DİNAMİK SİSTEMLER, ÇATALLANMA TEORİSİ VE UYGULAMALARI

<u>Deniz Alaçam</u>

KARMAŞIK SİSTEMLER VE VERİ BİLİMİ YAZ OKULU

18 Temmuz 2019

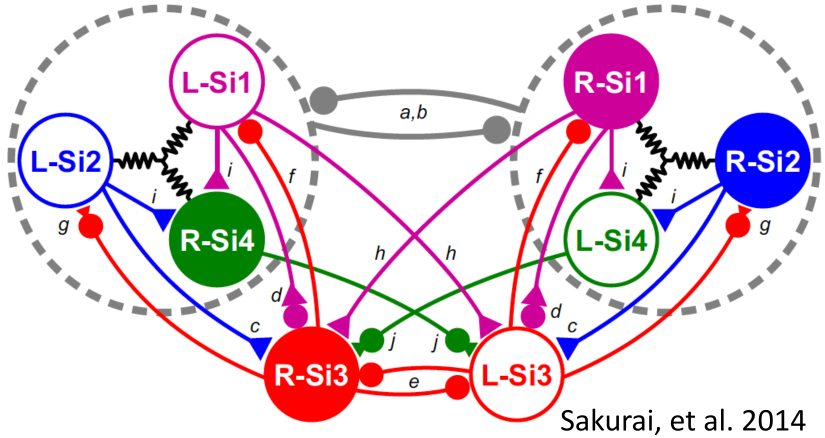
Kadir Has Üniversitesi, İstanbul

ULUDAĞ UNIVERSITY DEPARTMENT OF MATHEMATICS

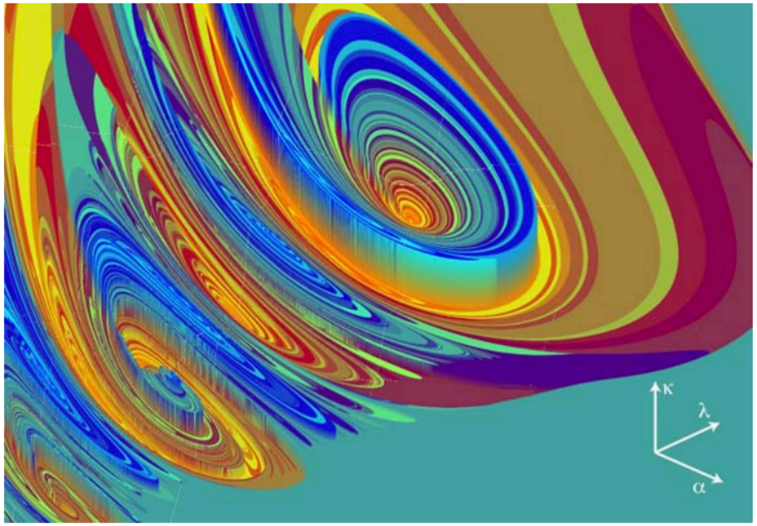
Georgia State University | Mathematics and Statistics

Ders Planı

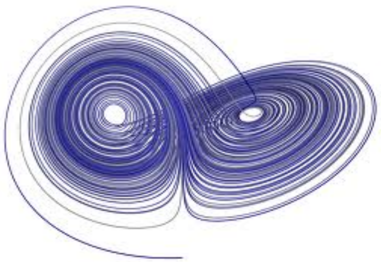
- Bölüm I :
  - Dinamik Sistemler
  - Sabit Nokta Analizi
  - Çatallanma(Bifurcation) Teorisi
- Bölüm II:
  - Uygulama: 3-Nod Network ve Ritim Üretimi

