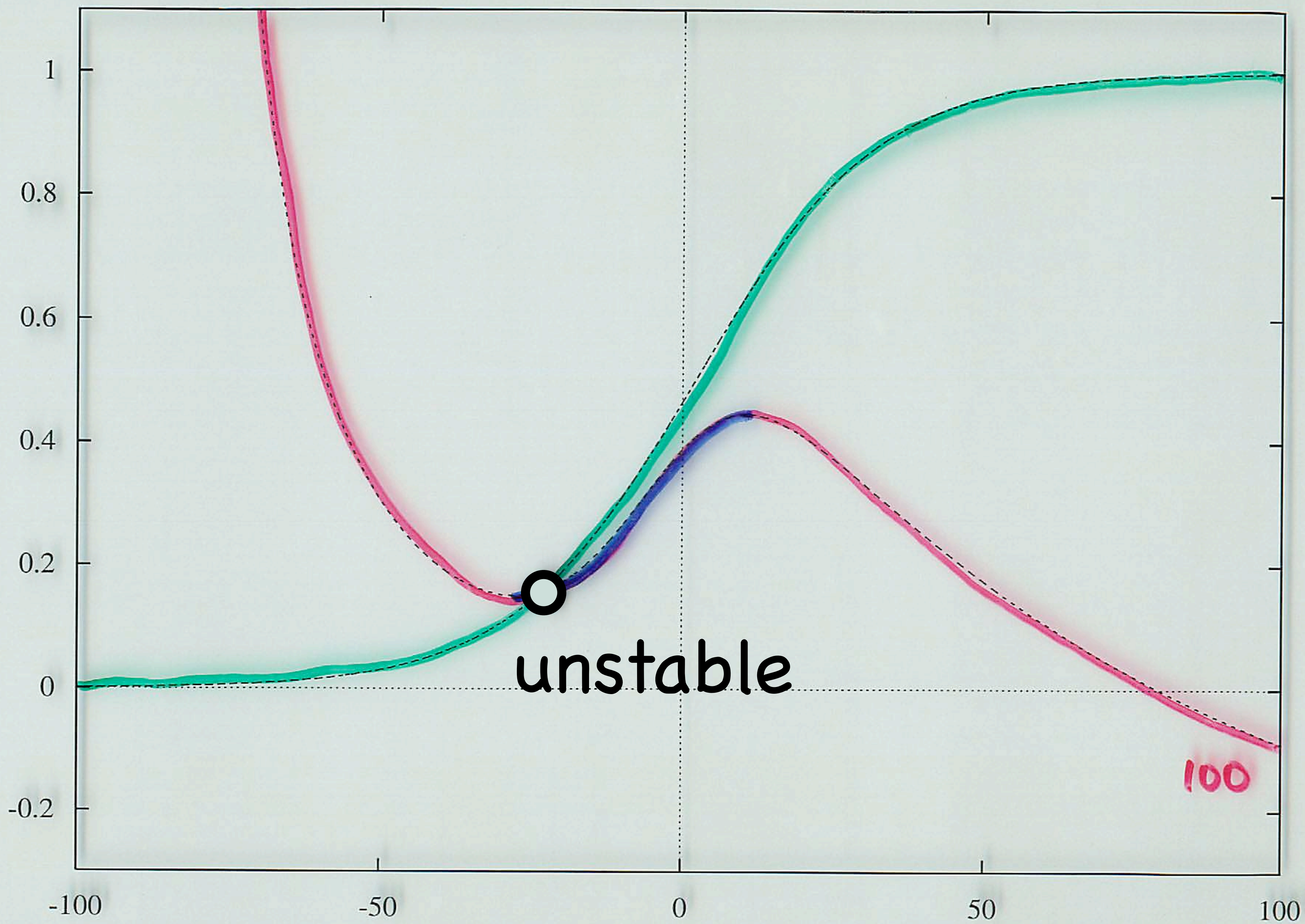
...the equilibrium is stable when the equilibrium occurs outside the “knees” of the voltage nullcline, and

...the equilibrium is unstable when the equilibrium occurs inside the “knees” of the voltage nullcline.

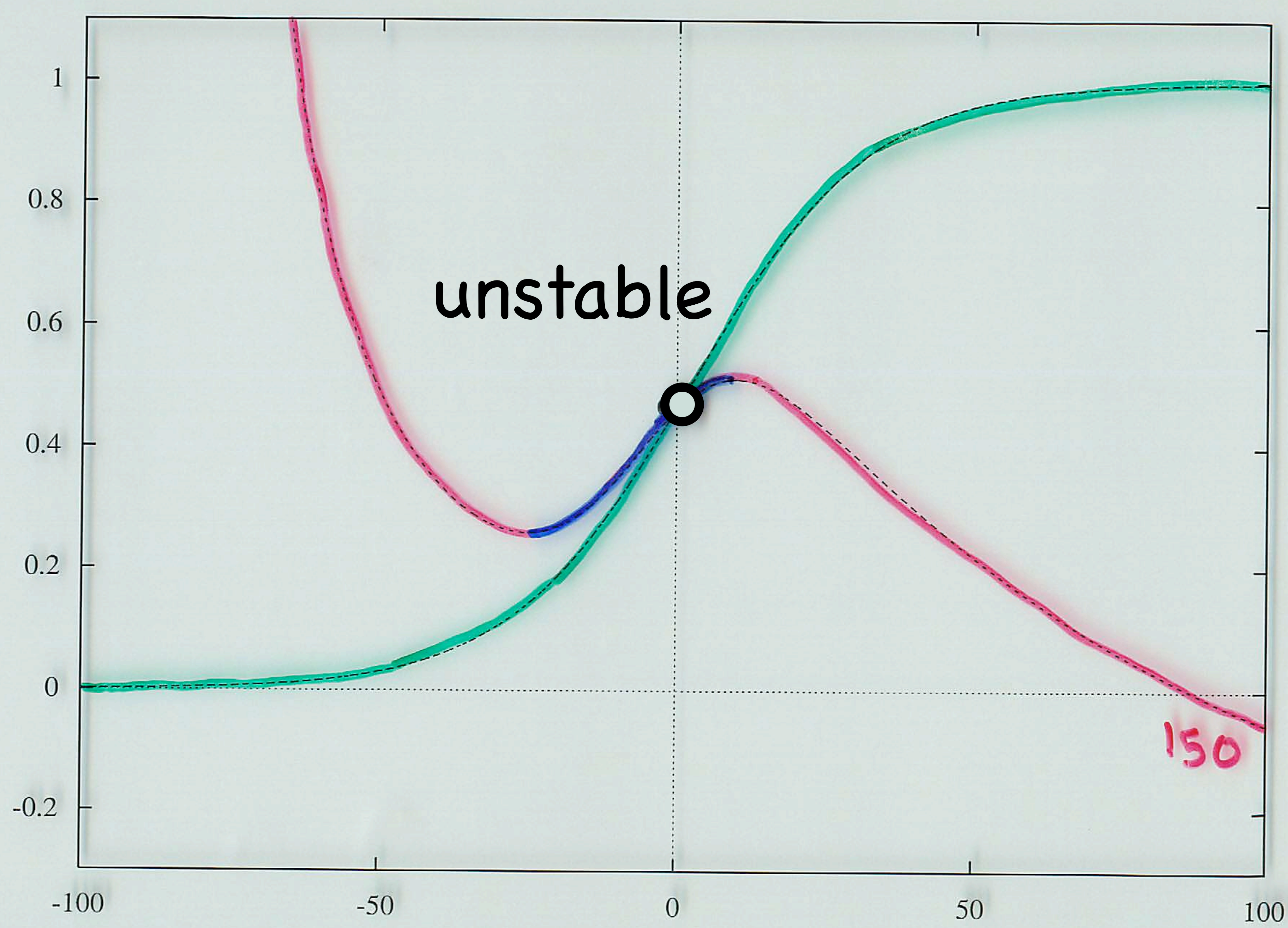
This is illustrated in the following slides.



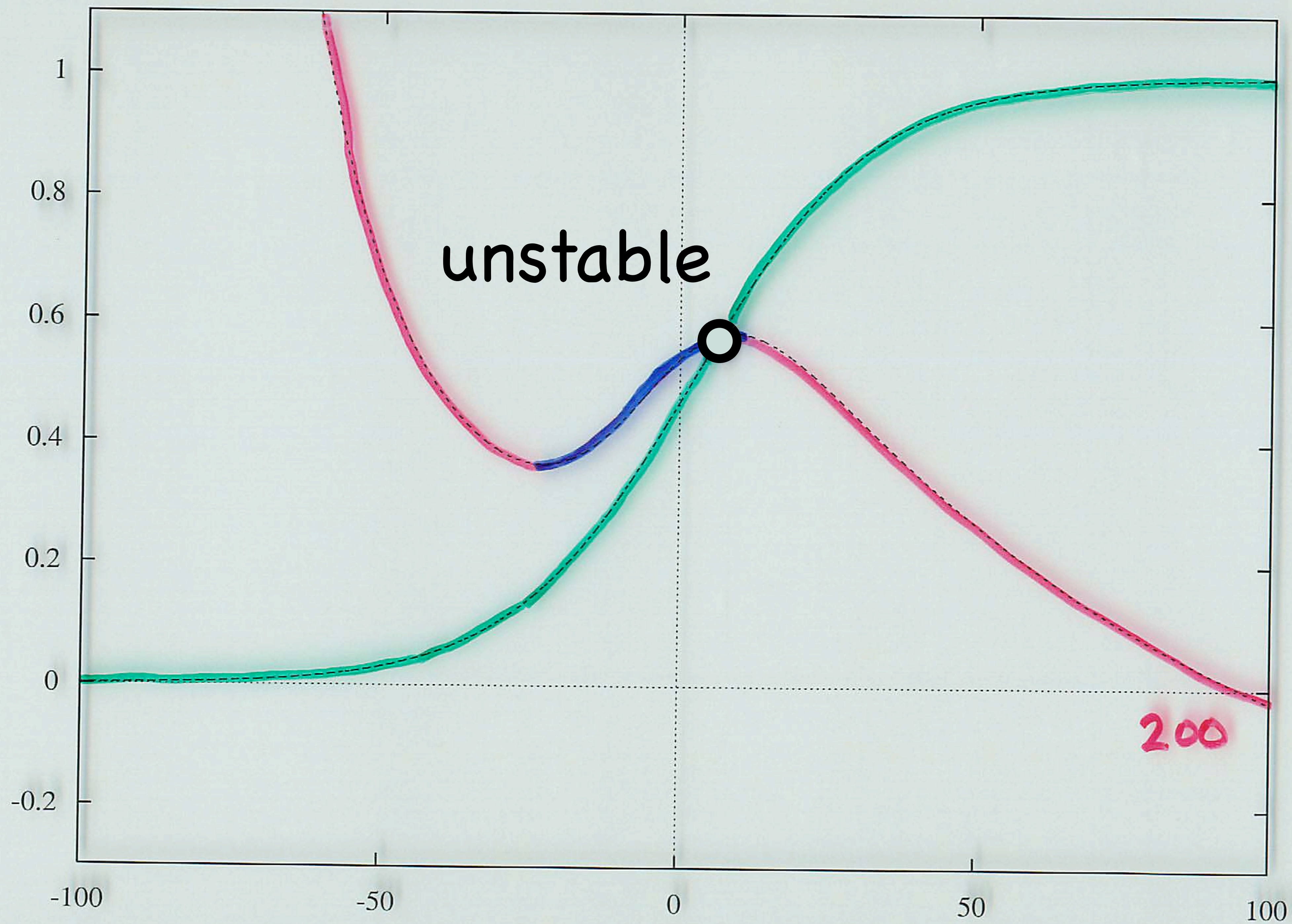
stable
50
1
0.8
0.6
0.4
0.2
0
-0.2
-100
-50
0
50
100



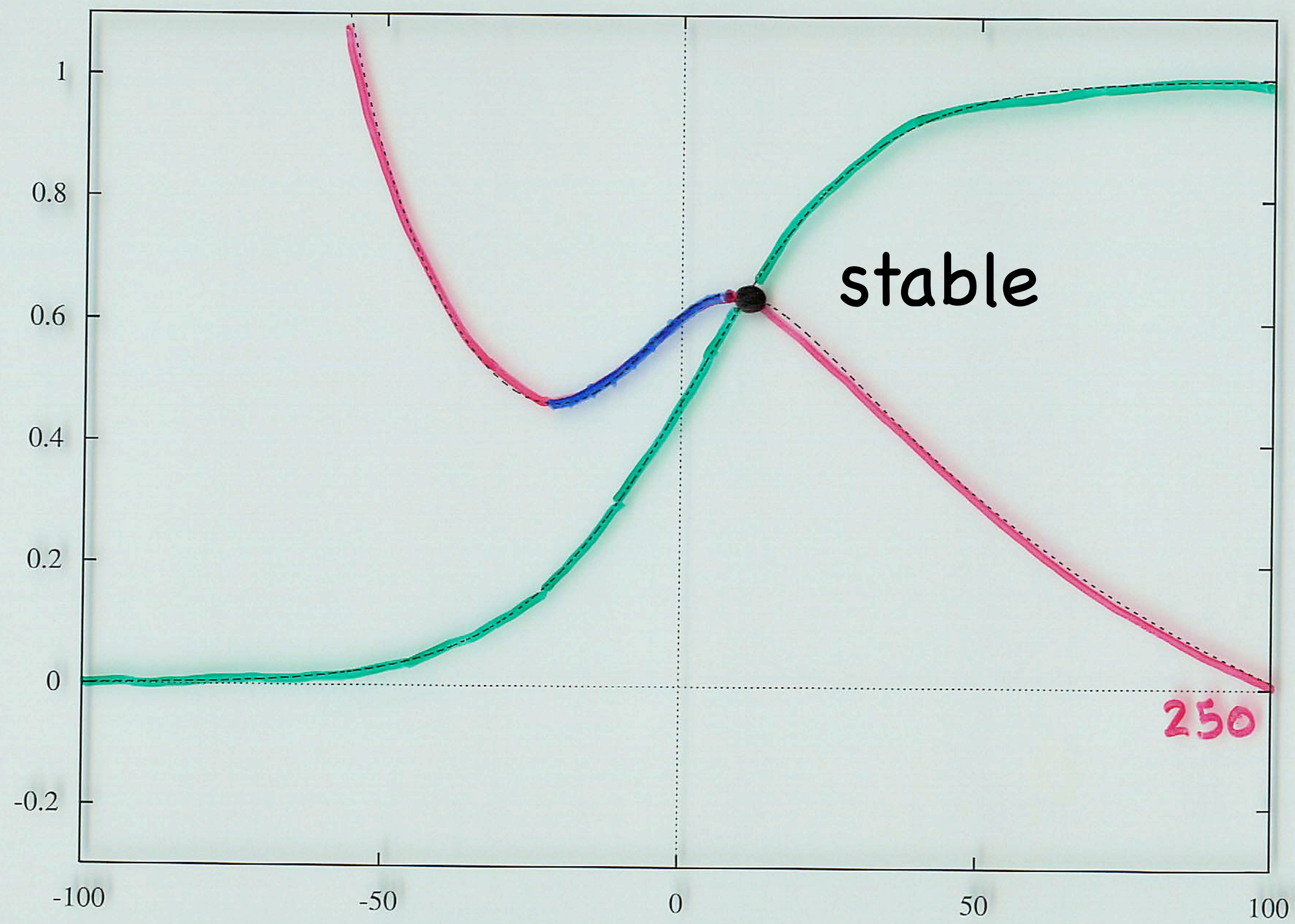
1
0.8
0.6
0.4
0.2
0
-0.2
-100
-50
0
50
100
unstable
100