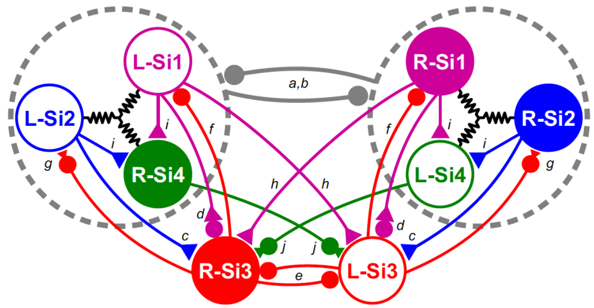


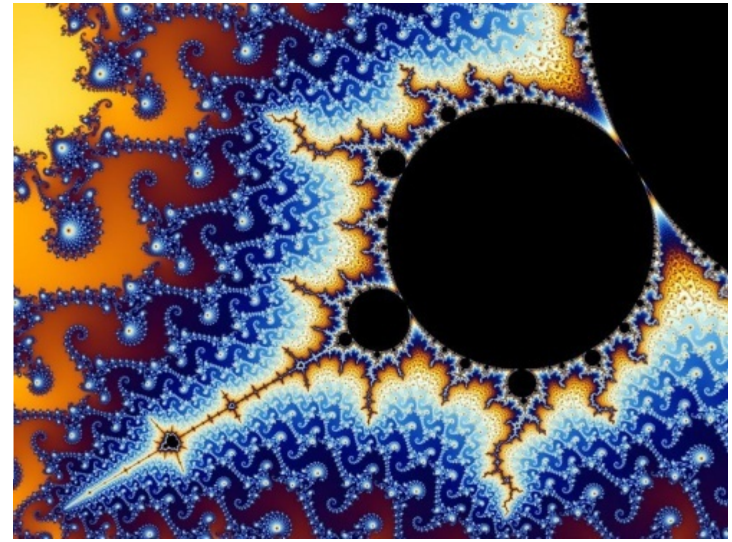
Sakurai, et al. 2014

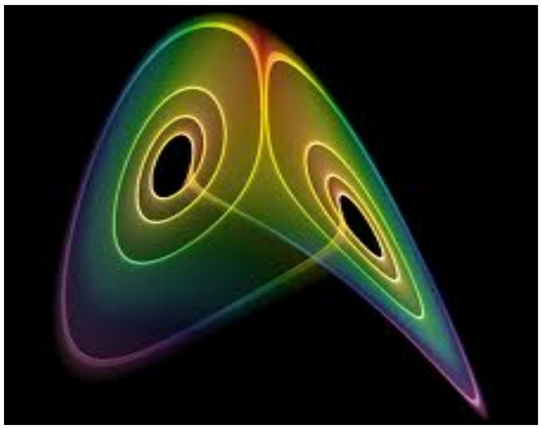


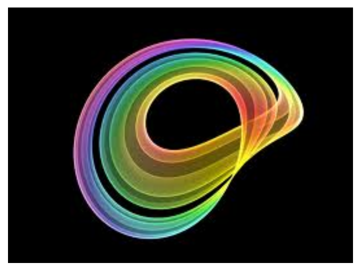
Dinamik Sistemler

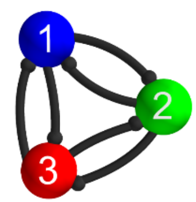


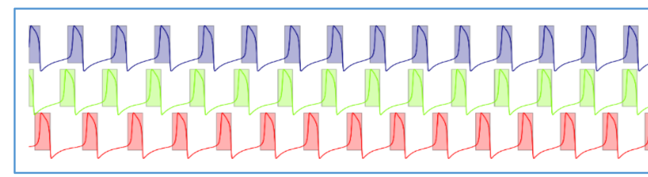


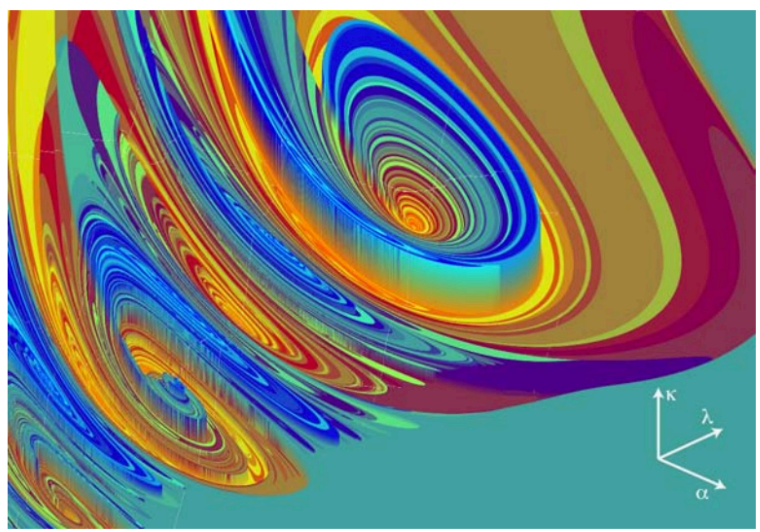


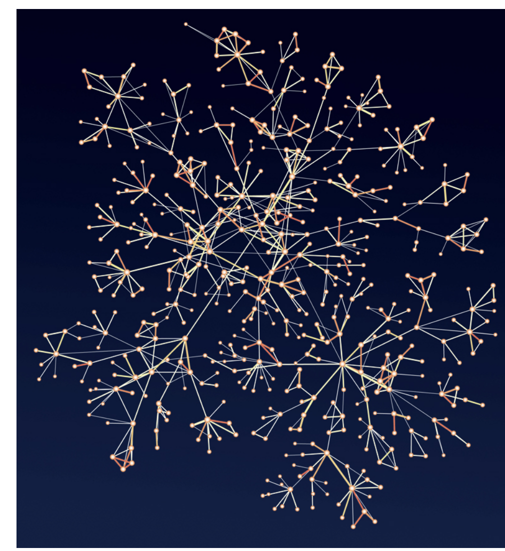




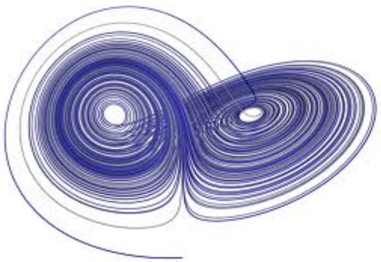


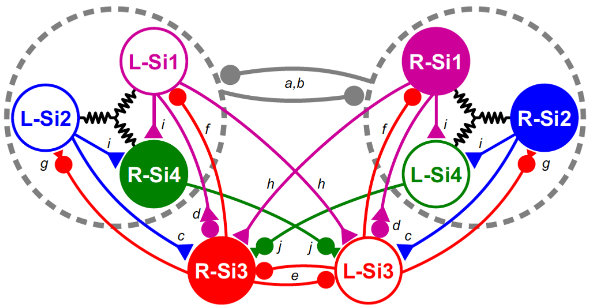


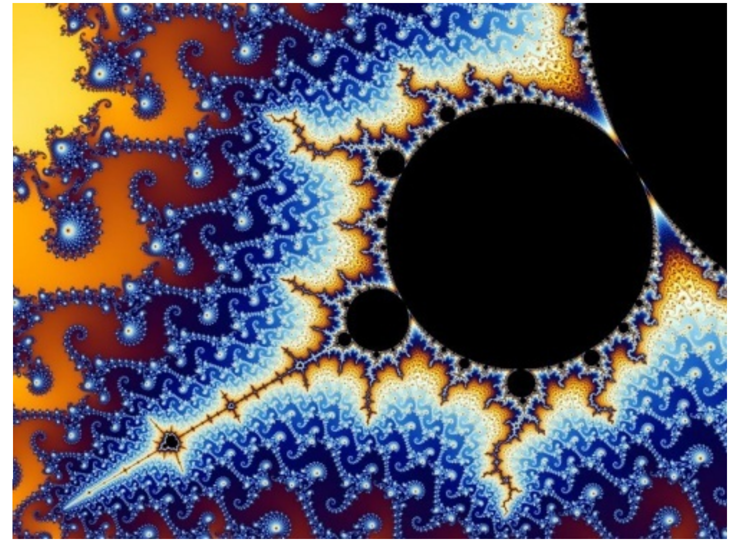


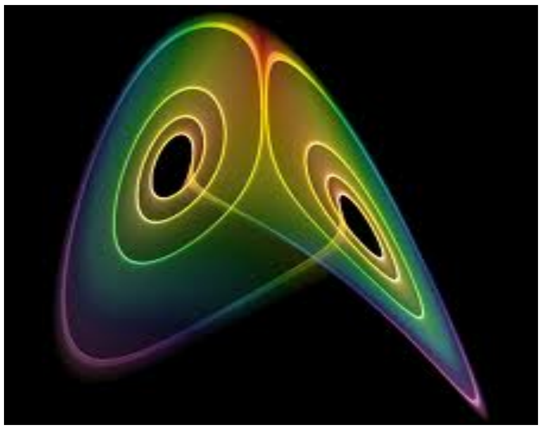


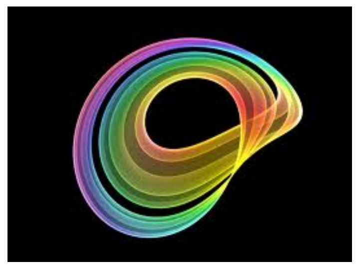
Dinamik Sistemler

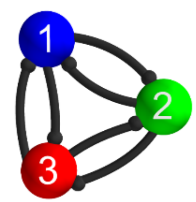


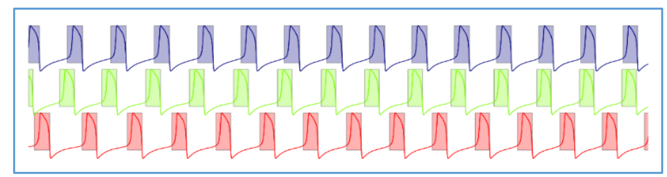




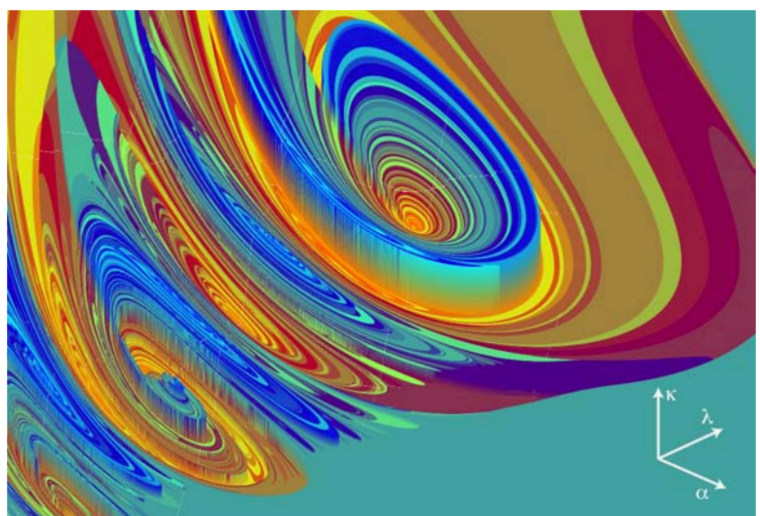


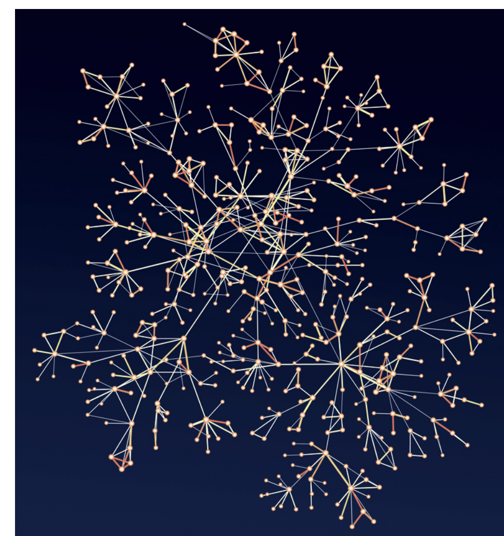






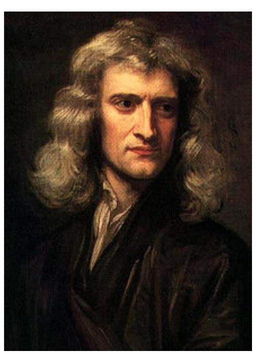
Dinamik sistem
belirlenmiş bazı kurallar gereğince zamana göre değişiklik gösteren sistemdir.





Dinamik Sistemler Tarihi

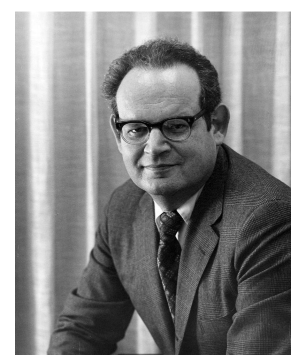
- 1600ler
  - Newton : ODEs, iki boyutlu problem, Gezengenlerin orbitleri
- 1800ler
  - Poincare : Geometrik yaklasım, Baslangıç degerlerine duyarlılık (Kaos)
- 1920 – 1950
  - Lineer olmayan osilatorler
- 1950ler
  - Hodgkin – Huxley: Nöral modelleme
- 1960lar
  - Lorenz : Kaotik sistemler, Hava tahmini
- 1970
  - Mandelbrot : Fraktal
- 1975
  - May : Logistik denklem
- 1980
  - Kaos, Non-lineer dinamik
- 1990
  - Muhendislik uygulamaları
- 2000
  - Kompleks sistemler, network


Newton


Poincare


Hodkin-Huxley


Lorenz


Mandelbrot


May

Dinamik Sistemler

$$\frac{dx}{dt} = f(x)$$

x asagidaki gibi tanımlanan bir vektor

$$\vec{x}(t) = [x_1(t), x_2(t), \ldots\ldots, x_n(t)]$$

f ise bir veya birden fazla boyutlu bir fonksiyon

$$f_1(x_1, x_2, \ldots., x_n), f_2(x_1, x_2, \ldots., x_n), \ldots., f_n(x_1, x_2, \ldots., x_n)$$

Tüm sistem ise bir dizi fonksiyon olarak tanımlanır.

$$\frac{dx_1}{dt} = \dot{x}_1 = f_1(x_1, x_2, \ldots., x_n)$$

$$\frac{dx_2}{dt} = \dot{x}_2 = f_2(x_1, x_2, \ldots., x_n)$$

.

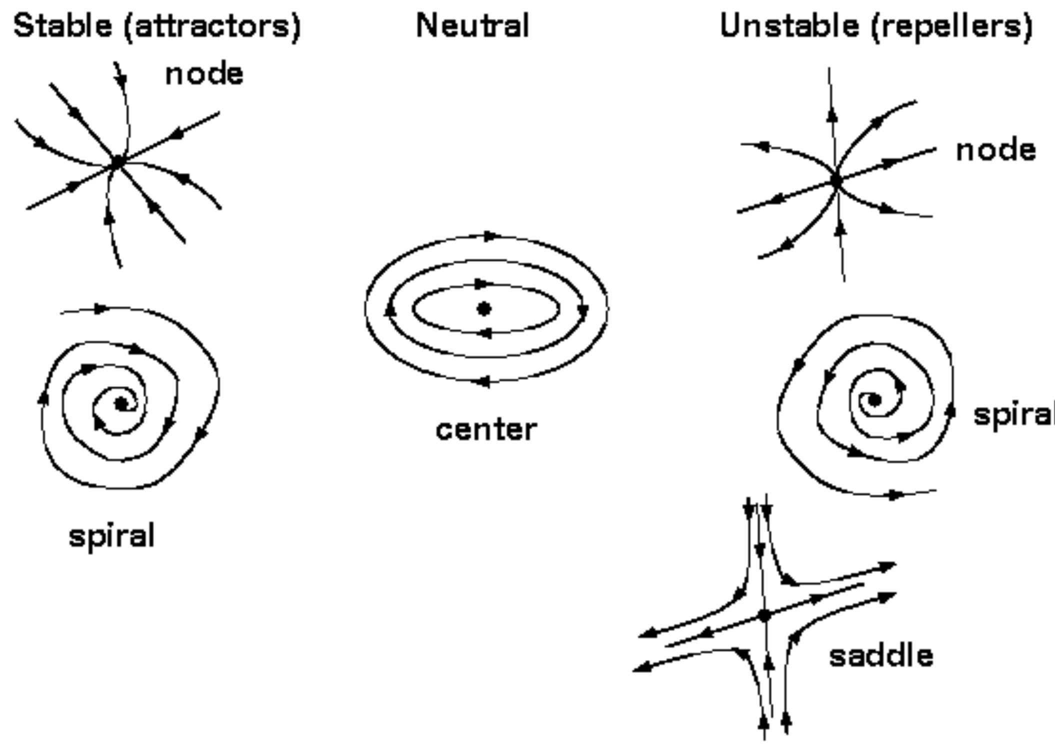
.

$$\frac{dx_n}{dt} = \dot{x}_n = f_n(x_1, x_2, \ldots., x_n)$$

Sabit noktalar ve Kararlılık

- Bir ***sabit nokta*** sistemin zaman karsısında degisim göstermedigi bir özel nokta olarak tanımlanır. Denge noktası veya kritik nokta olarak da adlandırılabilir.
- dx/dt = f(x) sistemini ele alırsak, sabit nokta olan x^*, $f(x^*)=0$ denkleminin çözüm olarak bulunur. Diskre sistemler için $x^*= f(x^*)$.

$$f(x^*)=0$$



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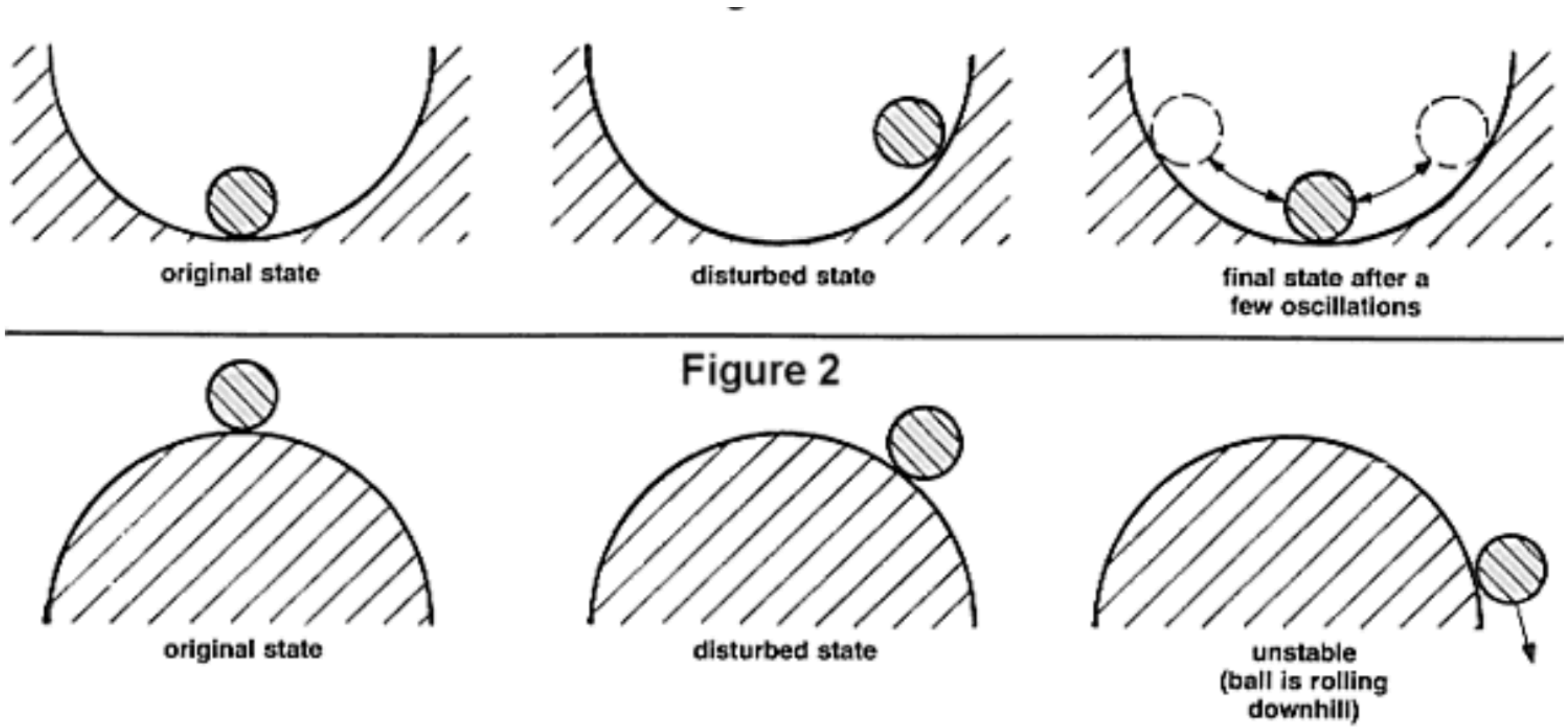

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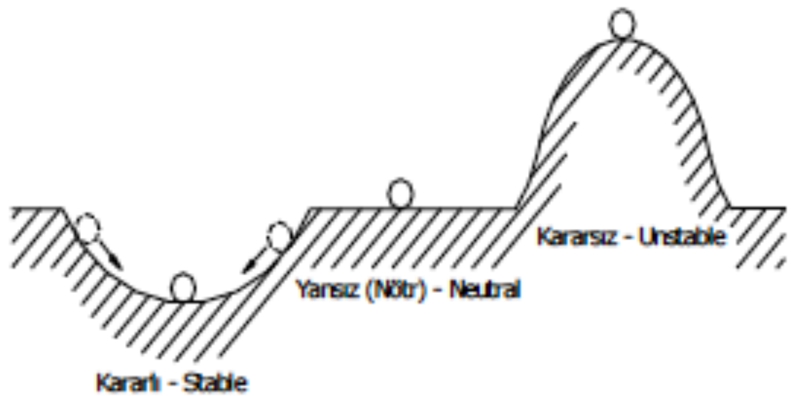
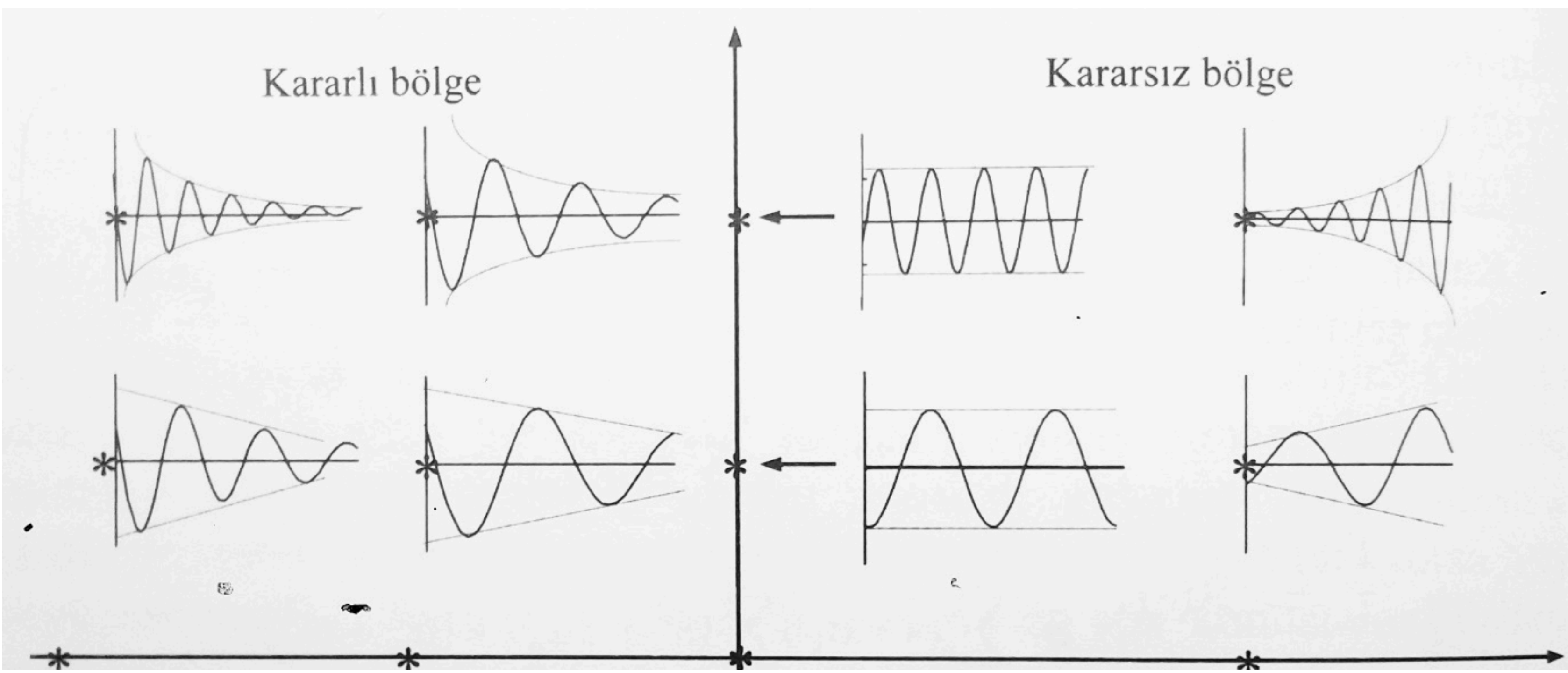
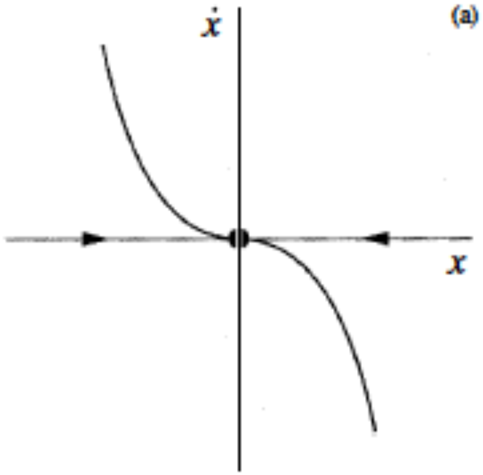
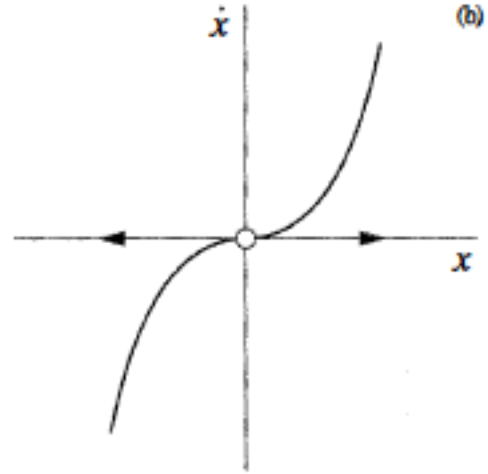




Sabit noktalar ve Kararlılık

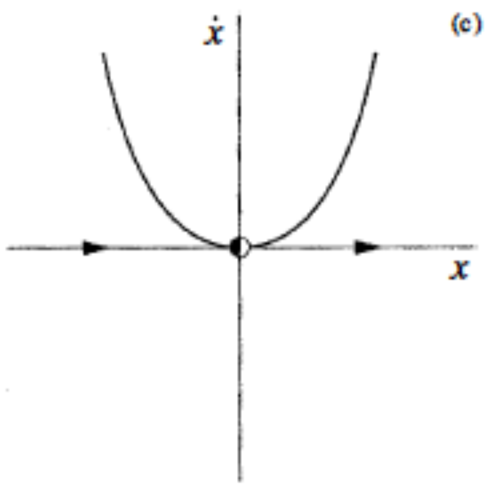
$$\frac{dx}{dy} = -x^3$$

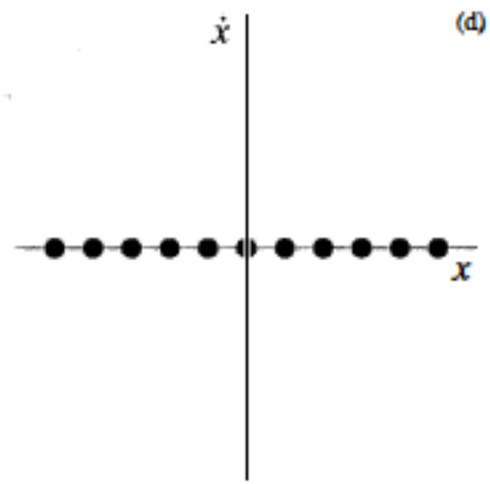




$$\frac{dx}{dy} = x^3$$

$$\frac{dx}{dy} = x^2$$





$$\frac{dx}{dy} = 0$$

Çatallanma(Bifurcation) Teoremi

- Bir sabit noktanın bir parametreye baglı olarak karakterindeki degisime çatallanma denir.

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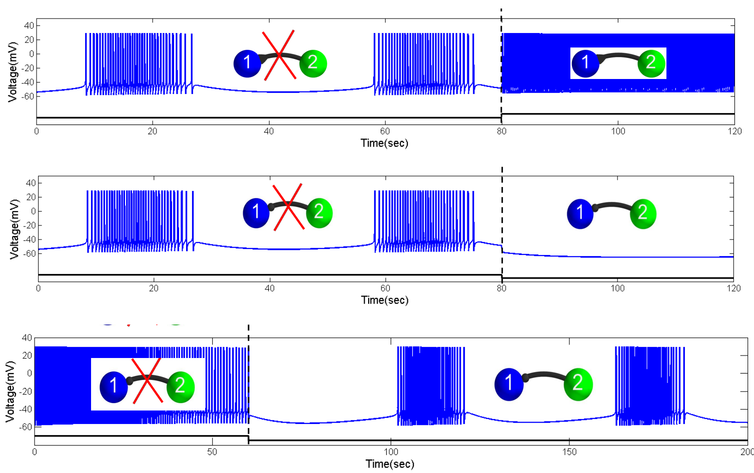

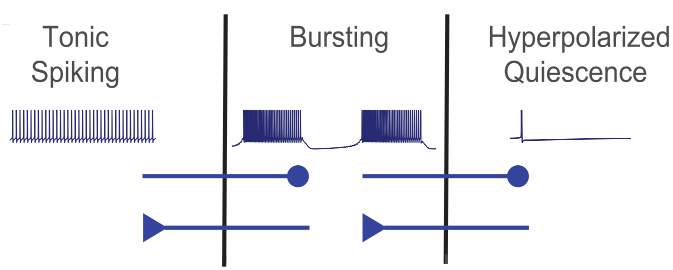

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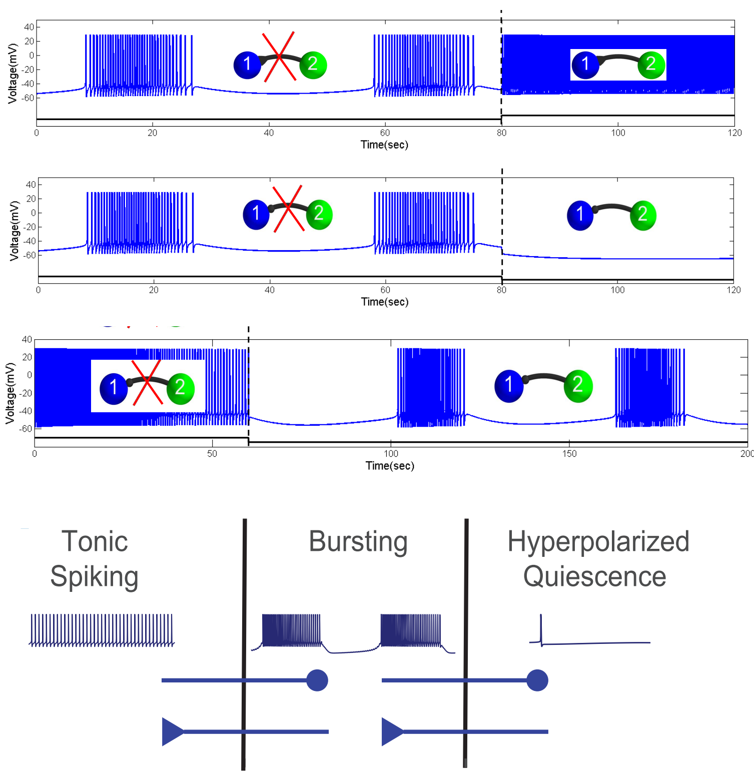
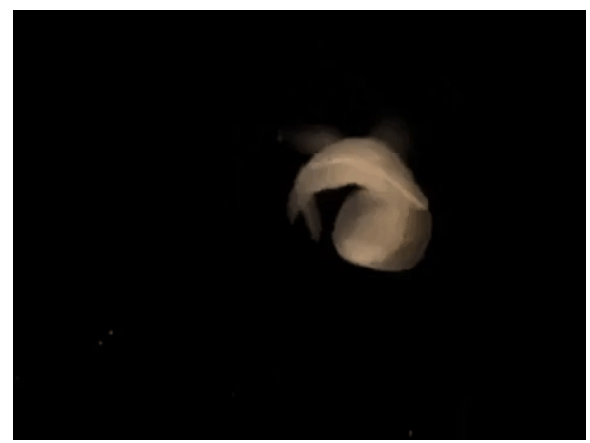
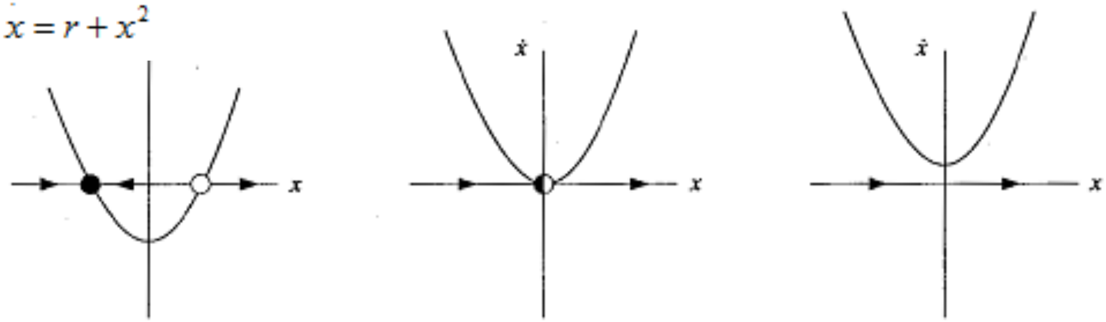




Çatallanma Türleri

Eger-Dügüm (Saddle Node) Çatallanması

$\dot{x} = r + x^2$



(a) $r<0$ (b) $r=0$ (c) $r>0$

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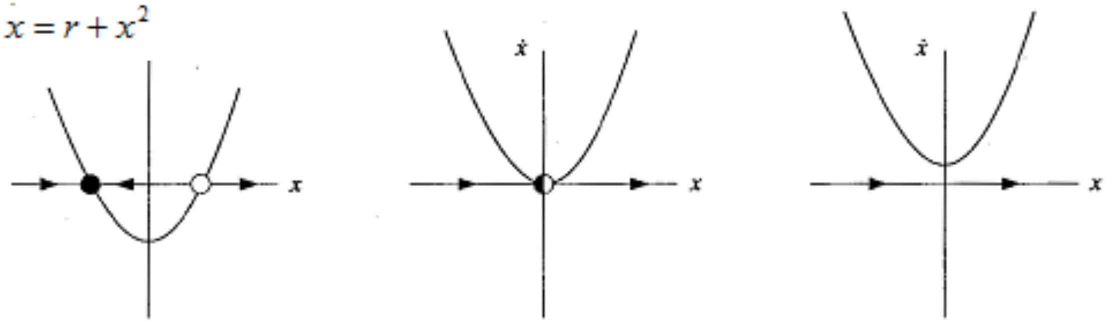

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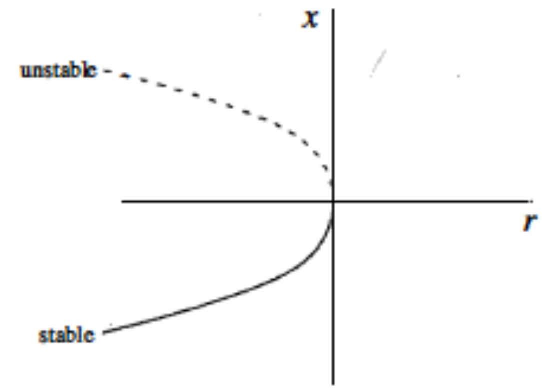

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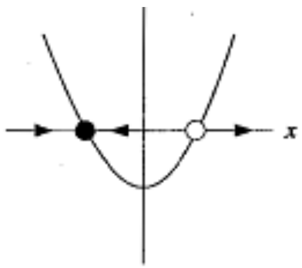
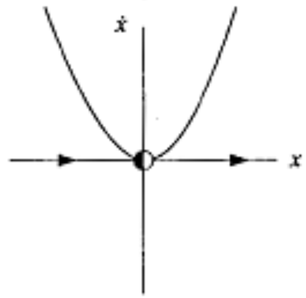
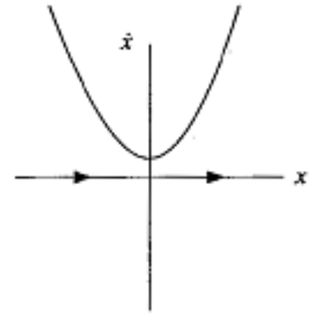