unstable
150
1
0.8
0.6
0.4
0.2
0
-0.2
-100
-50
0
50
100



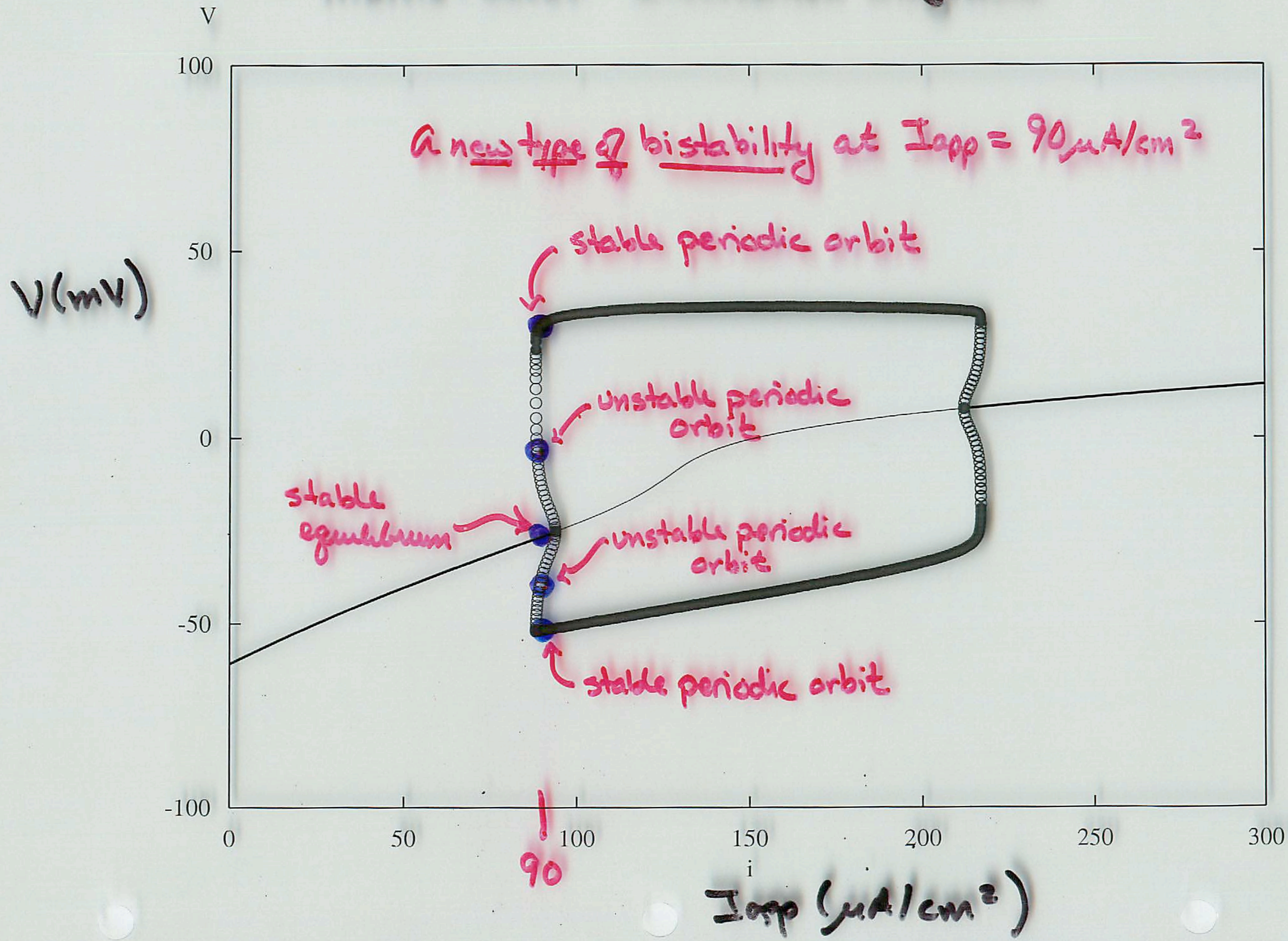
1
0.8
0.6
0.4
0.2
0
-0.2
-100
-50
0
50
100
unstable
200

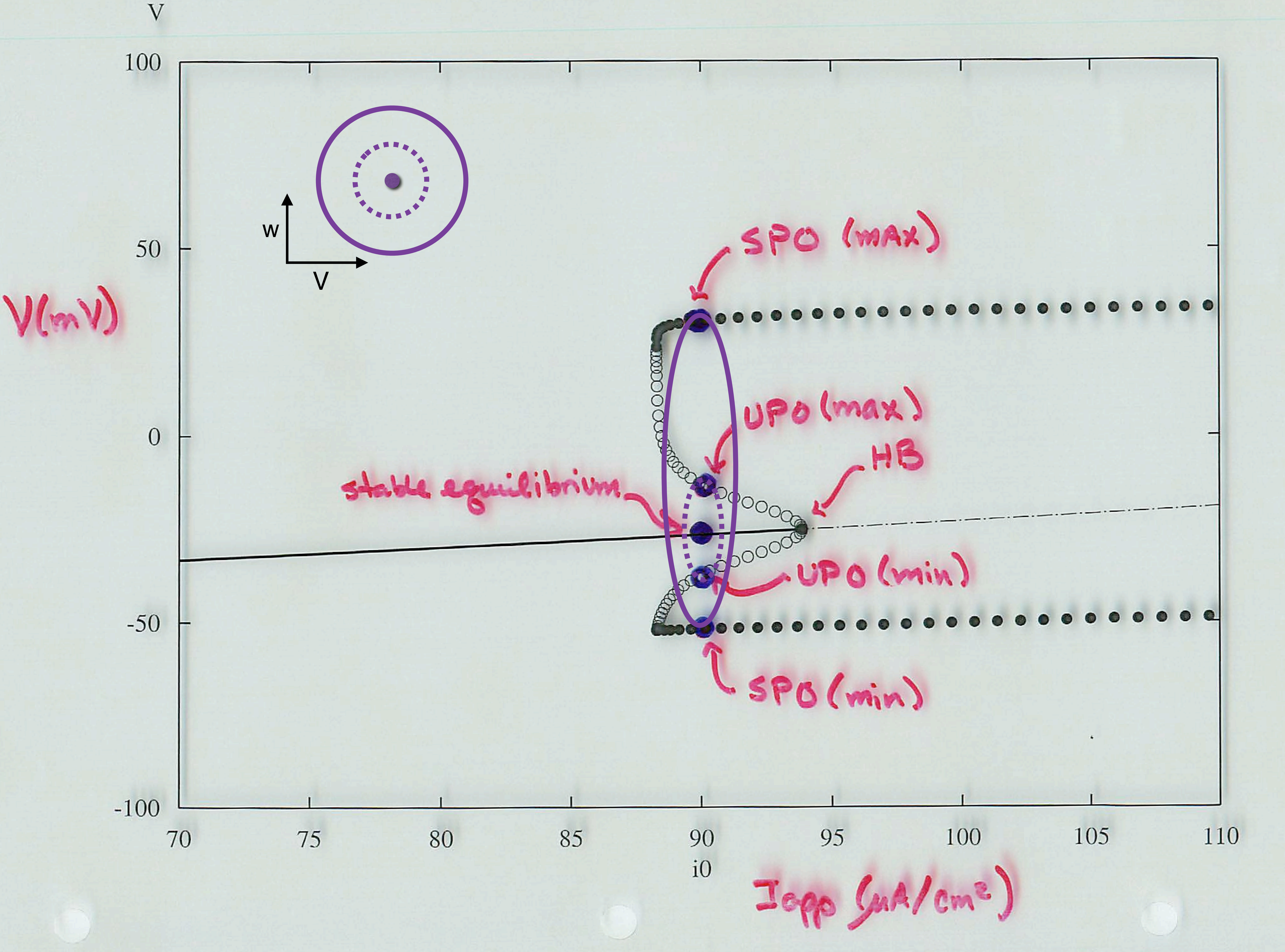


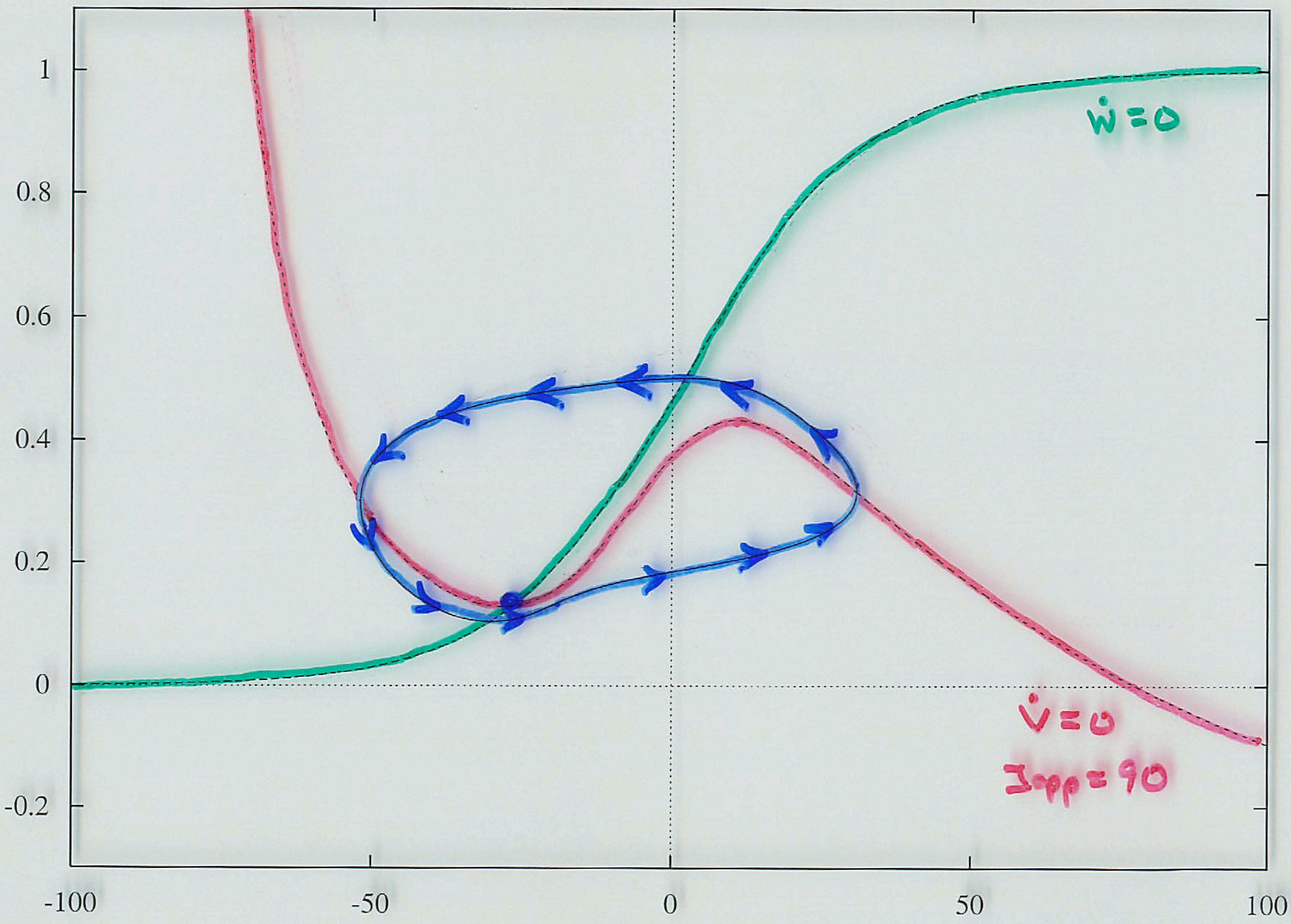
1
0.8
0.6
0.4
0.2
0
-0.2
-100
-50
0
50
100
stable
250

a new type of bistability...

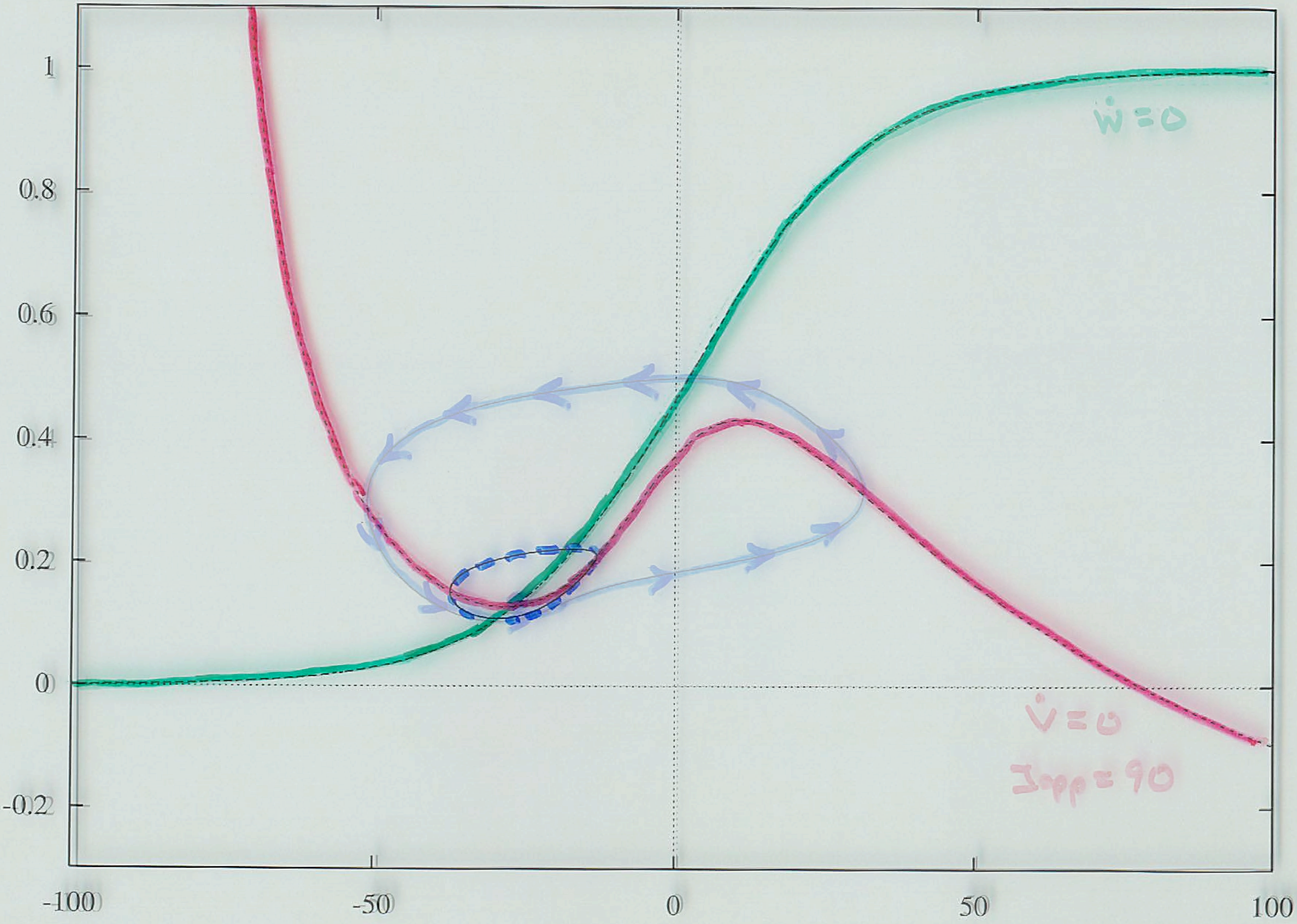
Morris-Lecar Bifurcation Diagram



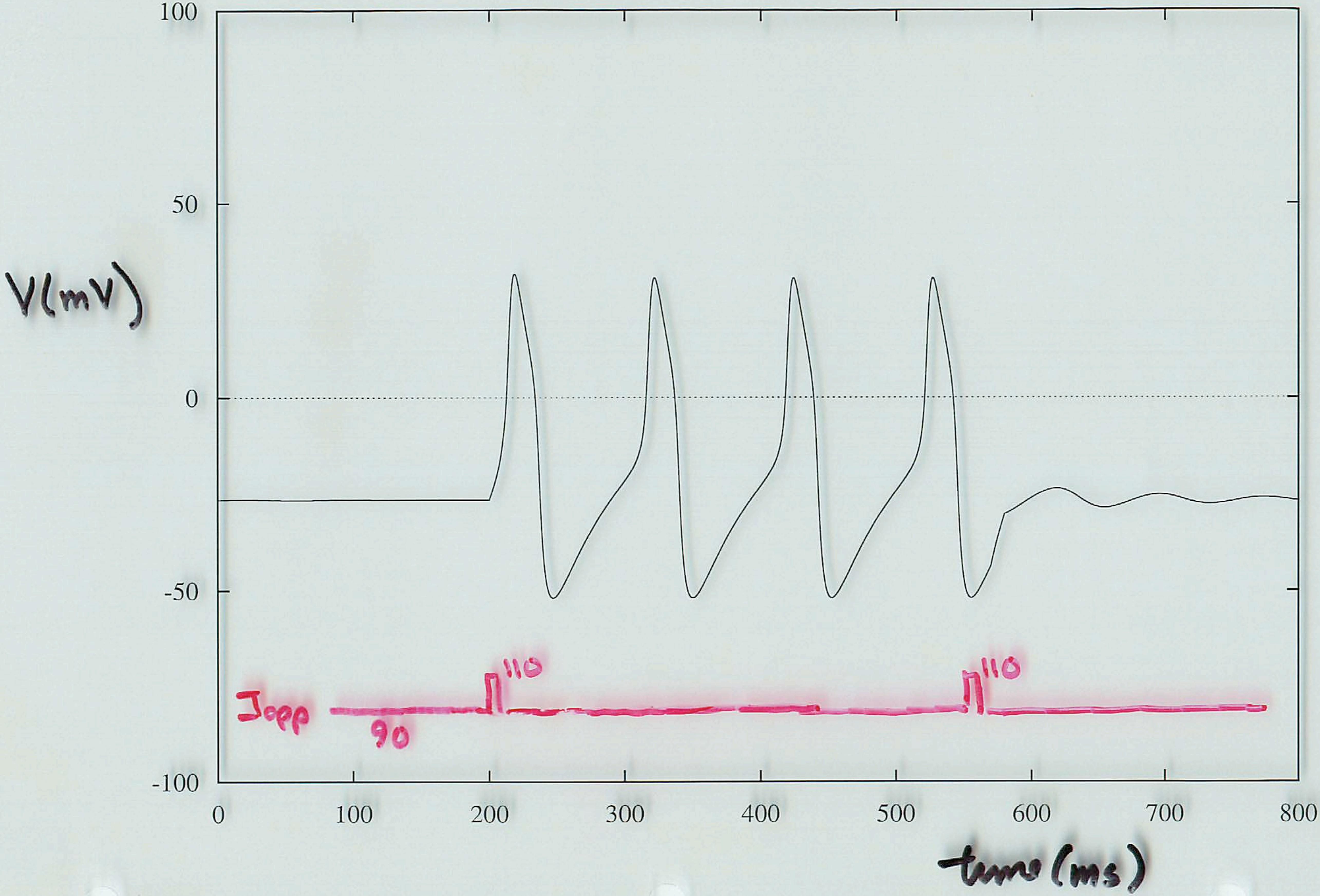

V
100
50
0
-50
-100
70
75
80
85
90
95
100
105
110
i0
V(mV)
Iapp (uA/cm²)
w
V
SPO (MAX)
UPO (max)
HB
stable equilibrium
UPO (min)
SPO (min)



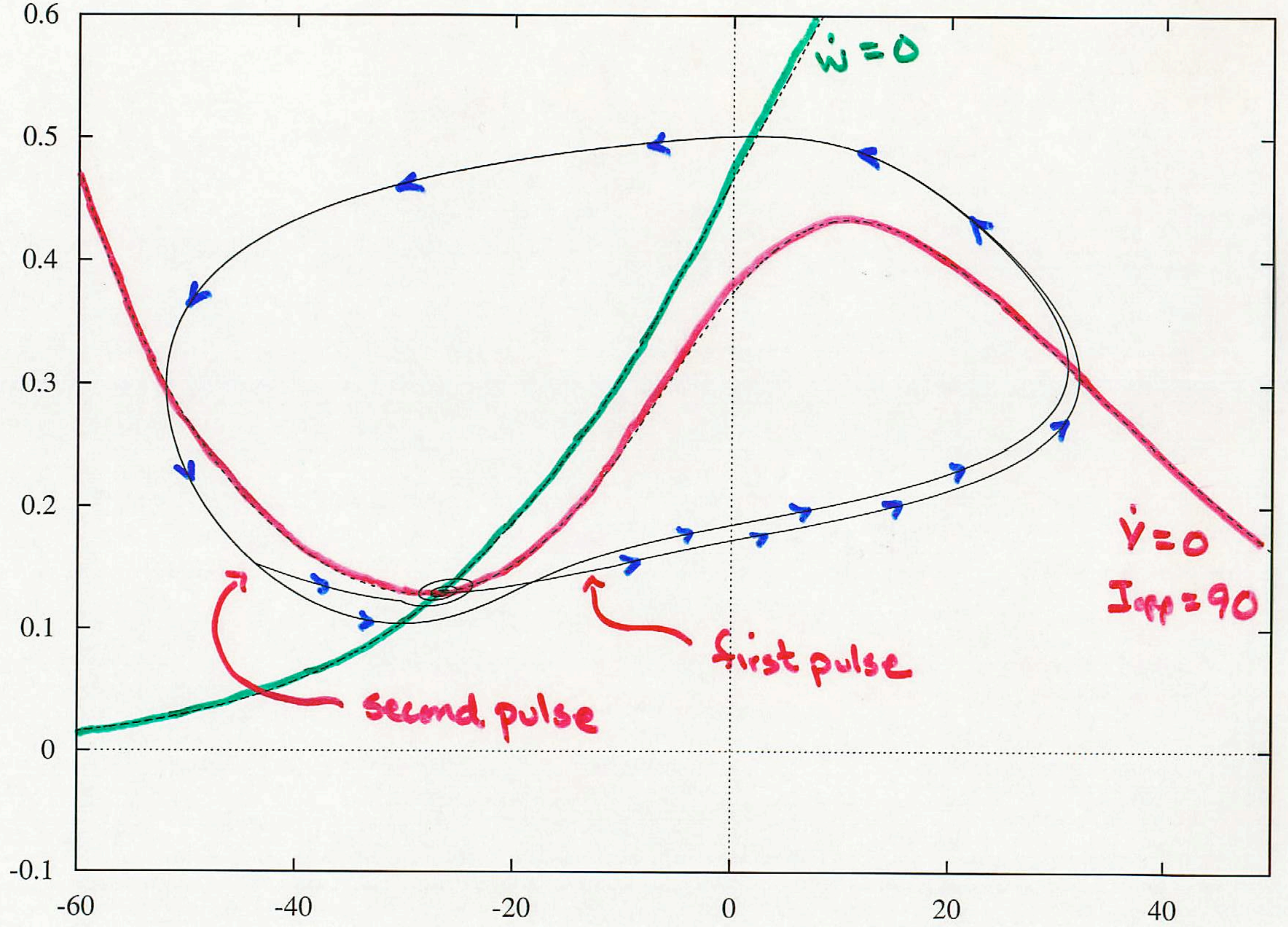
1
0.8
0.6
0.4
0.2
0
-0.2
-100
-50
0
50
100
ẇ = 0
v̇ = 0
Iapp = 90



1
0.8
0.6
0.4
0.2
0
-0.2
-100
-50
0
50
100
ẇ = 0
v̇ = 0
Iapp = 90



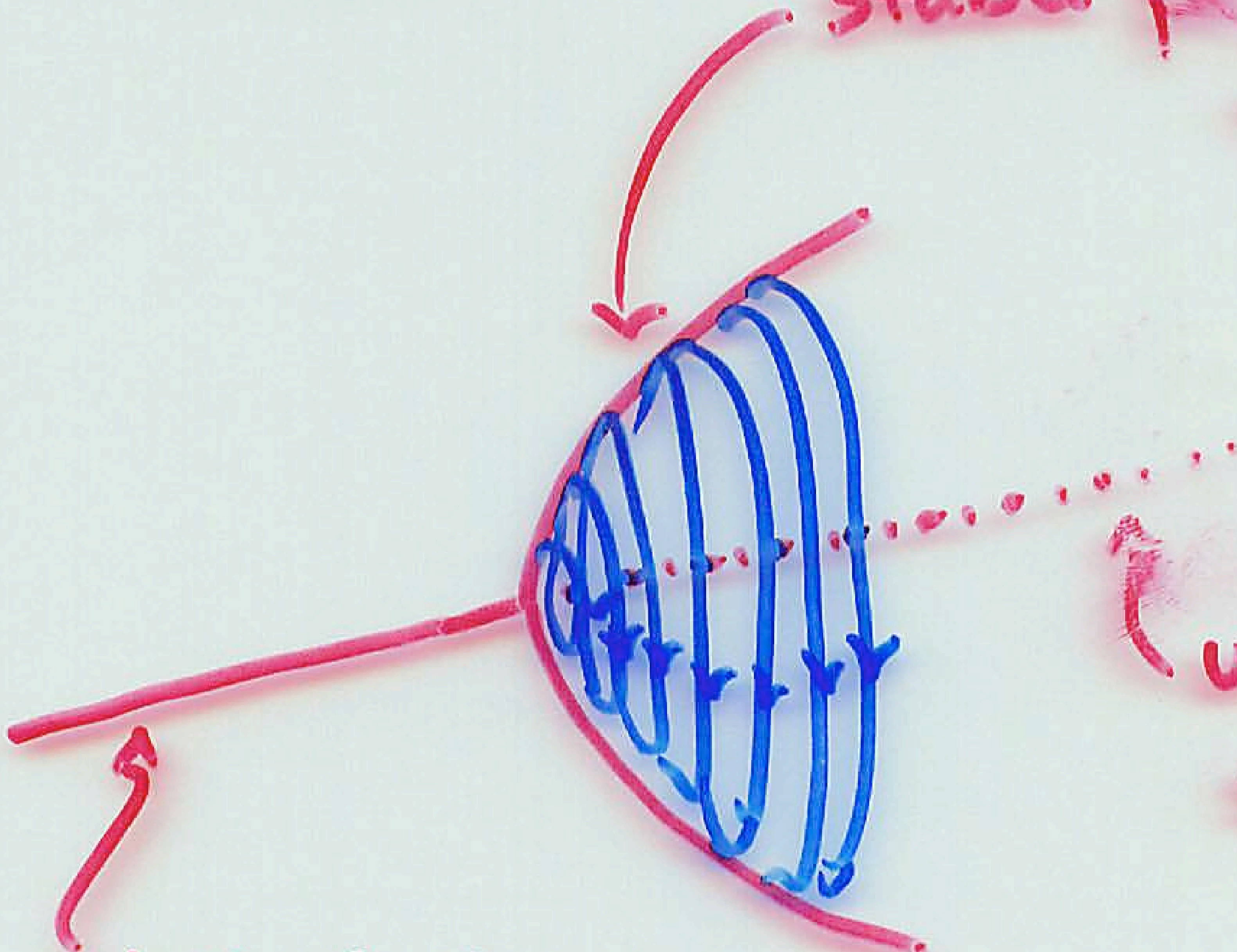
100
50
0
-50
-100
0
100
200
300
400
500
600
700
800
V(mV)
time (ms)
Iapp
90
110
110