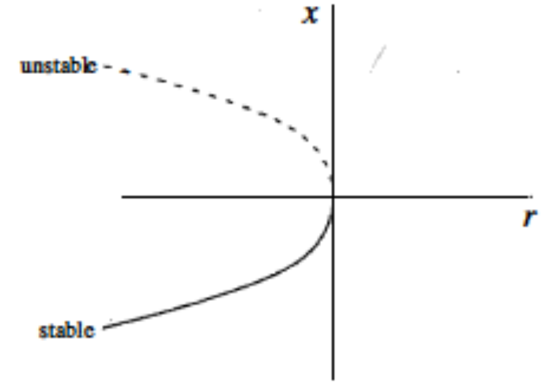
(a) $r<0$



(b) $r=0$

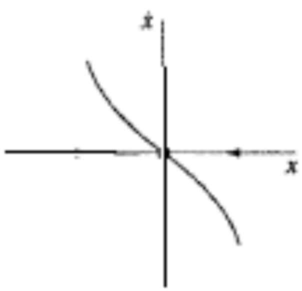


(c) $r>0$

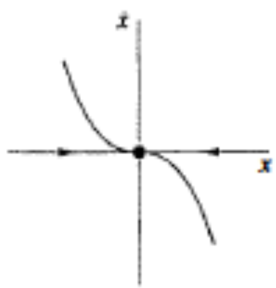


Pitchfork Çatallanması

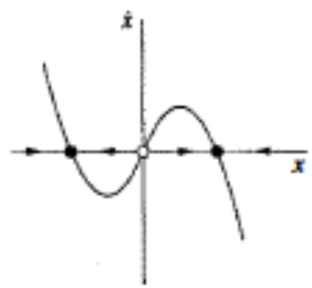
$\dot{x} = rx - x^3.$



(a) $r<0$



(b) $r=0$

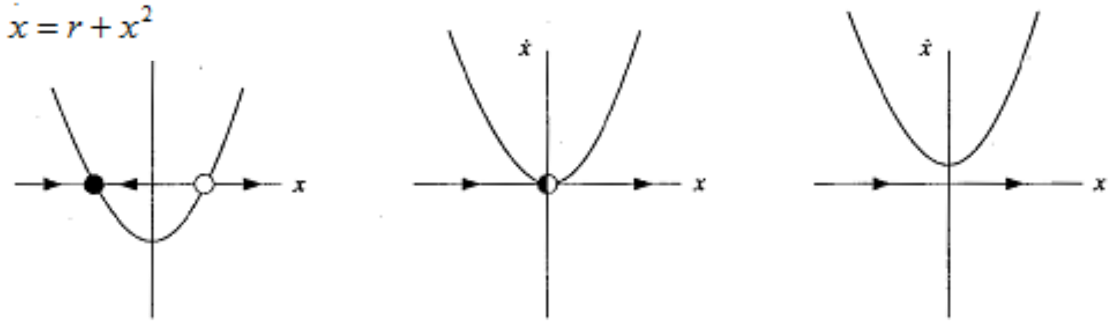


(c) $r>0$

Çatallanma Türleri

Eger-Dügüm (Saddle Node) Çatallanması

$\dot{x} = r + x^2$



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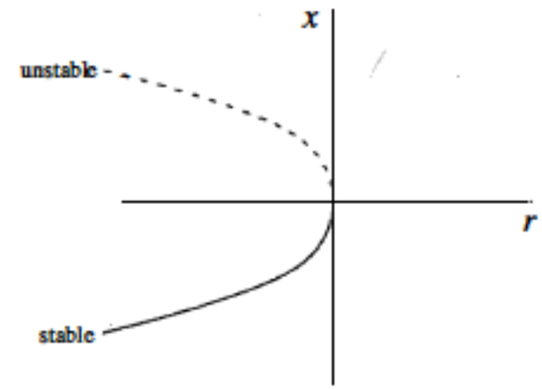

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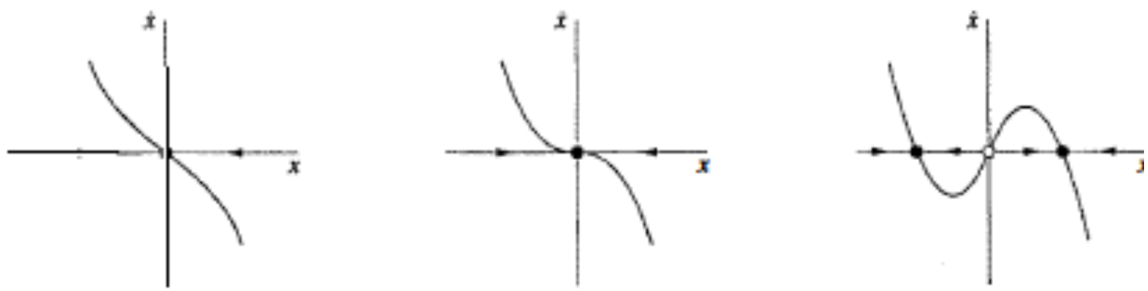

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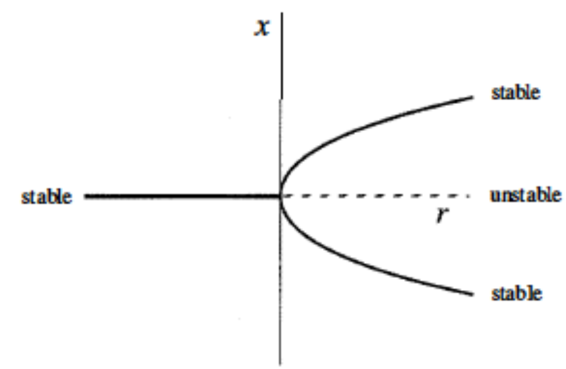
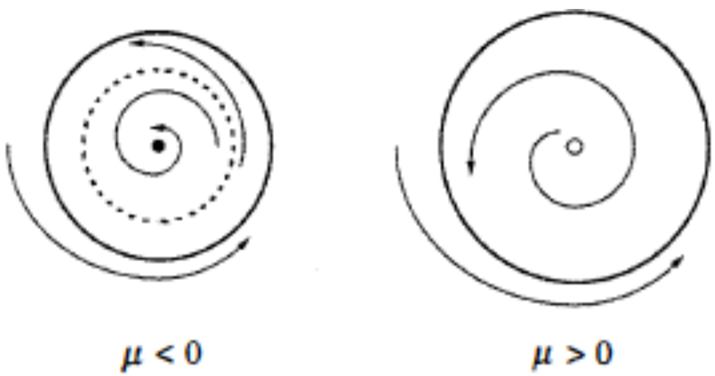
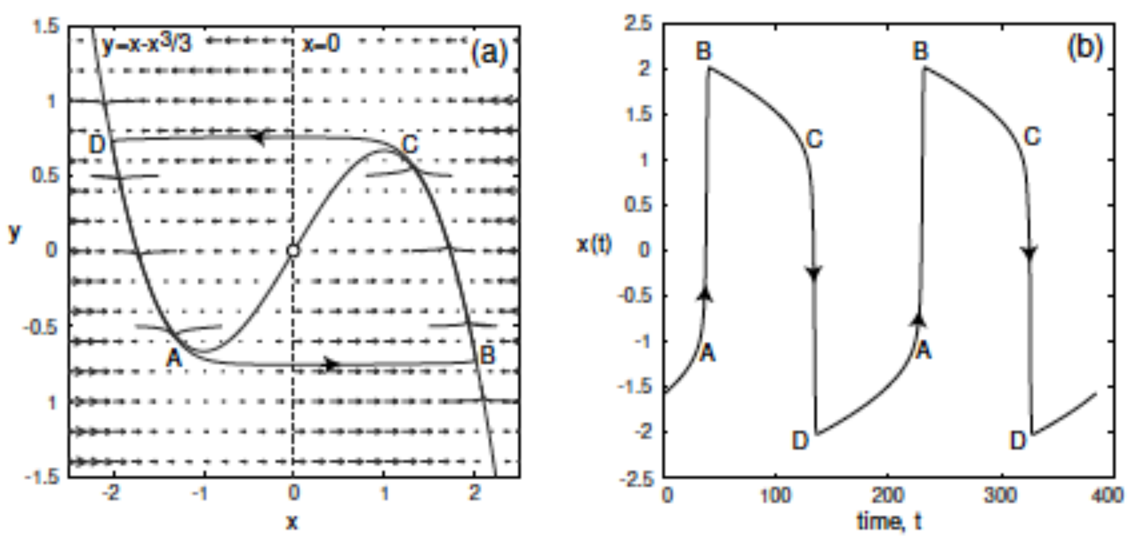


Çatallanma Türleri

Andronov - Hopf Çatallanması

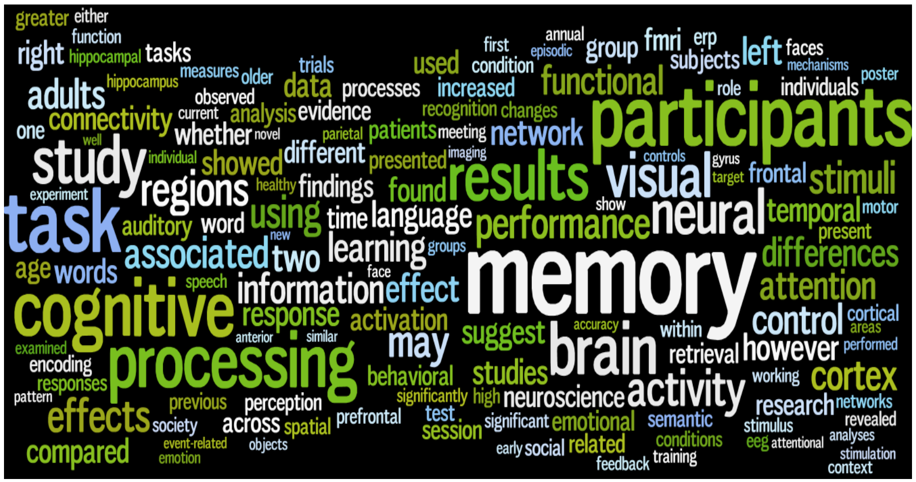


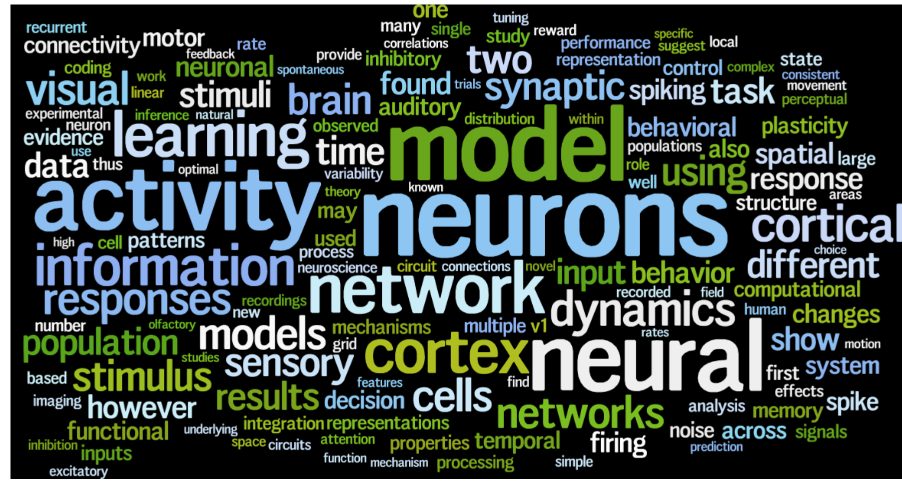
Kararlılıgını kaybeden sabit nokta kararlı bir çevirimin (limit cycle) olusmasına sebep olur.



Excitability

Neuroscience(Sinirbilim) nedir?



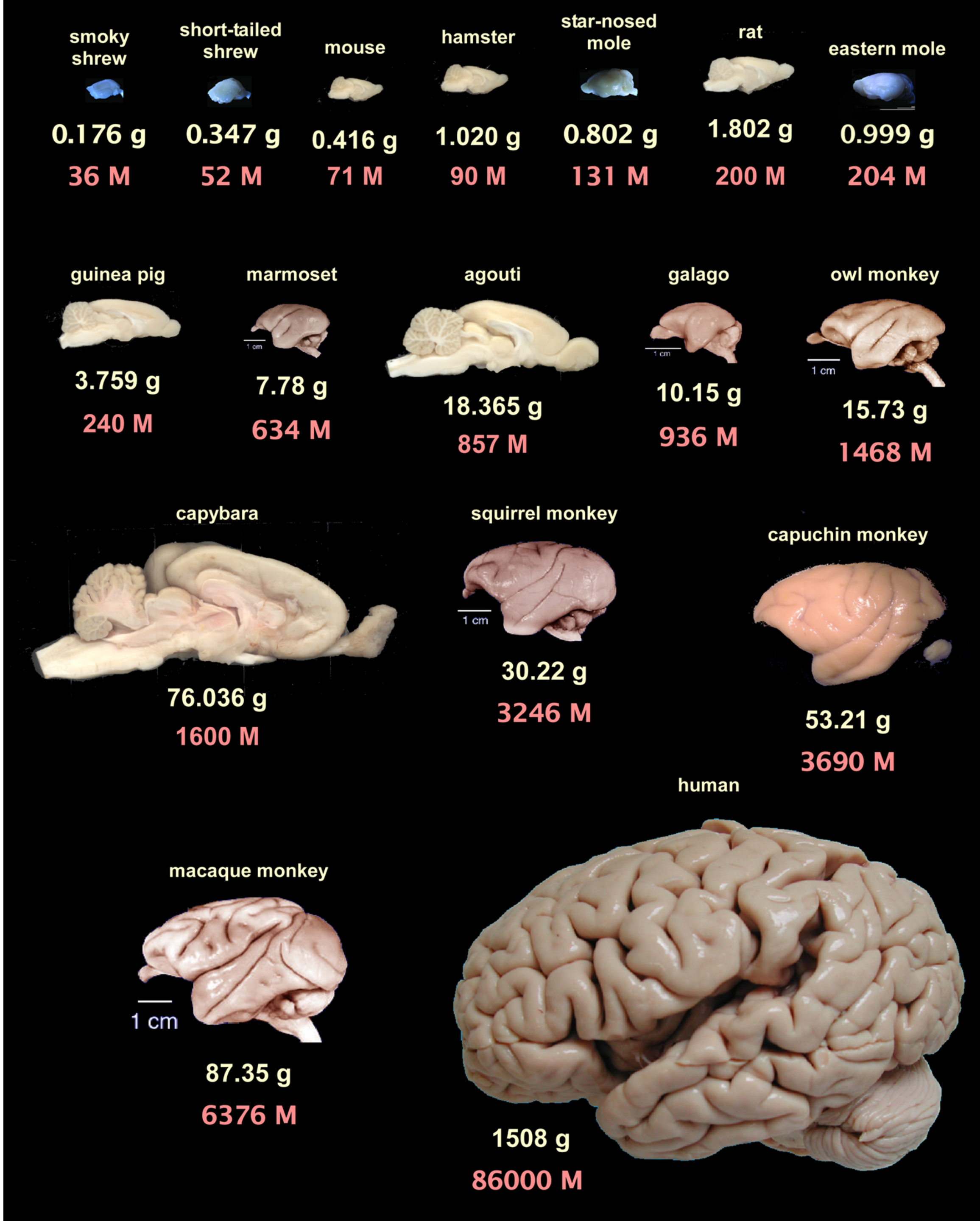


Neuroscience (sinirbilim) sinir sistemini inceleyen bilim dalidir. Biyoloji, sitoloji, psikoloji moleküler biyoloji gibi birden fazla dispilini bir araya getiren bilim dalidir. Temel amaci nöronlarin yapisini ve fonksiyonunu anlamaktir.

Computational neuroscience (hesaplamali sinirbilim veya matematiksel sinirbilim) ise sinirbilimin matematiksel modelleri ve metodlari kullanarak nöronlarin ve networklerinin yapisini analiz eden alt dalidir.

Beyin ve Fonsiyonlari

- Insan Beyni ≈ 86 trilyon nöron
- Herbir nöron ~10000 diger nöron ile baglantilidir.
- 1 mm^3 of cortekste ~1 trilyon sinaps



Tarihi

Camillio Golgi (1843 - 1926)

- Neurons are continuous with one another
- Nearly endless network of connected tubes
- Revolutionary staining technique

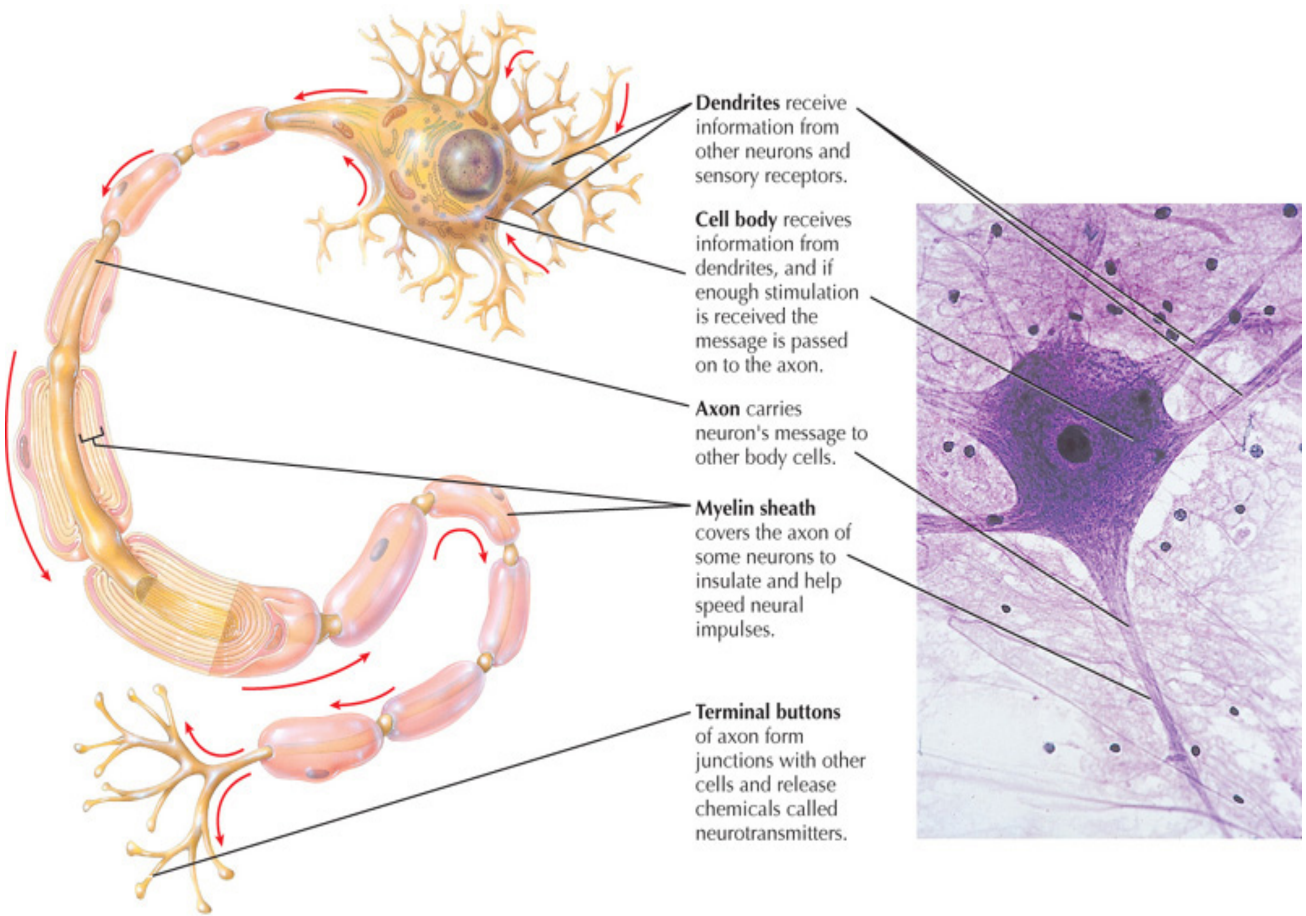
Santiago Ramon Cajal (1852 - 1934)

- Used Golgi staining technique
- Neurons are not continuous with one another
- Small gaps exist

Both received Nobel Prize in Phsiology in 1906

Nöron

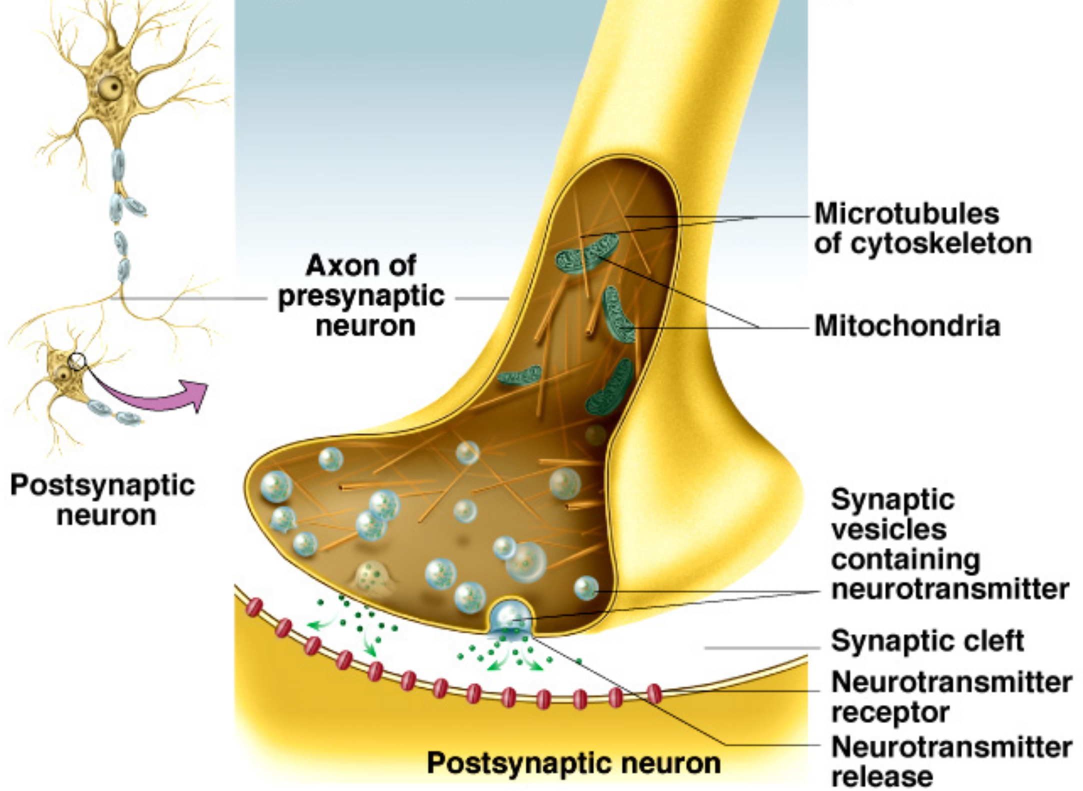
- A neuron (nerve cell) is an electrically excitable cell that processes and transmits information by electrical or chemical signaling.
- Neurons are core components of the nervous system, which includes the brain, spinal cord, and peripheral ganglia



Sinaps

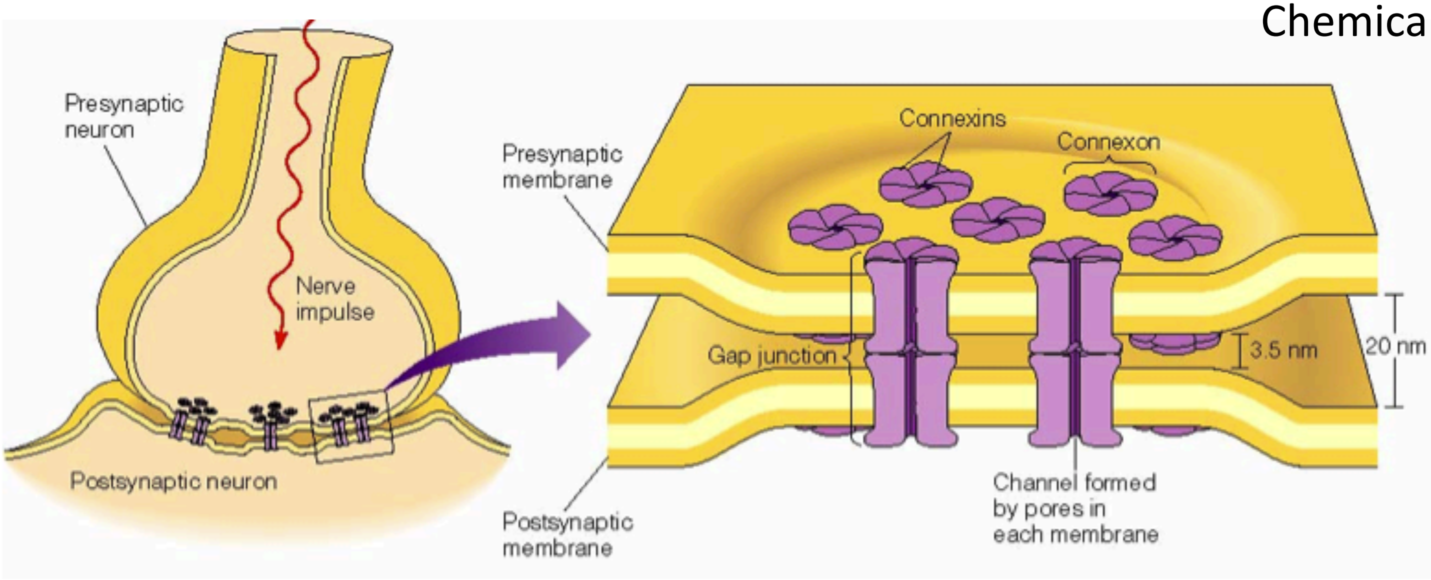
- Chemical Synapses: Presynaptic neurons have synaptic vesicles with neurotransmitter and postsynaptic have receptors