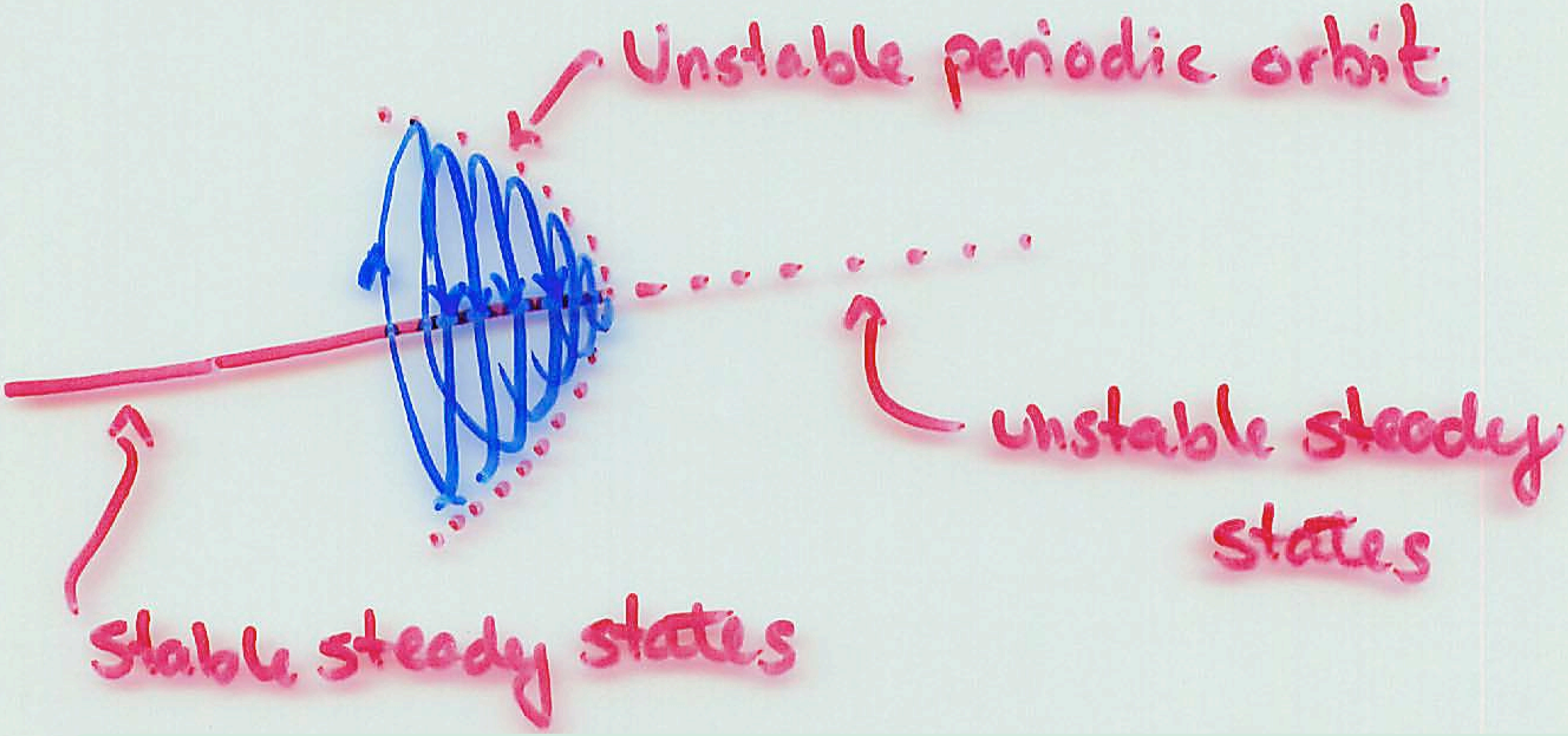
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
-60
-40
-20
0
20
40
ẇ = 0
V̇ = 0
Iapp = 90
first pulse
second pulse

Slow passage through Hopf bifurcations

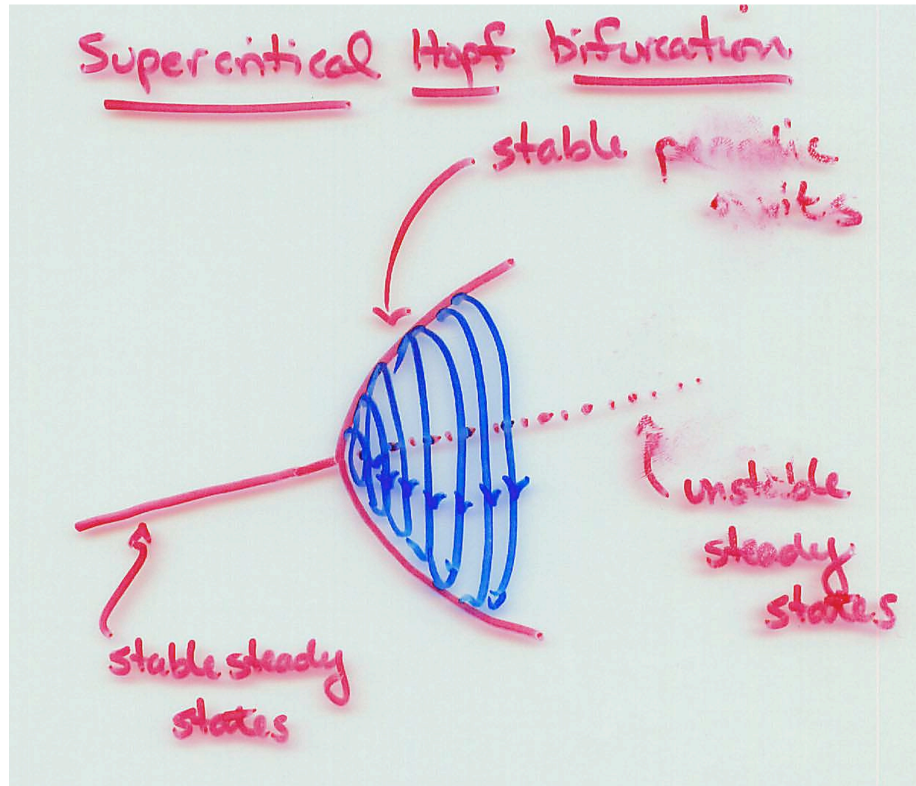
Supercritical Hopf bifurcation

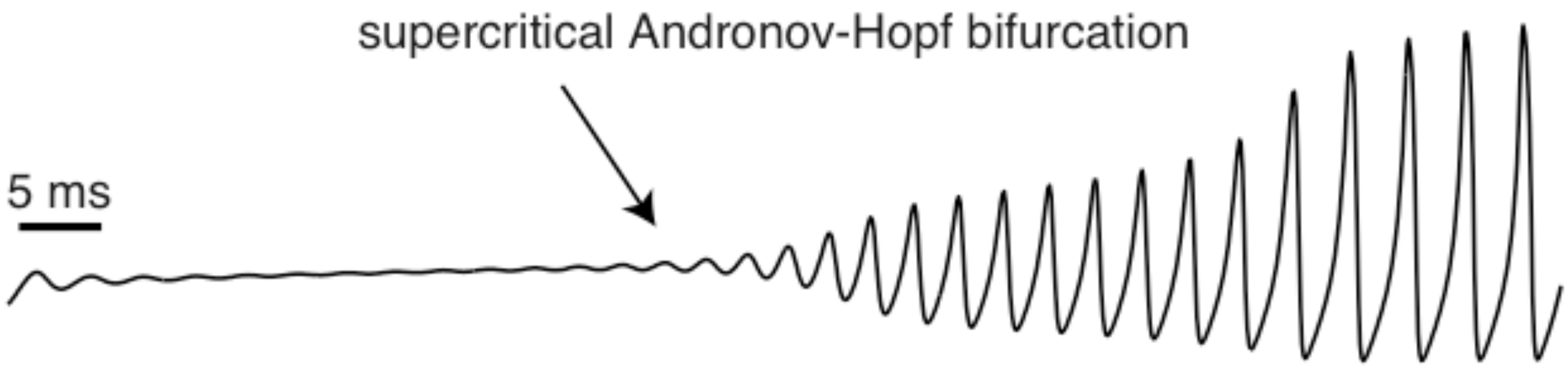


Subcritical Hopf bifurcation

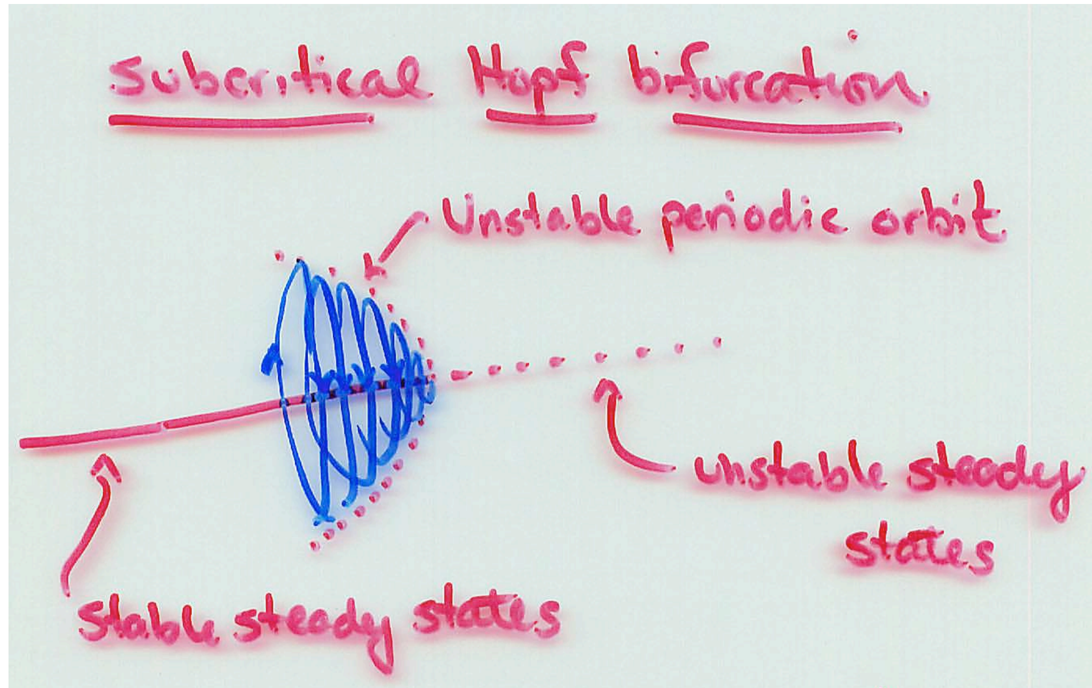


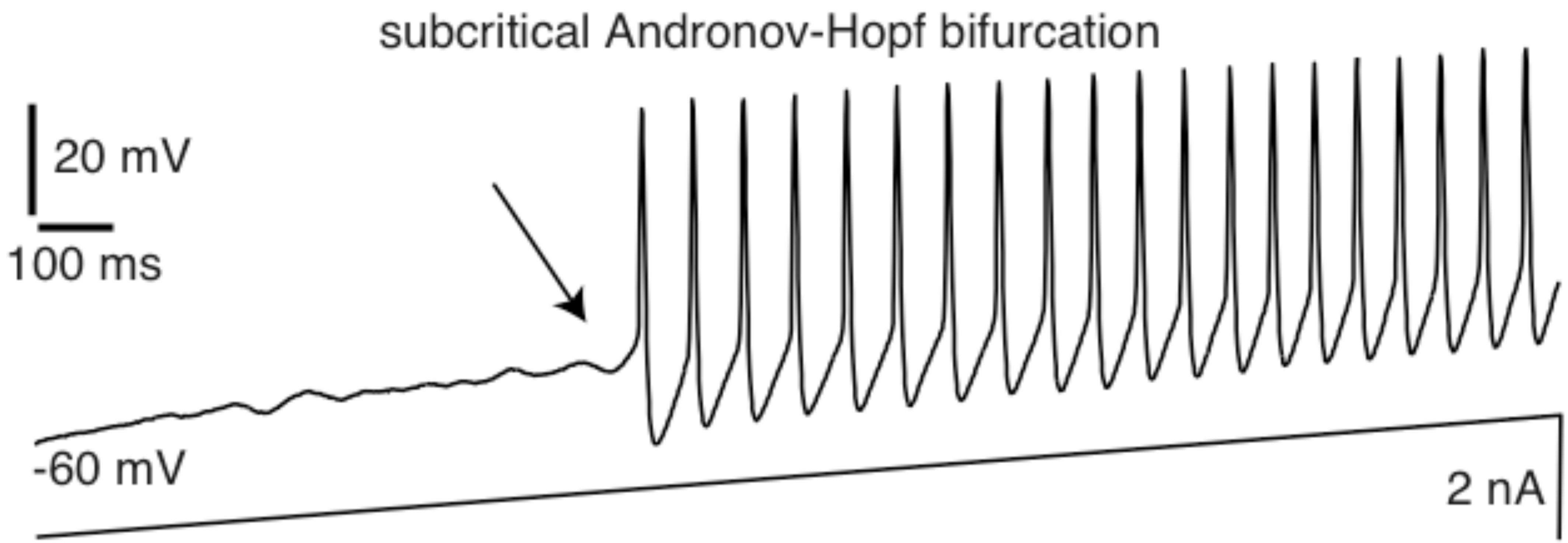
Starting from stable equilibrium Iapp increases through a supercritical Hopf bifurcation





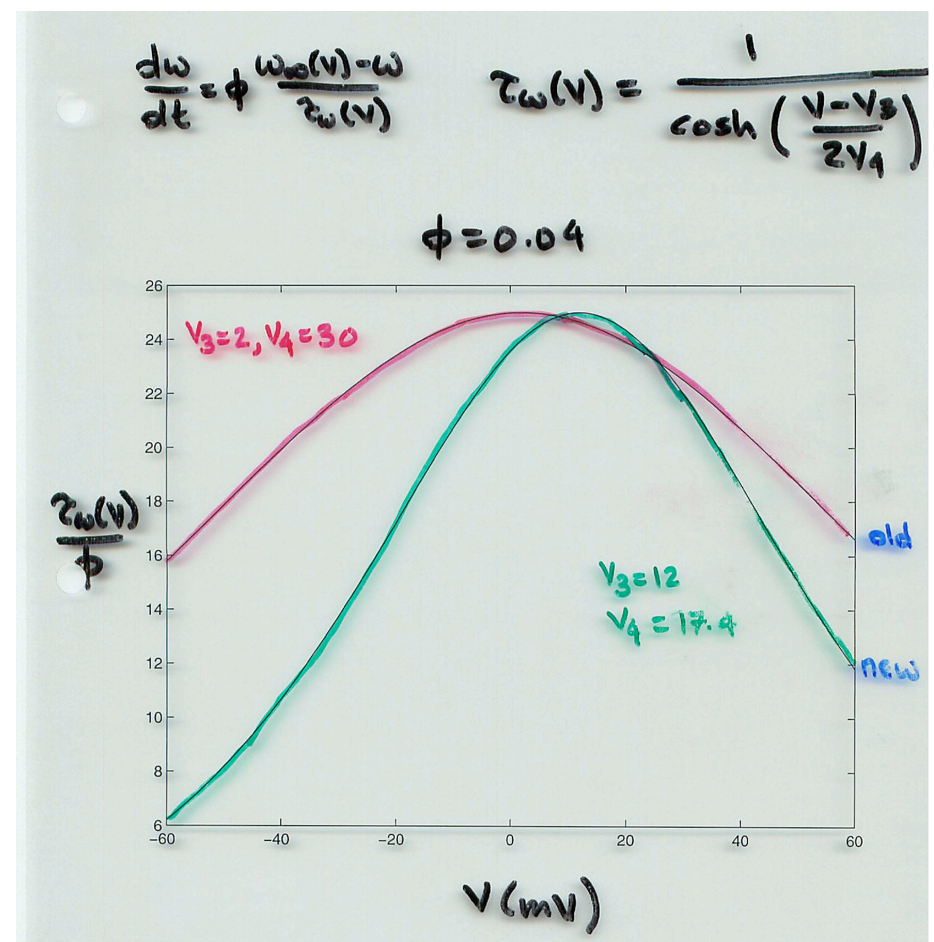
Starting from stable equilibrium Iapp increases through a subcritical Hopf bifurcation



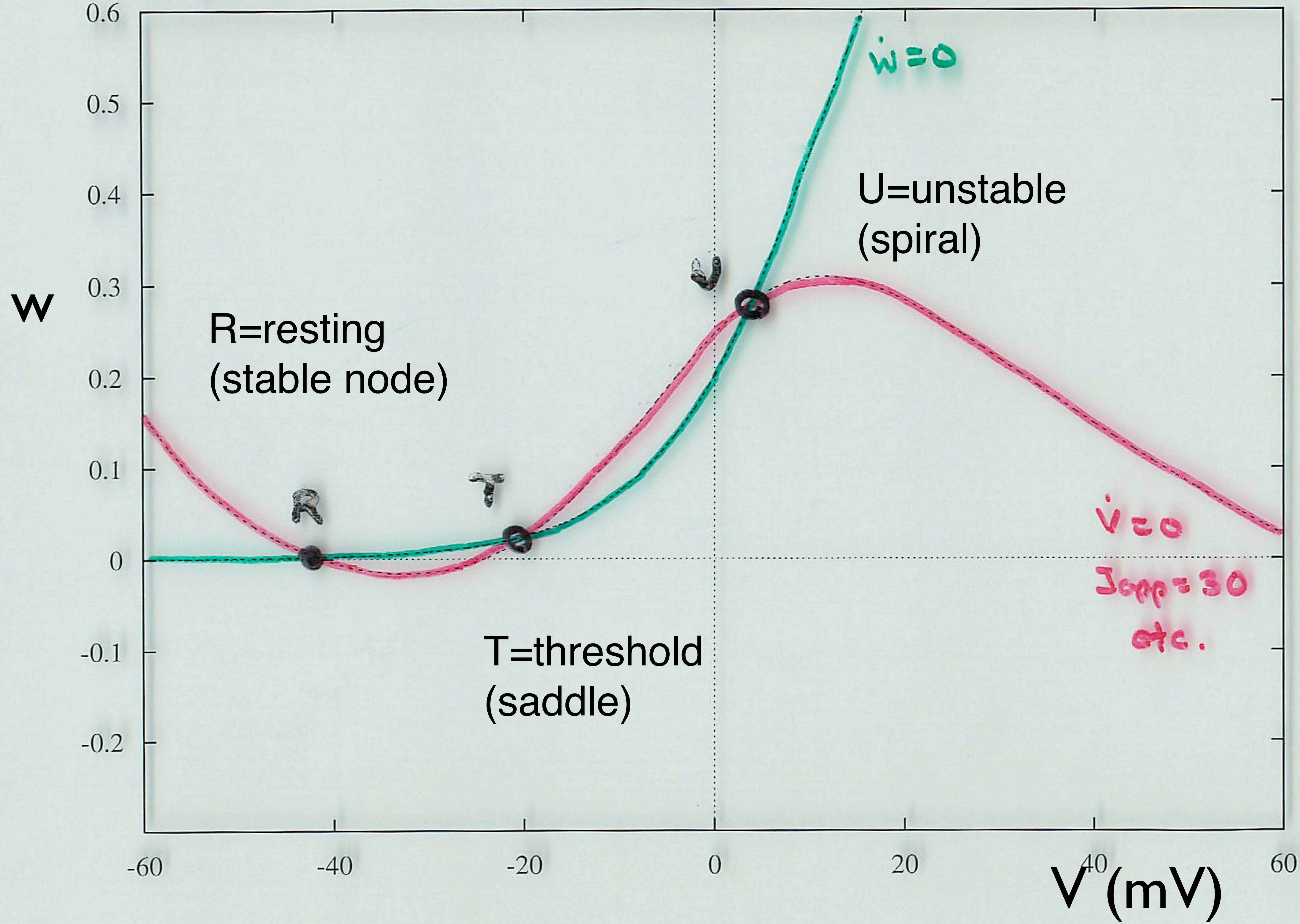


type 1 excitability and oscillations in the Morris-Lecar model

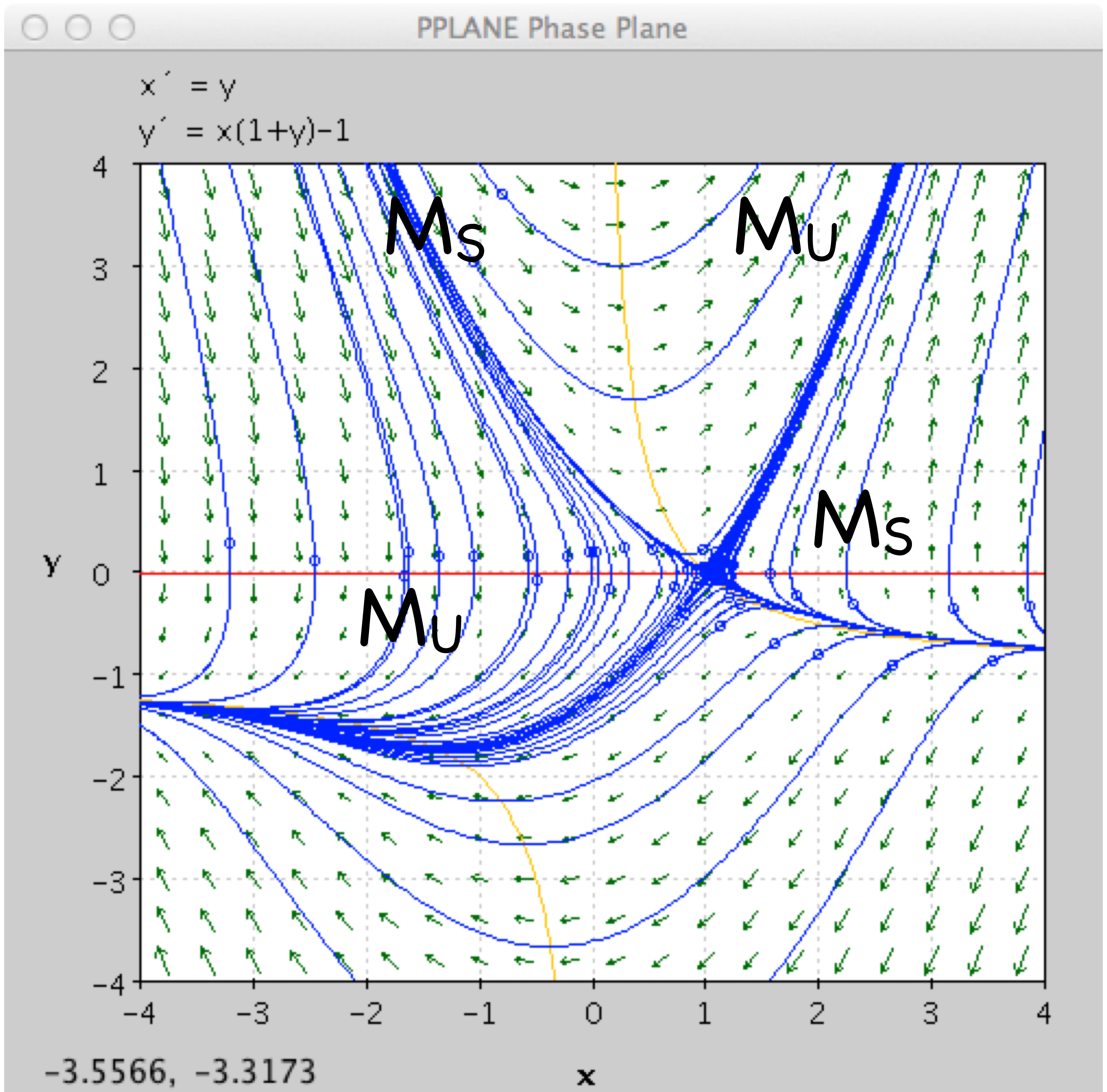
voltage-dependent time constant for activation of the potassium channels changed to transition from type 2 to type 1



sub-critical applied current - type I excitability



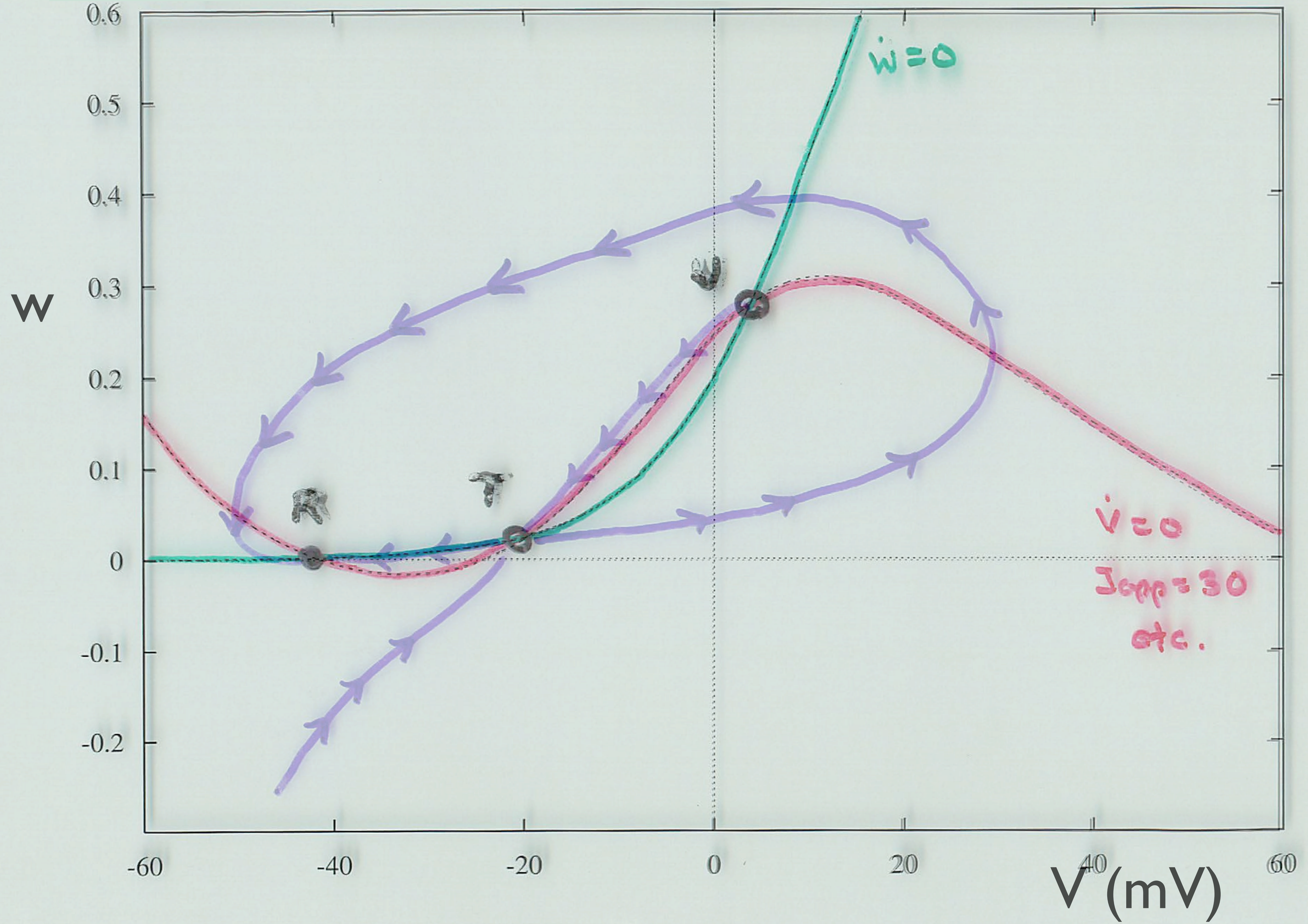
saddle points have stable and unstable manifolds