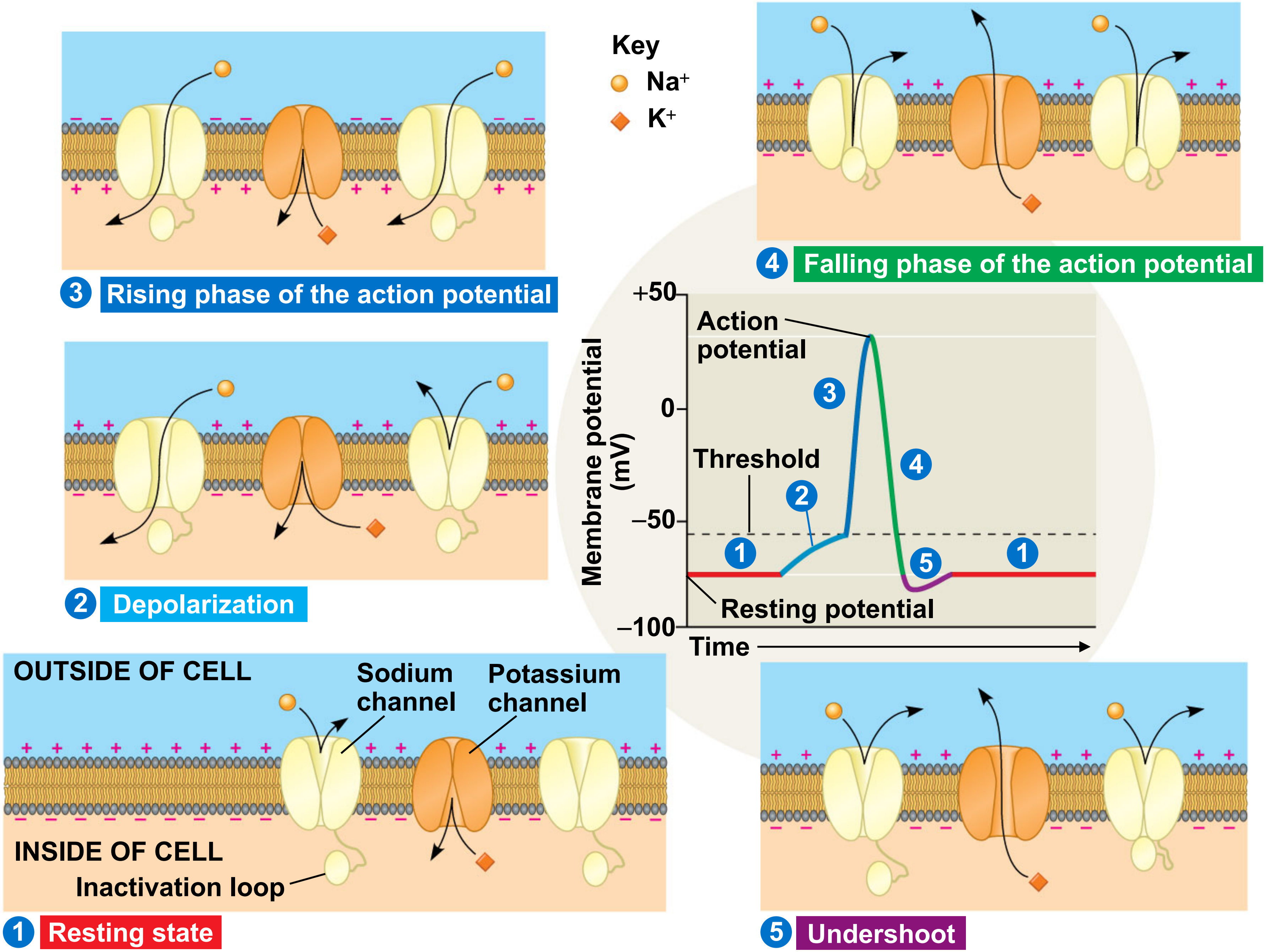
- Gap Junctions: Protein connections between the presynaptic and postsynaptic neuron



Gap Junction

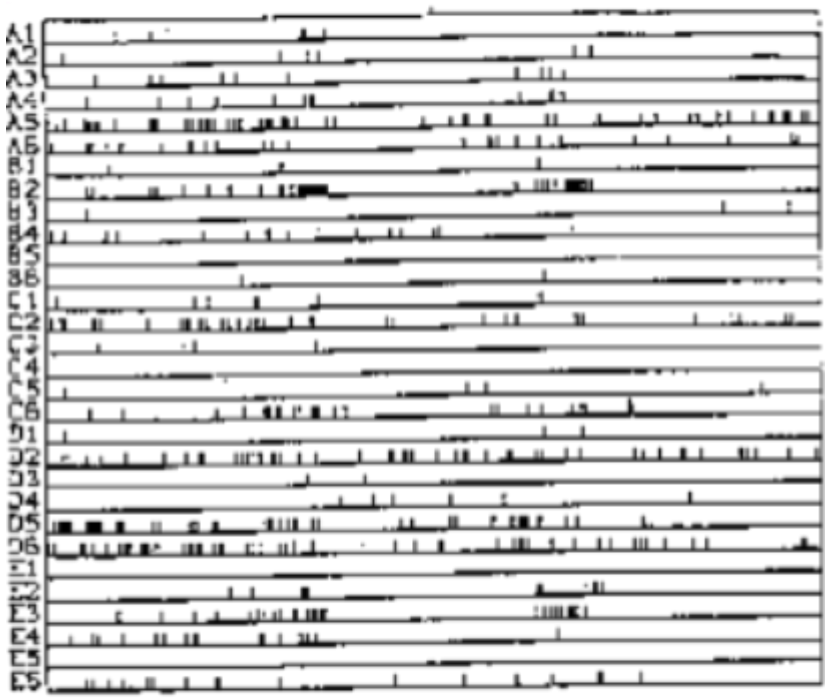
Chemical Synapse



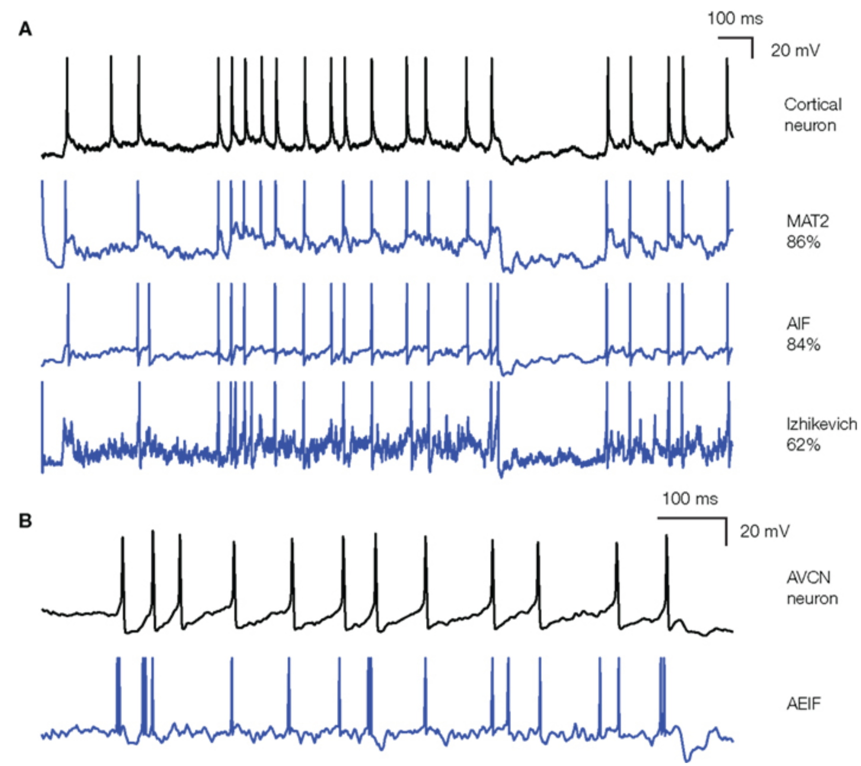


Key
Na+
K+
Rising phase of the action potential
Falling phase of the action potential
Depolarization
+50
0
−50
−100
Action potential
Threshold
Resting potential
Membrane potential (mV)
Time
OUTSIDE OF CELL
Sodium channel
Potassium channel
INSIDE OF CELL
Inactivation loop
Resting state
Undershoot

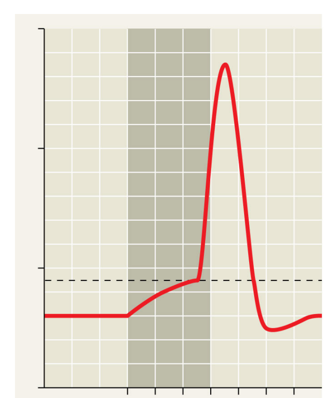
Action Potential (Spike)



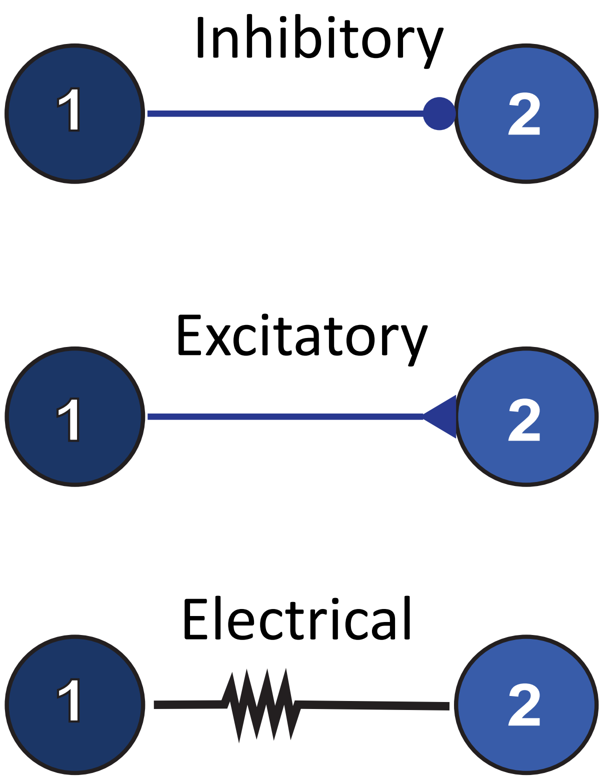
Spike trains from 30 neurons from a monkey cortex. Short vertical bars represent spikes; horizontal axis represents time. Source: [Krüger and Aiple, 1988](#).

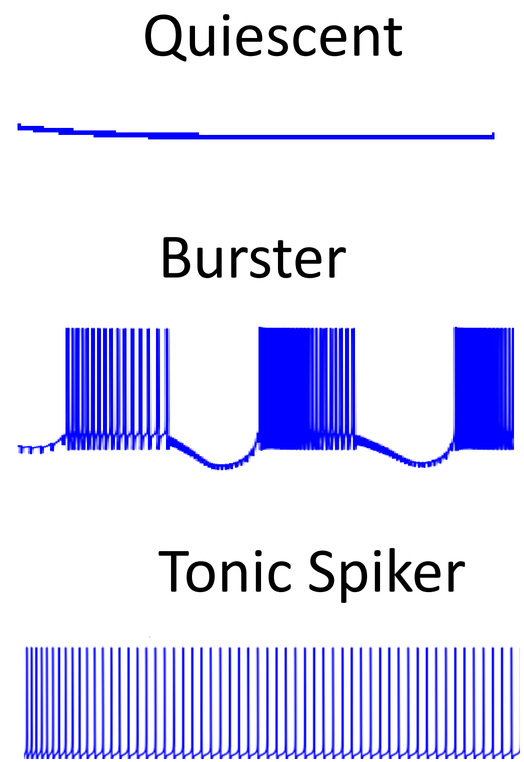


- If a depolarization shifts the membrane potential sufficiently, it results in a massive change in membrane voltage called an **action potential.**