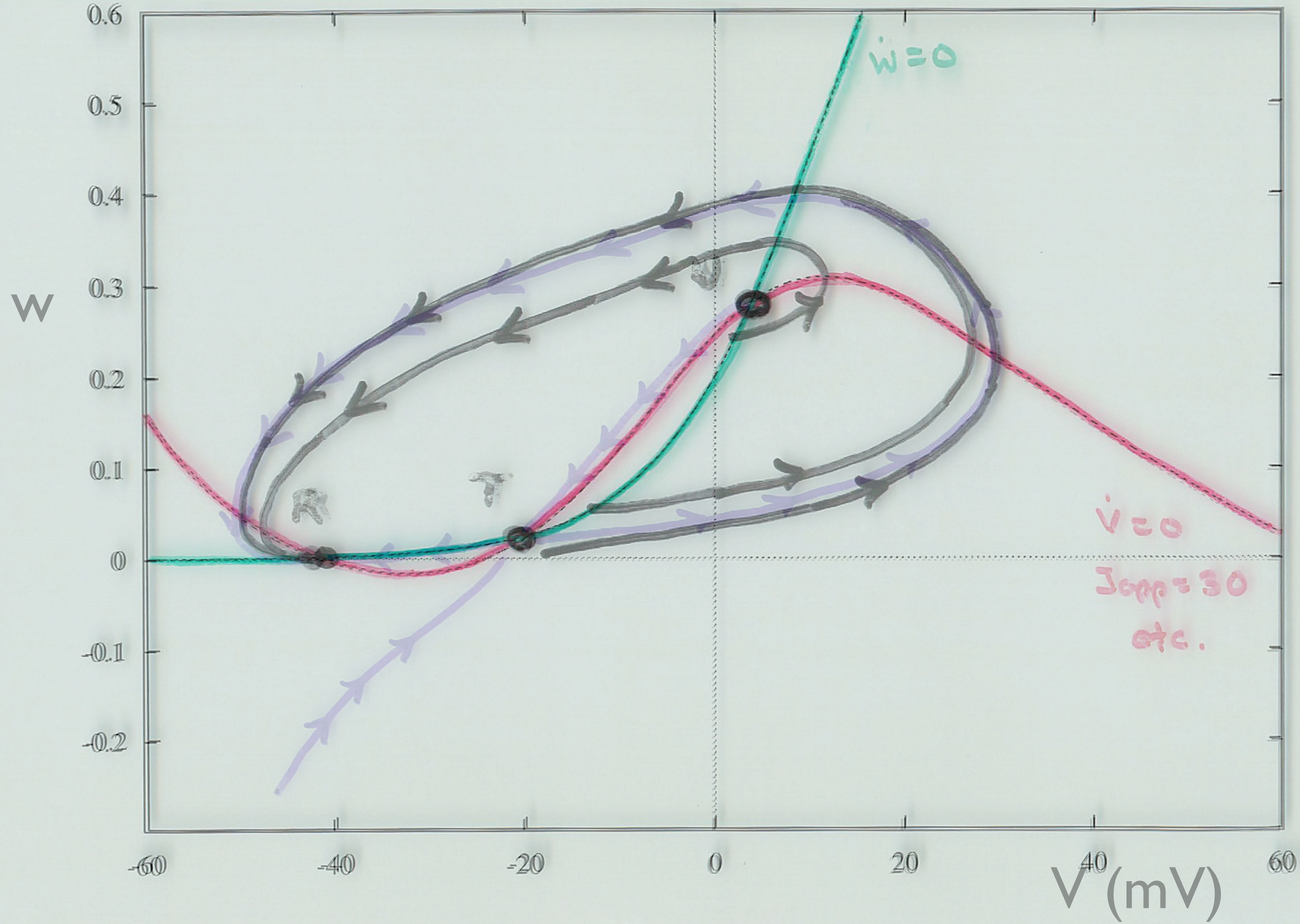
M_U = unstable manifold

M_S = stable manifold

stable manifold of saddle is a separatrix

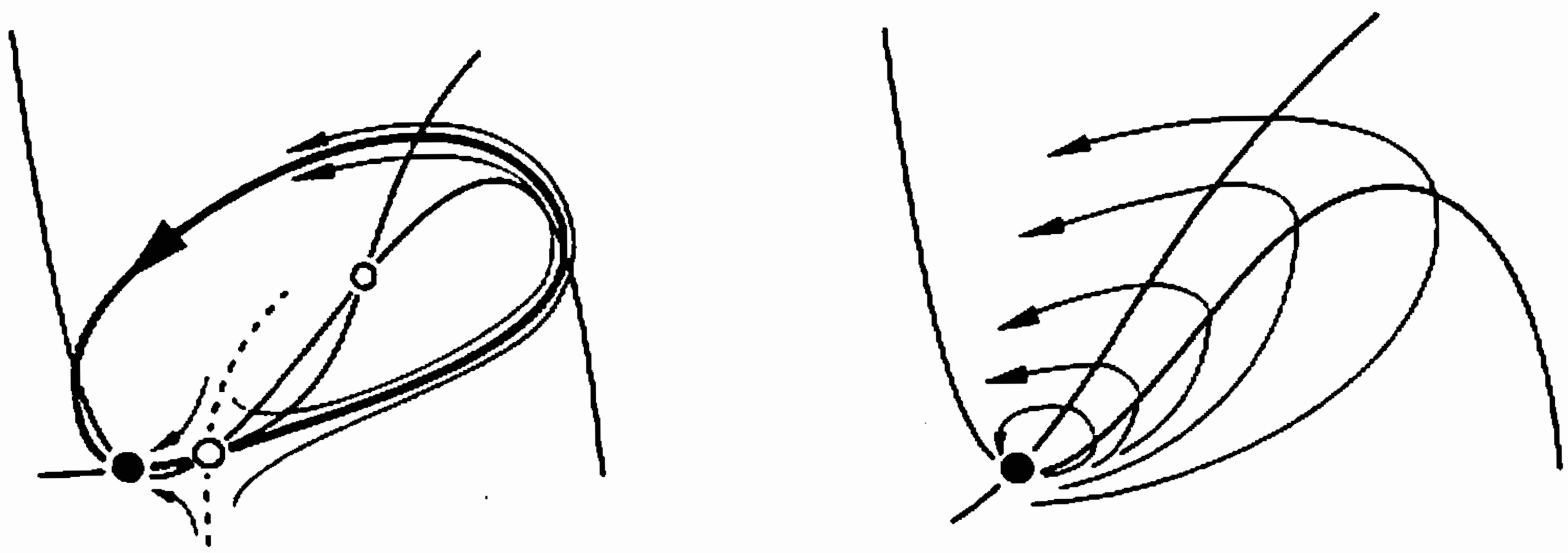


stable manifold of saddle is a separatrix



type 1 excitability

type 2 excitability



a

b

Figure 2.50. a. Class 1 neurons have action potentials of fixed amplitude. b. Class 2 neurons can have action potentials of arbitrary small amplitude.

type 1 excitability   type 2 excitability

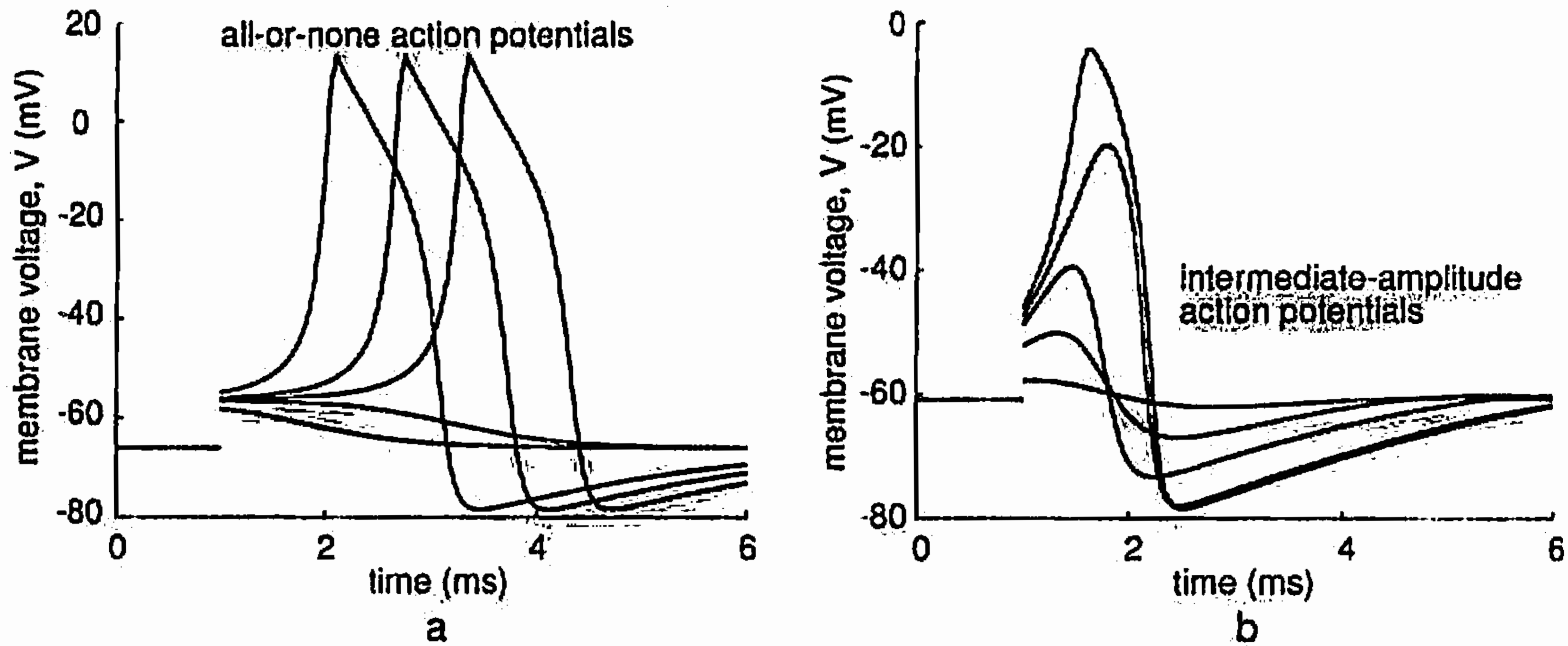
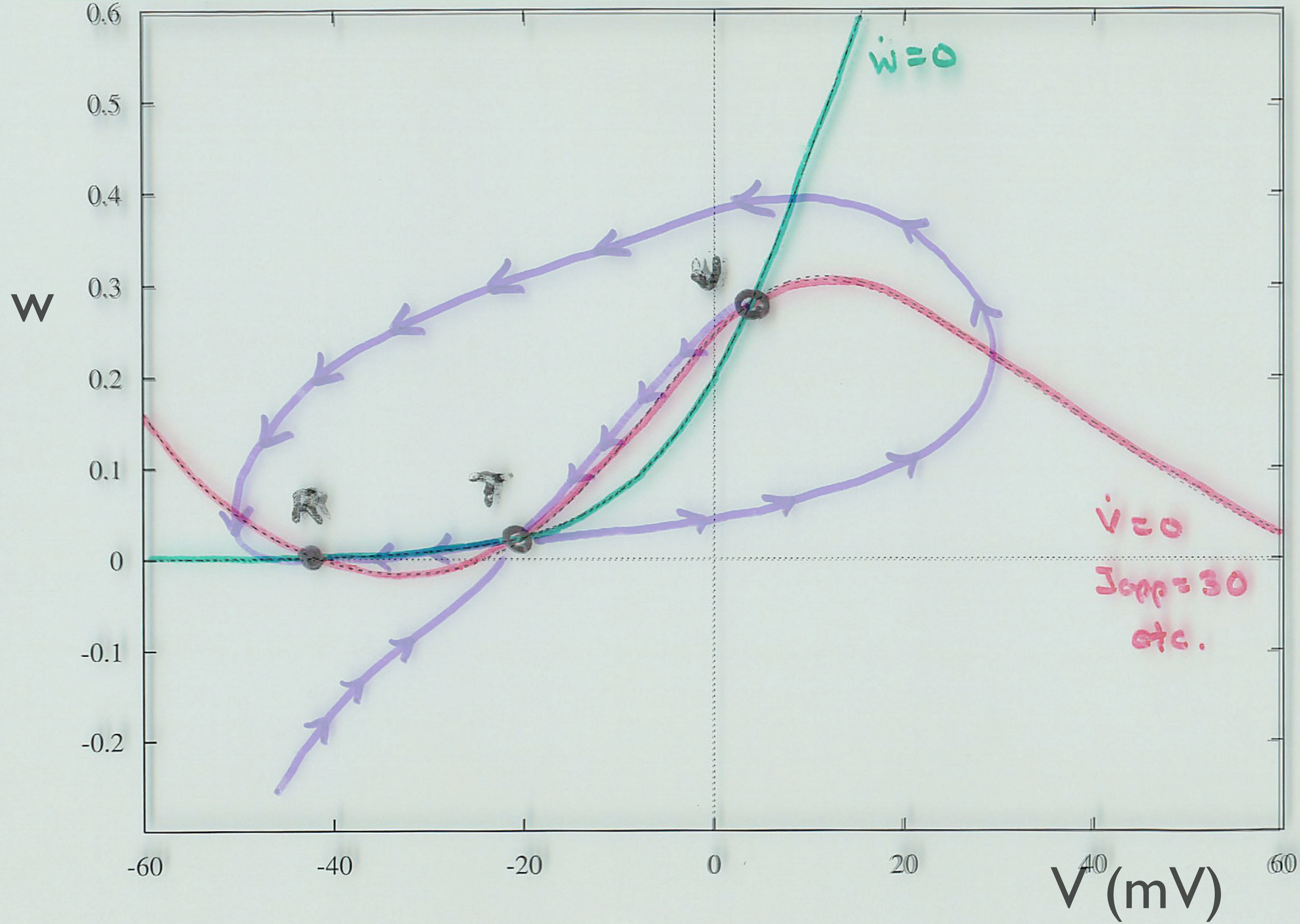


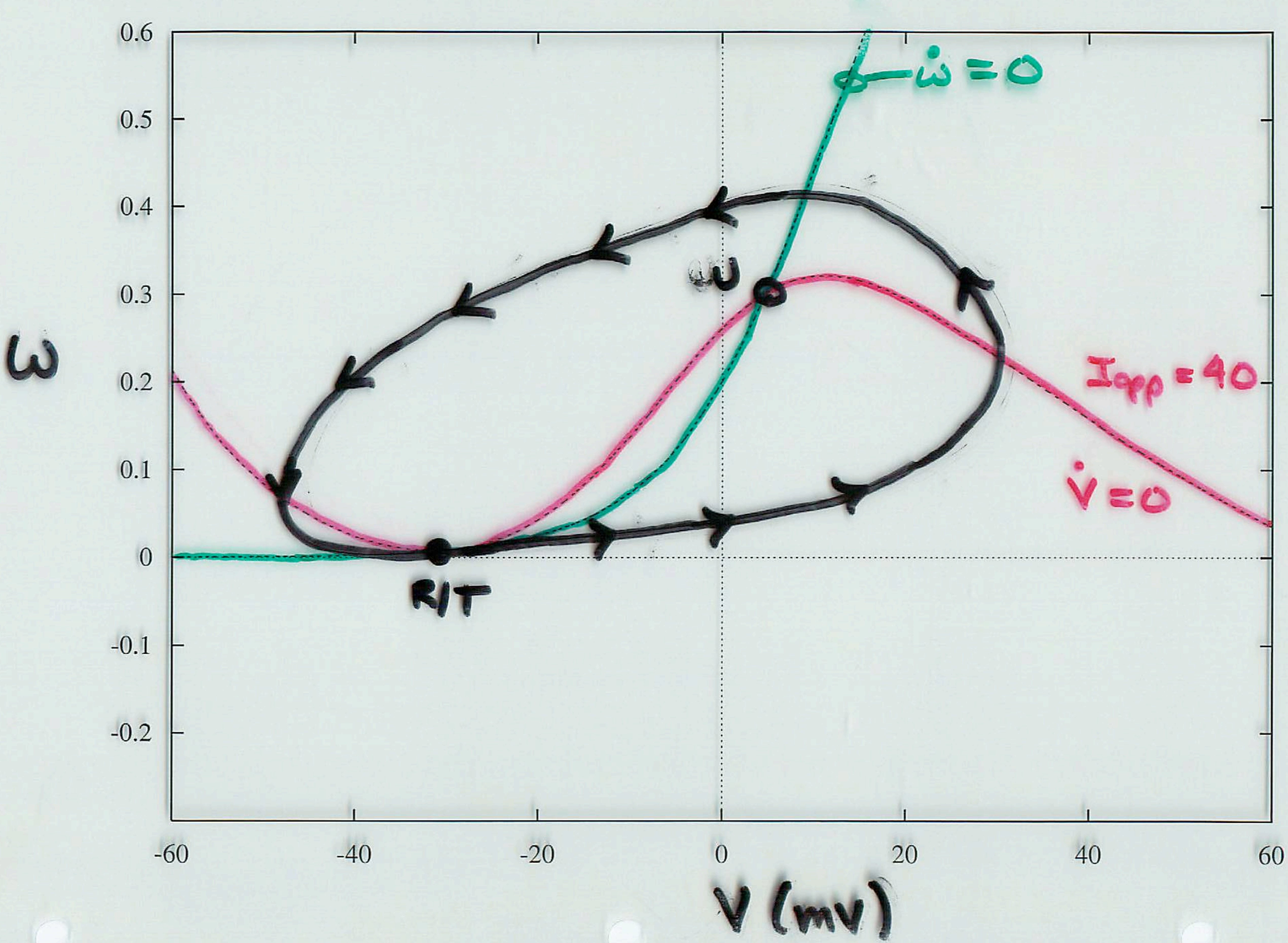
FIGURE 4.2. a. All-or-none action potentials in the $I_{\mathrm{Na,p}}+I_{\mathrm{K}}$-model (4.1,4.2) with high-threshold K^+ current. b. Failure to generate all-or-none action potentials in the $I_{\mathrm{Na,p}}+I_{\mathrm{K}}$-model with low-threshold K^+ current.

type I oscillations in the phase plane

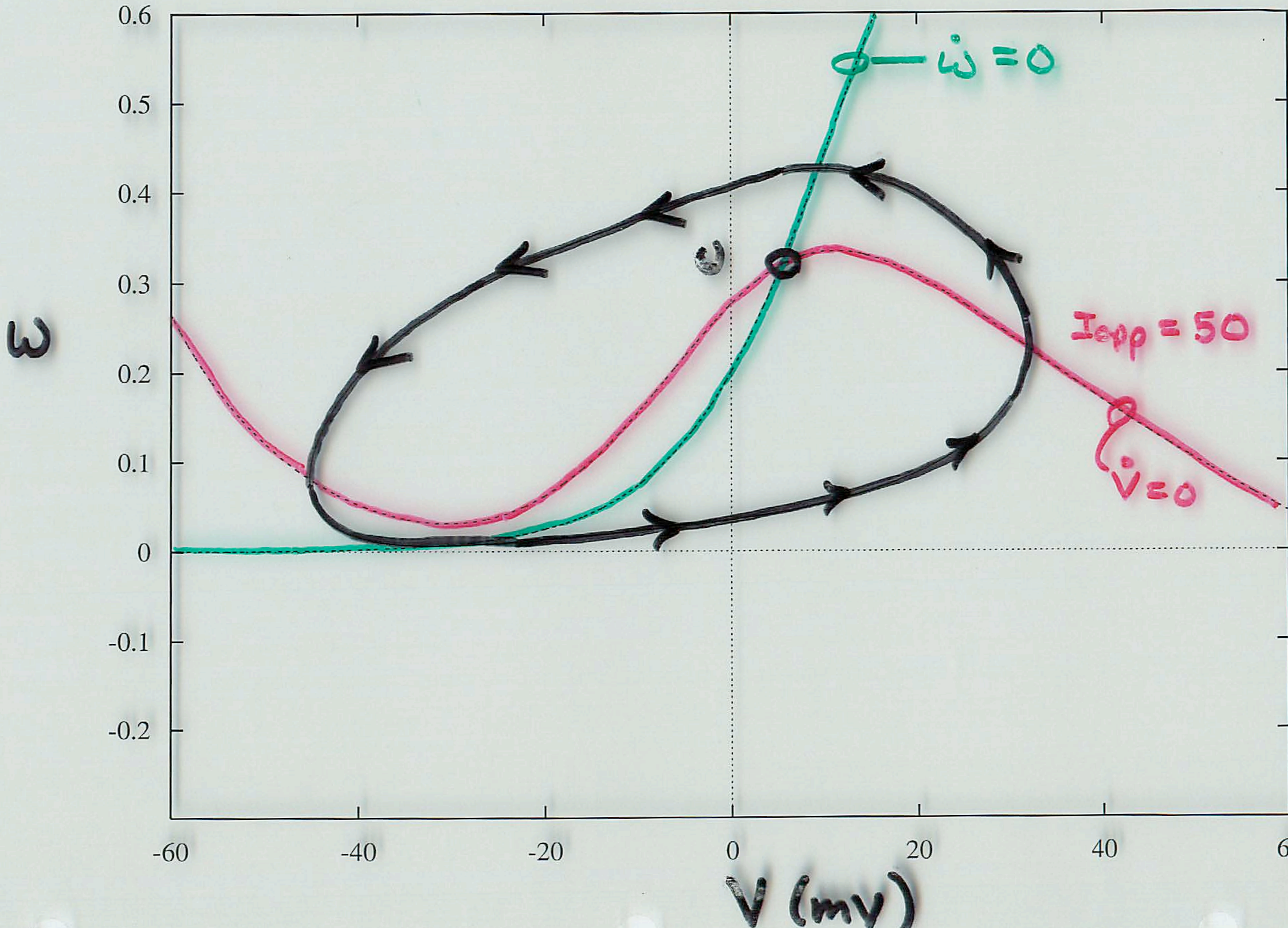
unstable manifold of saddle is also a separatrix