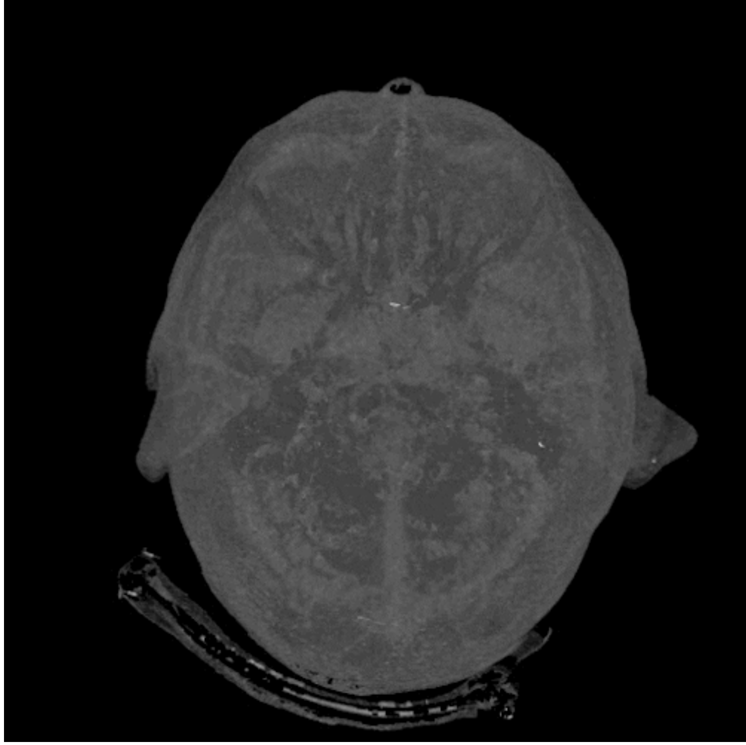
Sinaps ve Hücre Tipleri





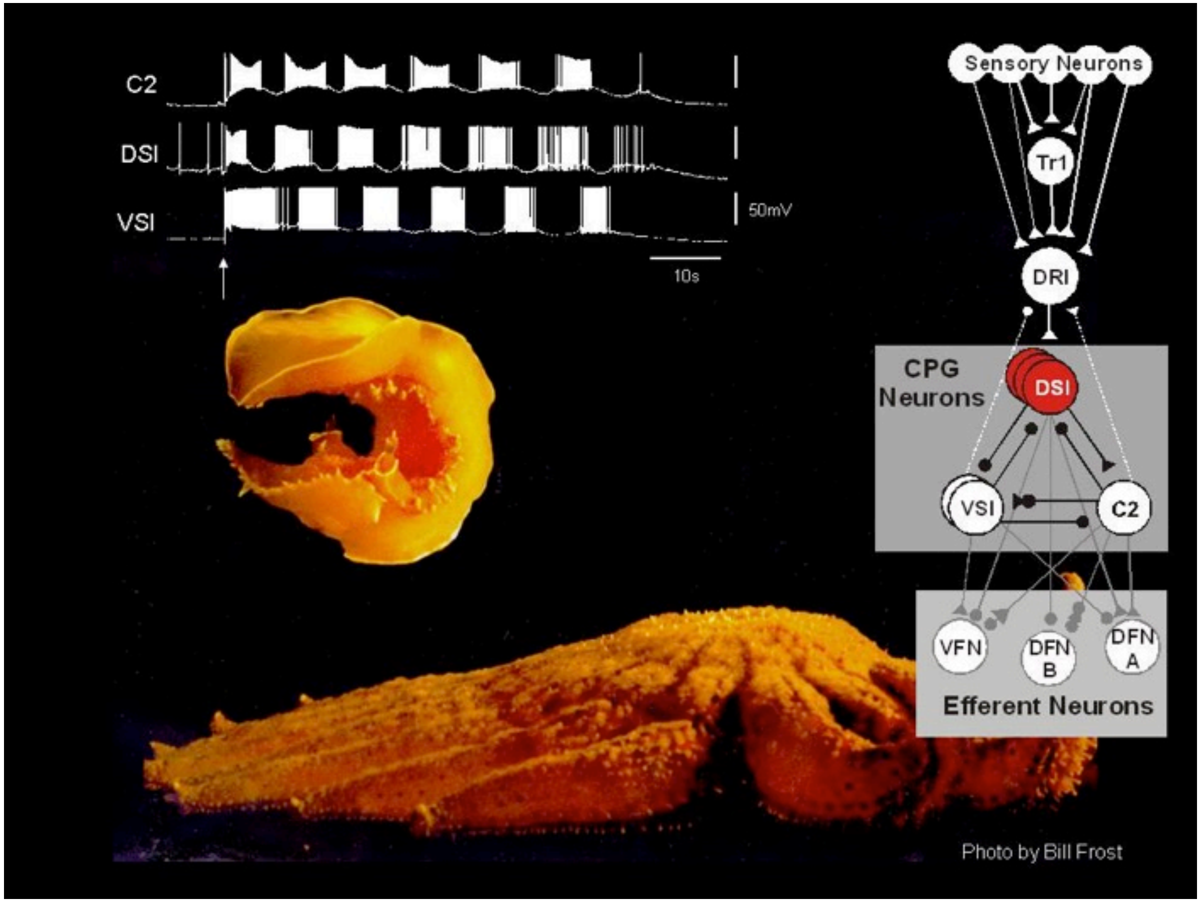
Matematiksel modellleme

- Temel Materyal
  - Anatomi ve fizyoloji
  - Deneyler
  - Pataloji ve lezyonlar
- Hipotez
  - Basitlestirme
  - Paralel programlama
  - Dinamik sistemler
- Dogrulama
  - Tahminler
  - Aciklamalar



Küçük Networkler :
Central Pattern Generators (CPGs)

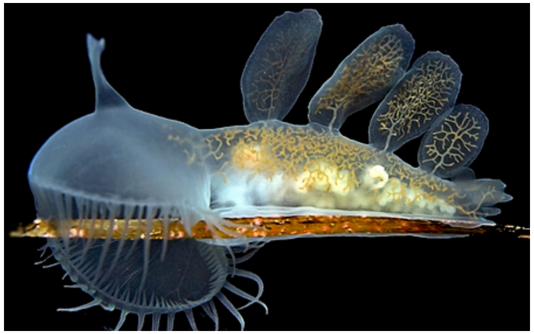
- Yürüme, nefes alma, uçma, yüzme gibi ritmik hareketlerden sorumludur.
- Daha büyük networklerin temelini olusturur.
- Çalisma mekanizmalari hala tam olarak bilinmiyor.



Katz, et al , 2007

Sea Slug Swim CPGs

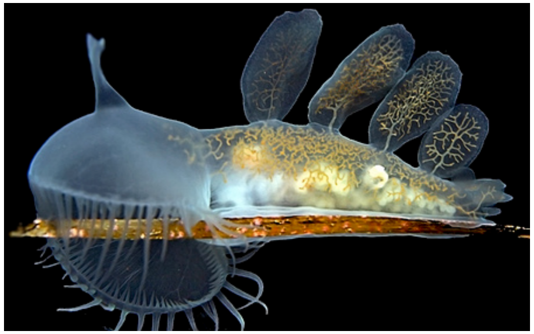
Melibe Leonina

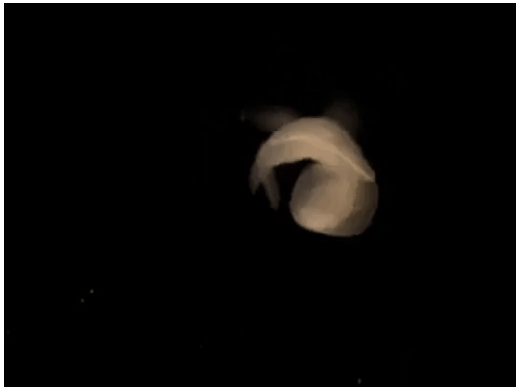


Dendronotus Iris

Sea Slug Swim CPGs

Melibe Leonina

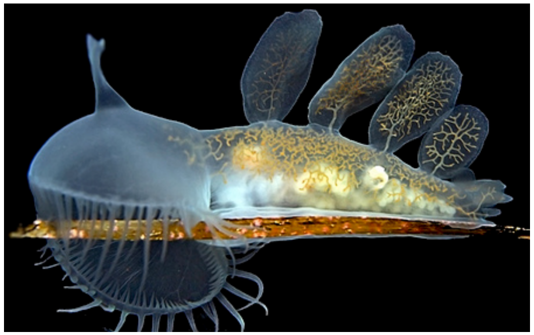


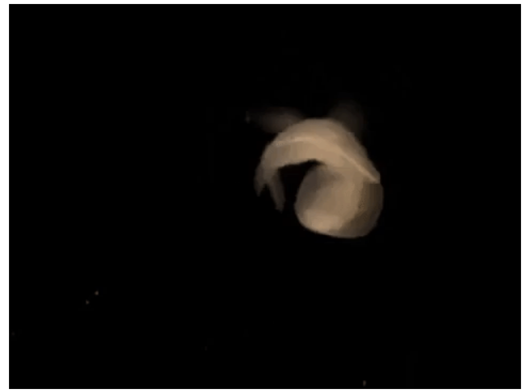


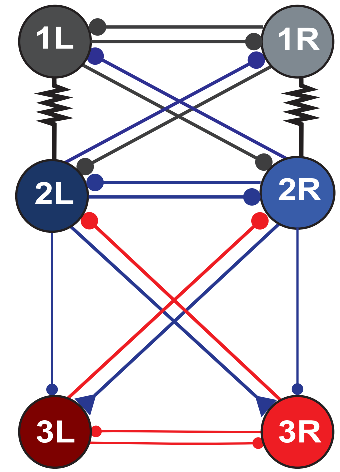
Dendronotus Iris

Sea Slug Swim CPGs

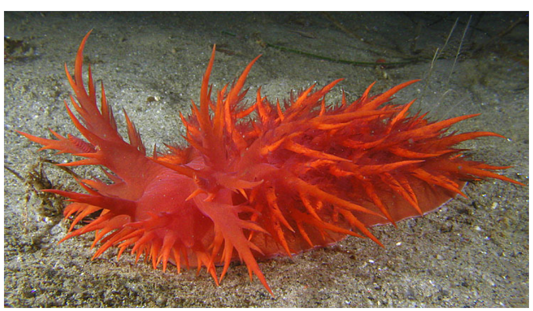
Melibe Leonina

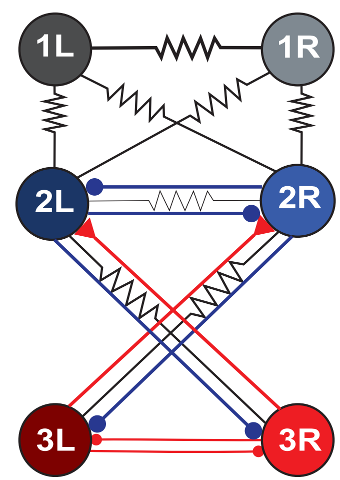






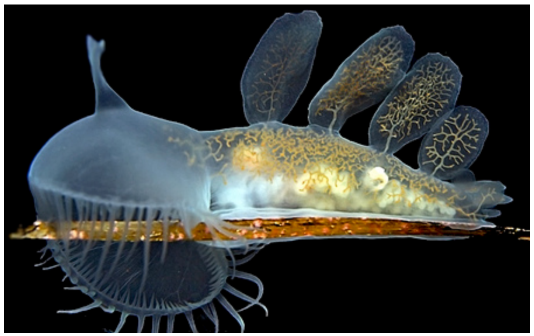
Dendronotus Iris

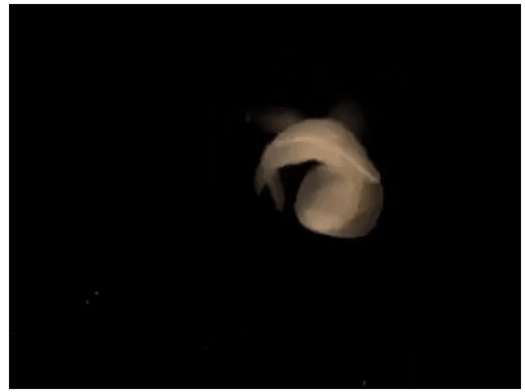


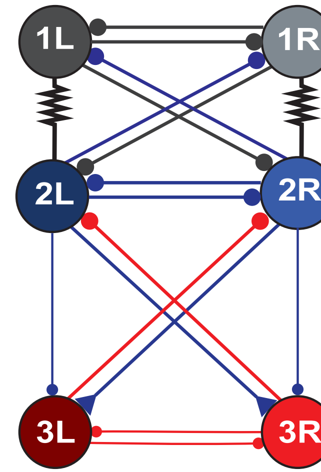


Sea Slug Swim CPGs

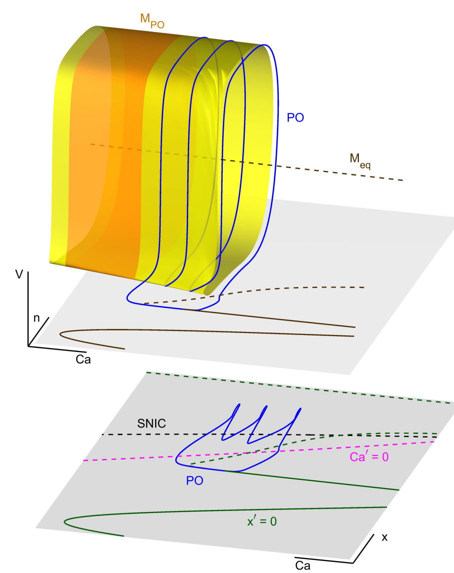
Melibe Leonina





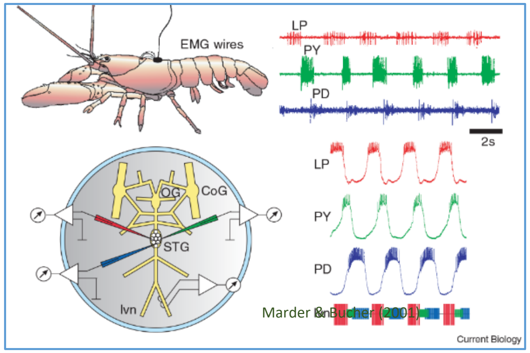


$$C_m V' = -\bar{g}_{Na} m_\infty^3(V) h (V - V_{Na}) - \bar{g}_{Ca} x (V - V_{Ca}) - \bar{g}_h ((1/(1+e^{-(V-63)/7.8})))^3 y (V - V_h)$$
$$-[\bar{g}_K n^4 - \bar{g}_{KCa} Ca/(0.5+Ca)](V - V_K) - \bar{g}_L (V - V_L)$$
$$h' = \lambda[h_\infty(V) - h]/\tau_h(V)$$
$$n' = \lambda[n_\infty(V) - n]/\tau_n(V)$$
$$x' = [x_\infty(V) - x]/\tau_x$$
$$y' = [y_\infty(V) - y]/\tau_y(V)$$
$$Ca' = \rho[K_c x(V_{Ca} - V + shift) - Ca]$$
$$S' = \alpha(1 - S)/(1 + e^{-k(V_i - th)}) - \beta S$$
$$M' = (0.01 + 0.9/(1 + e^{(-(V+10))}) - M)/\tau_M$$