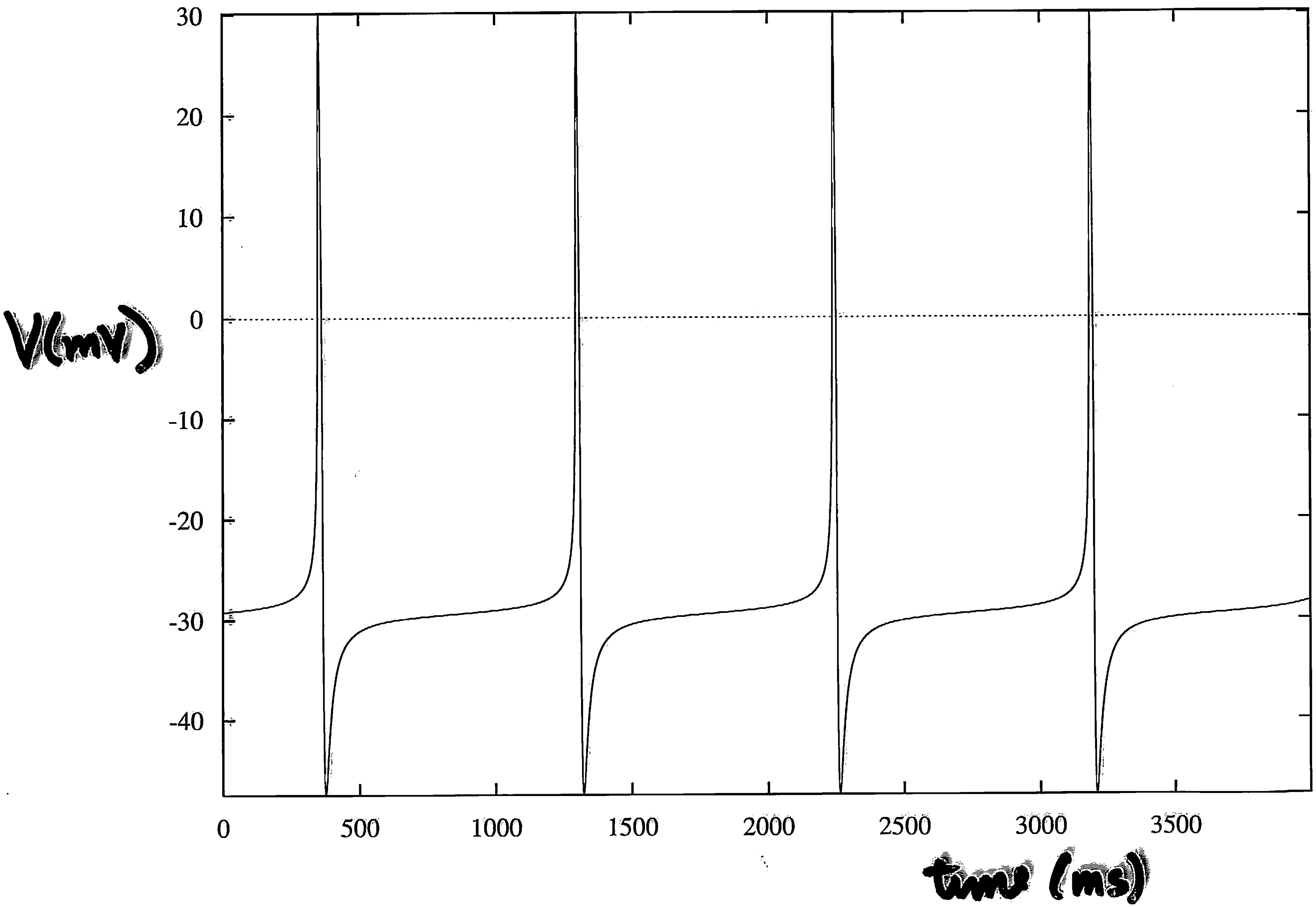
critical applied current

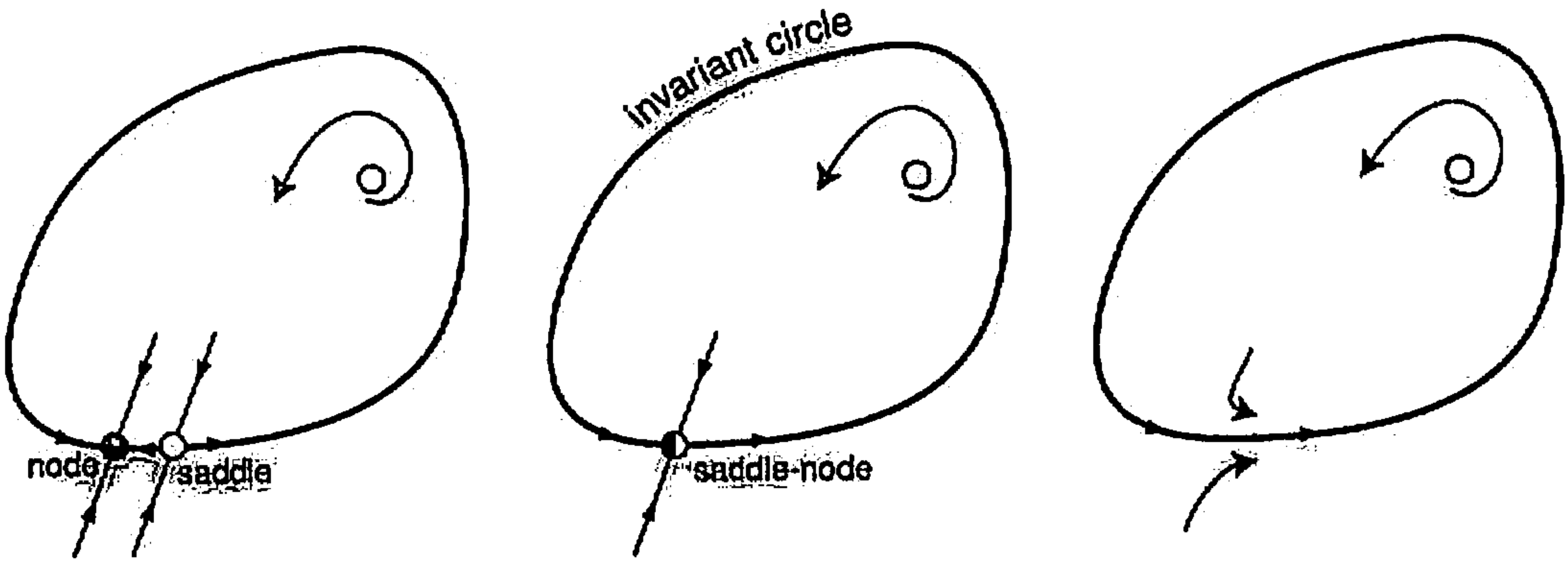


super-critical applied current

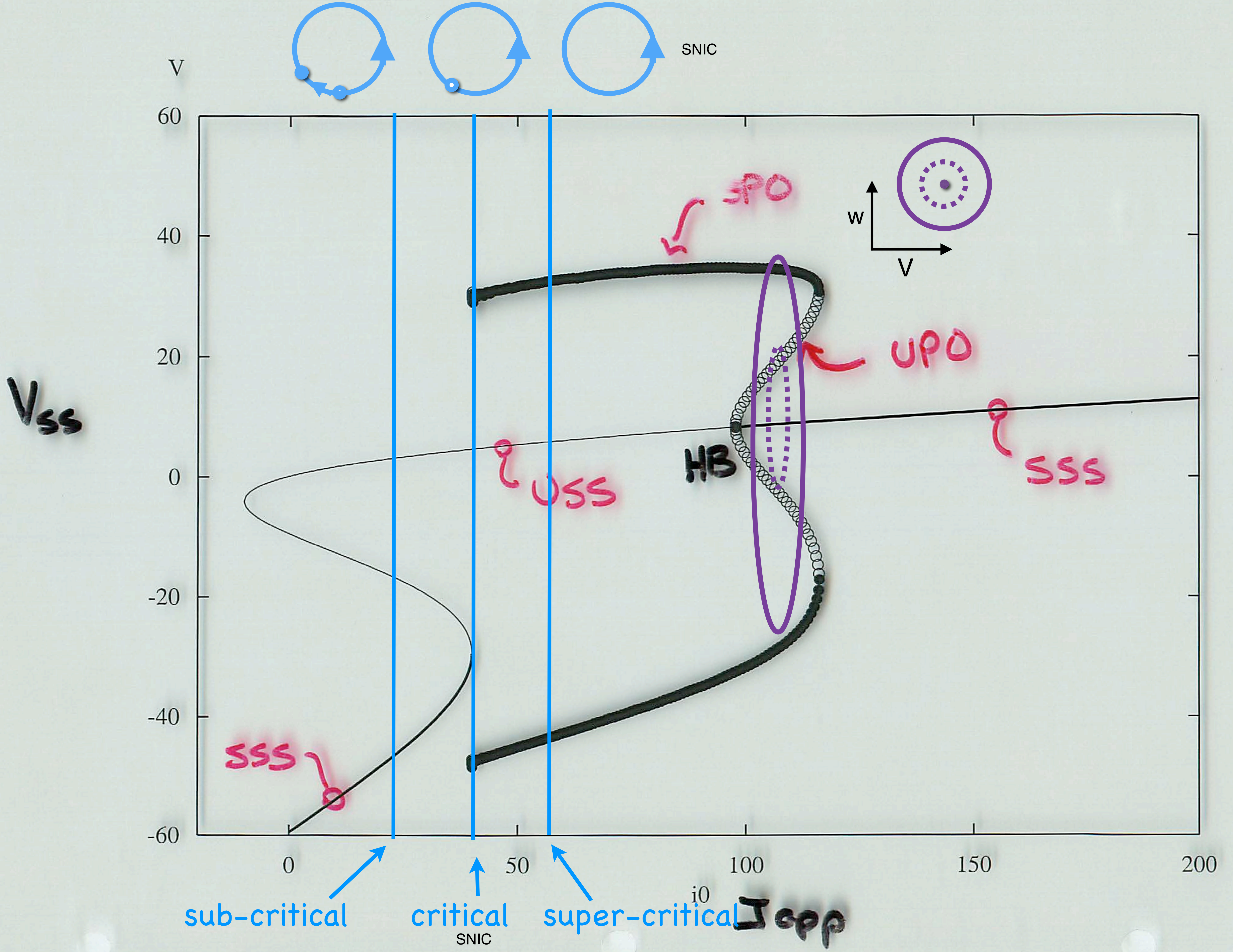


Type 1 oscillations with Iapp ≈ critical



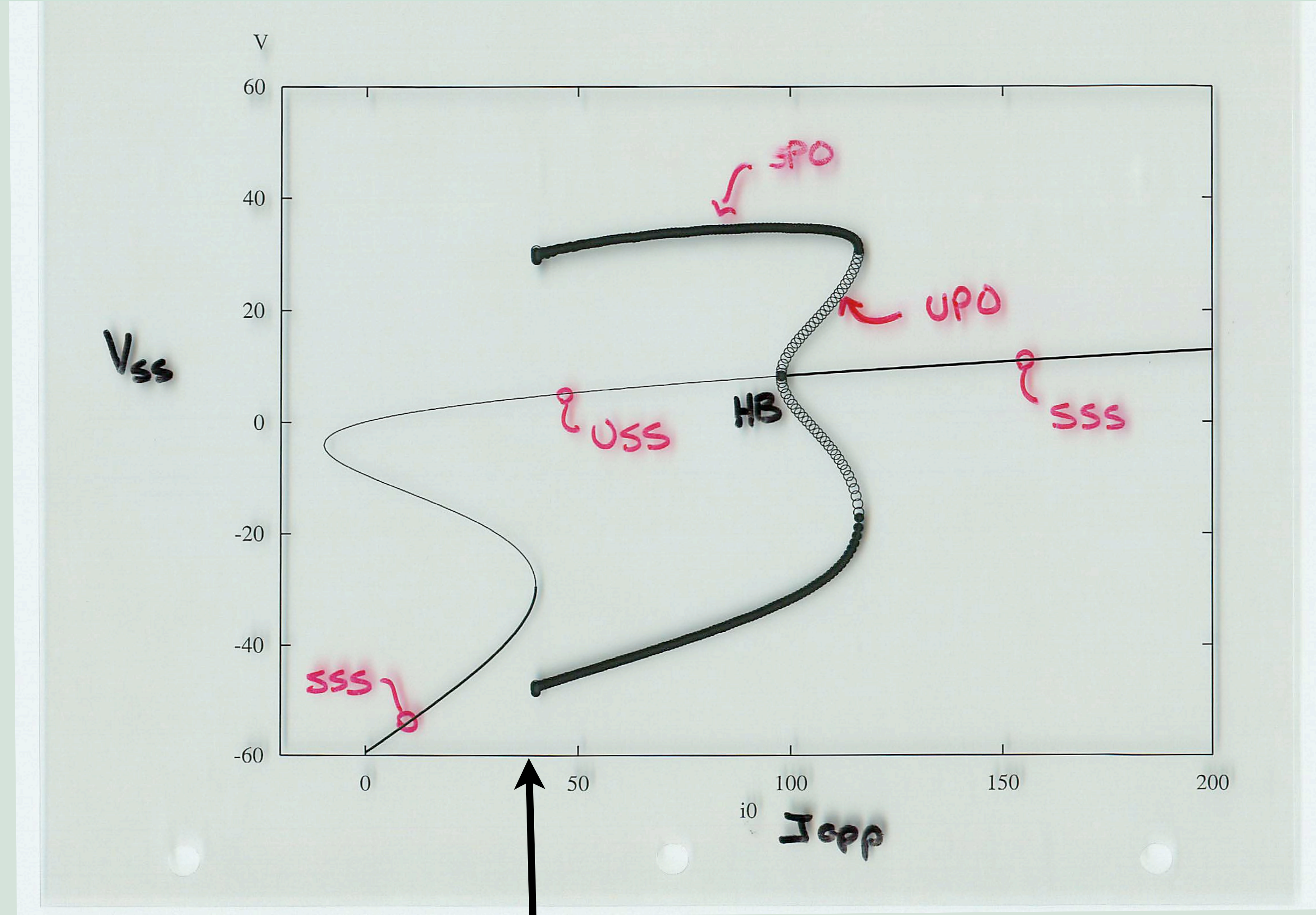


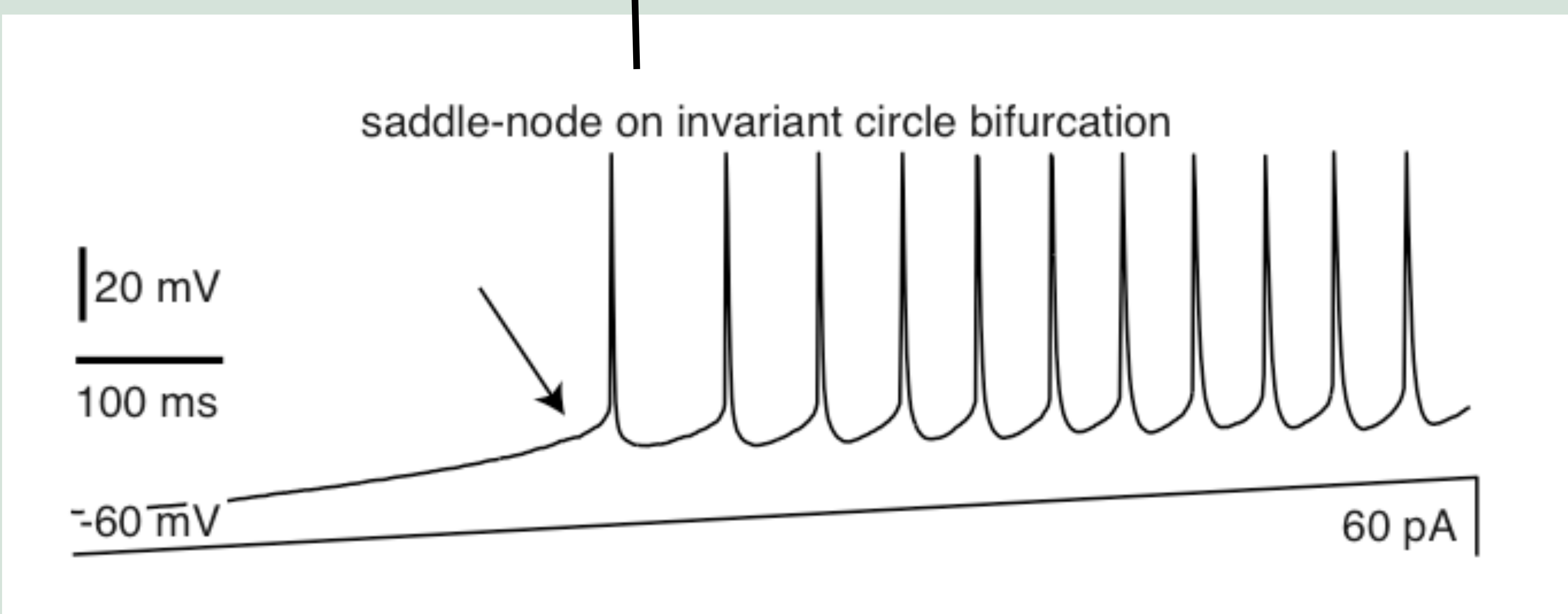
saddle-node on invariant circle (SNIC) bifurcation



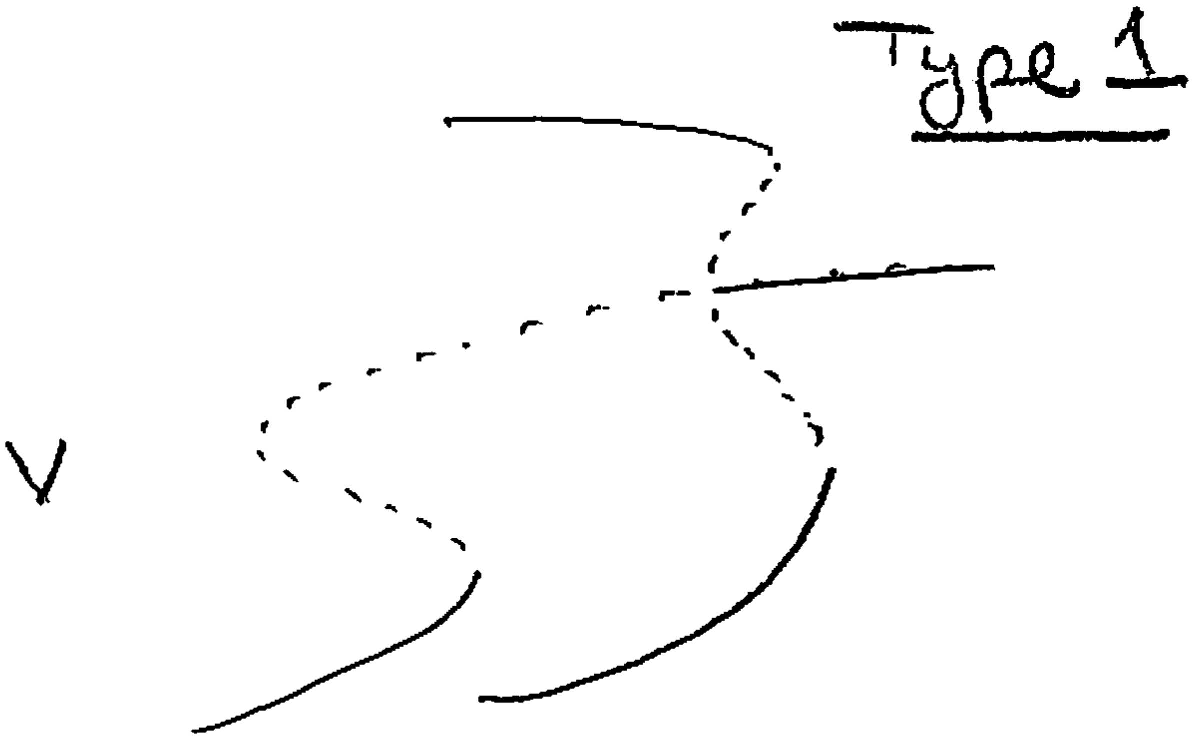
SNIC
V
60
40
20
0
-20
-40
-60
Vss
SPO
UPO
HB
USS
SSS
SSS
w
V
0
50
100
150
200
i0
Iapp
sub-critical
critical
SNIC
super-critical

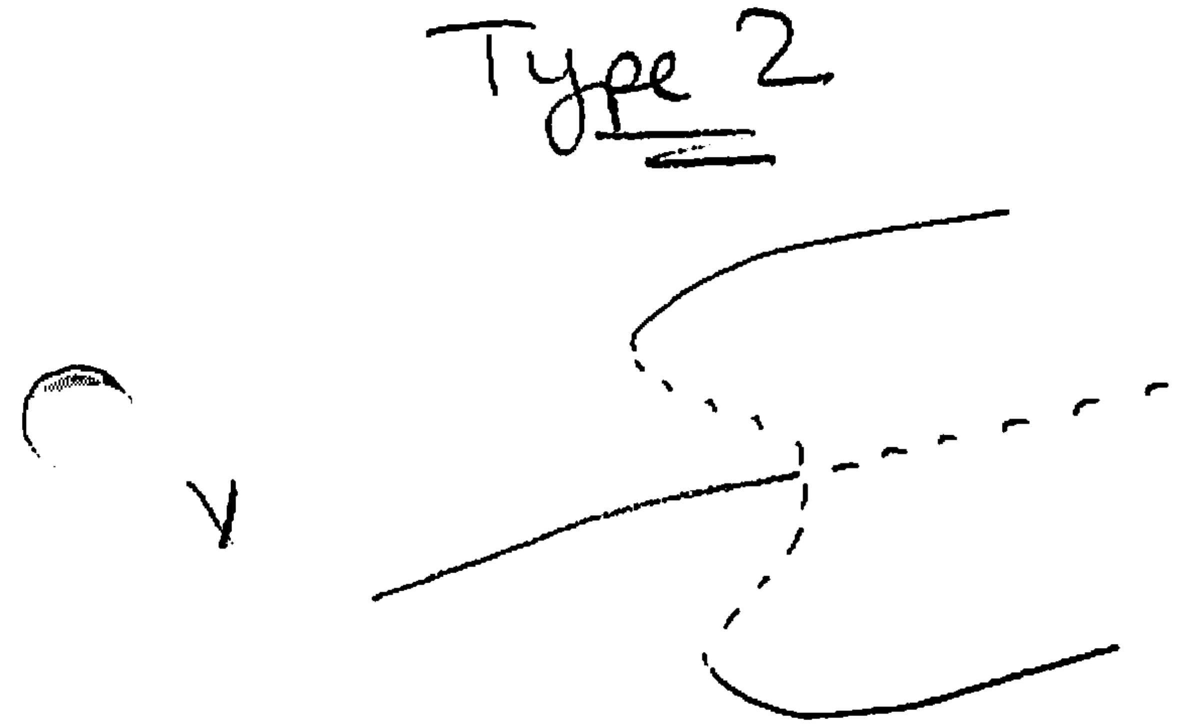
Passage through SNIC bifurcation





bifurcation diagrams showing emergence of oscillations





SNIC bifurcation
"saddle-node on an invariant circle"

Hopf bifurcation
(sub-critical)