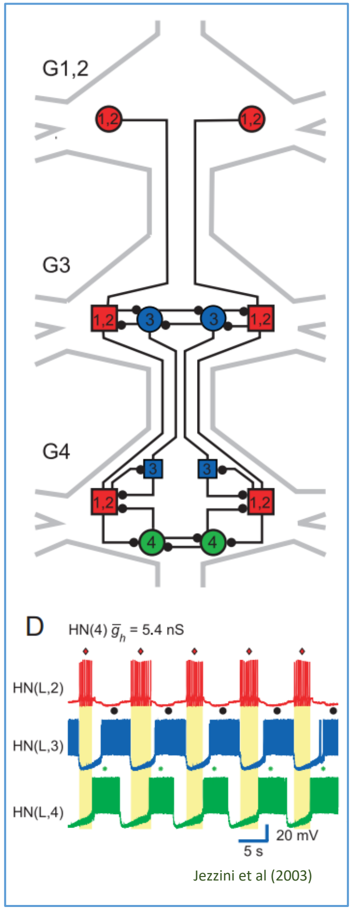
3-Nodlu Ağlarda Ritim Üretimi

Locomotion – Lobster



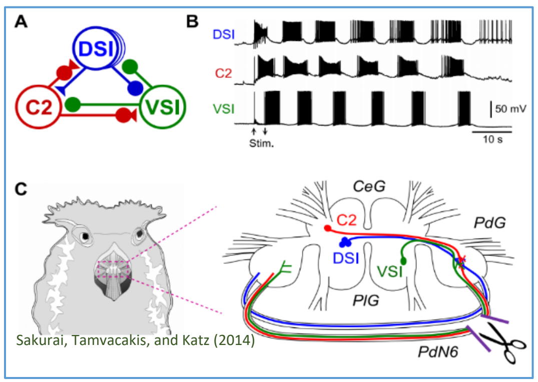
Marder & Bucher (2001)

Heartbeat – Leech



Jezzini et al (2003)

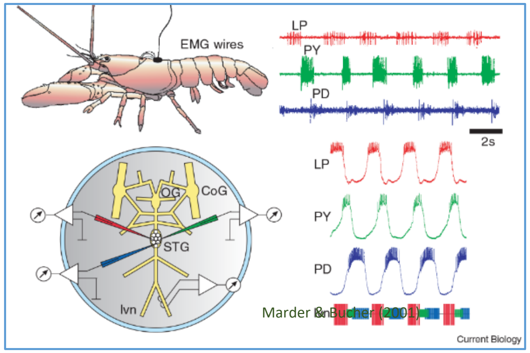
Swimming – Tritonia



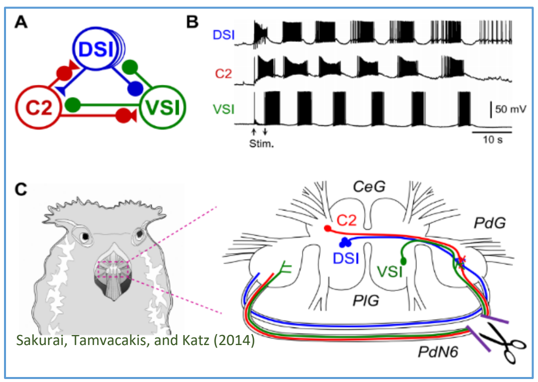
Sakurai, Tamvacakis, and Katz (2014)

3-Nodlu Ağlarda Ritim Üretimi

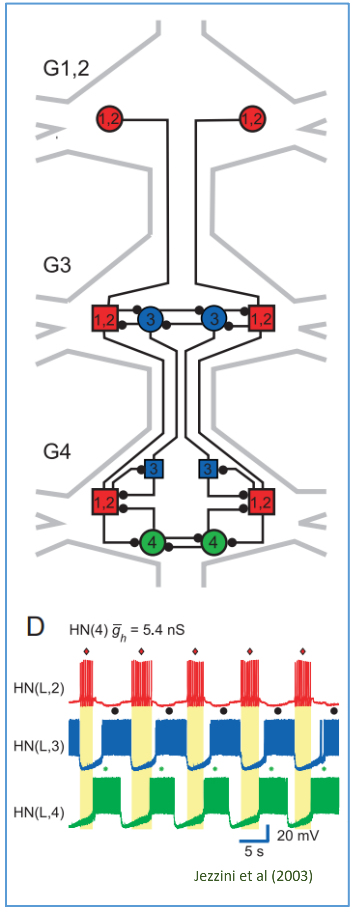
Locomotion – Lobster

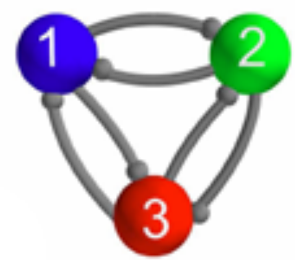


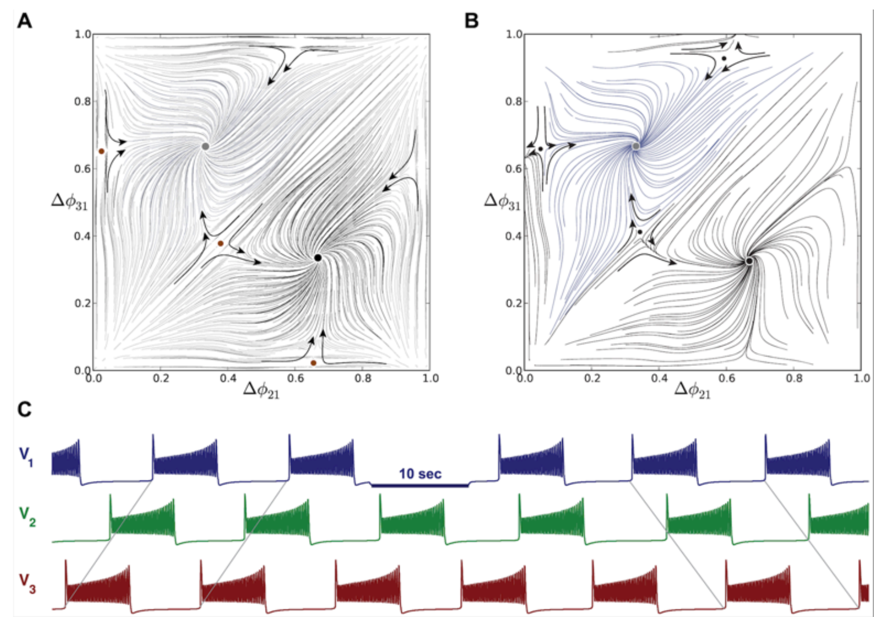
Swimming – Tritonia



Heartbeat – Leech

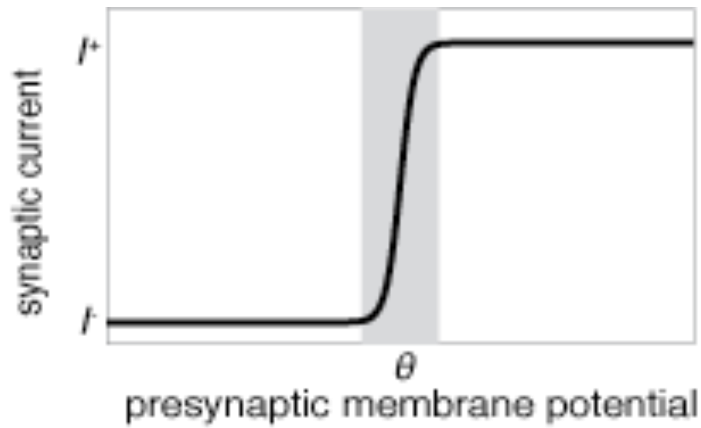






Half-Center Oscillators (HCOs)

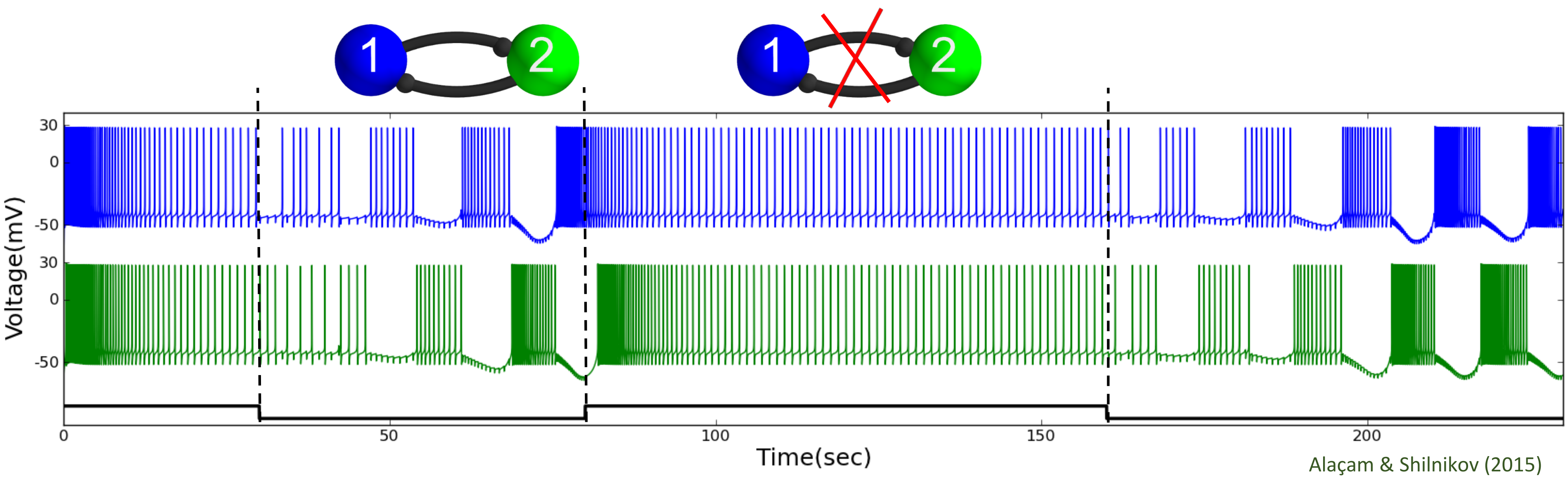
Kopell, et al, 1993



Fast-Threshold Modulations (FTM)

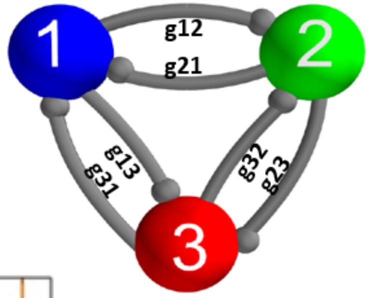
$$I_{syn} = g_{ij}\frac{V - E}{1 + e^{-k(V_i - \theta_{th})}}$$

- Reciprocal inhibition between coupled cells permits rhythmogenesis and anti-phase oscillations



Alaçam & Shilnikov (2015)

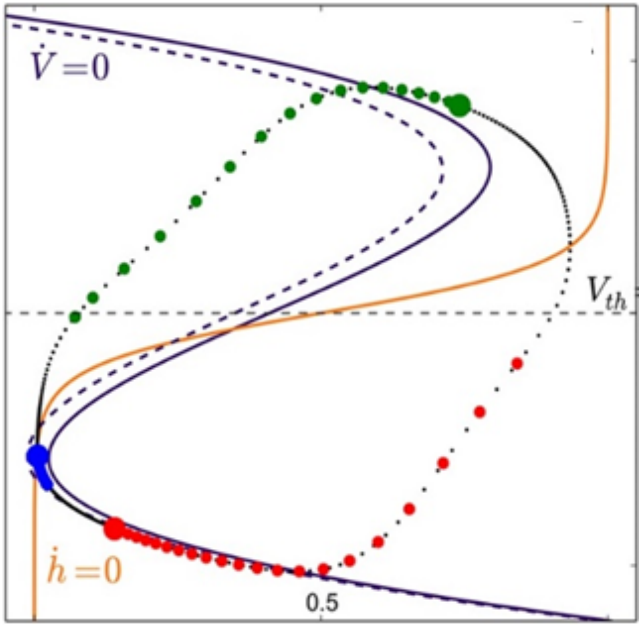
gFN Nöronlarının Özellikleri



$$\dot{V}_i = m(V_i - V_i^3) - x_i + I + \Sigma G_{ij},$$

$$\dot{h}_i = \epsilon[\frac{1}{1+e^{-k(V_i - V_0)}} - h_i],$$

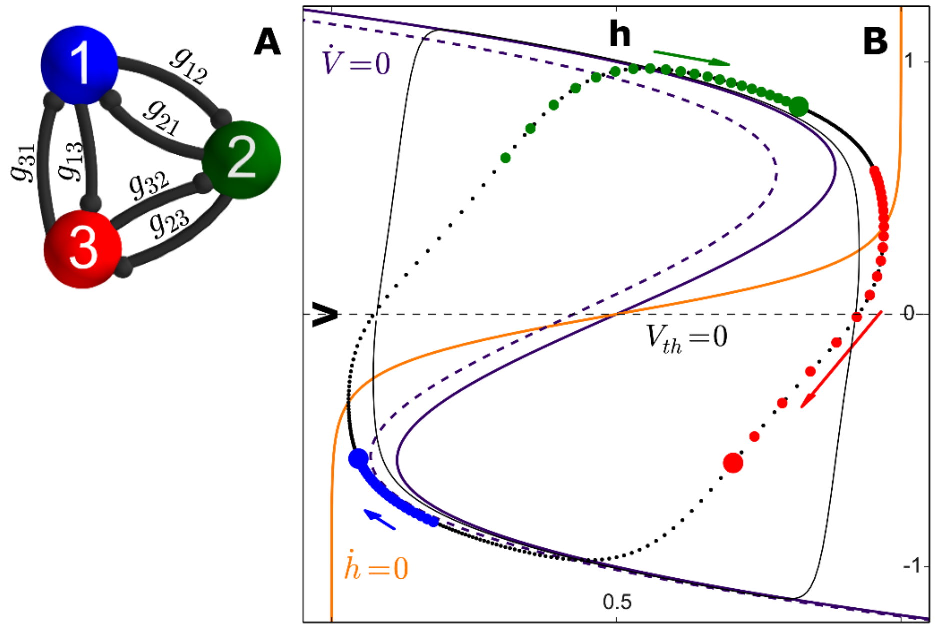
$$G_{ij} = g_{ij}(\frac{V_{syn} - V_i}{1+e^{-k(V_i - V_0)}})$$

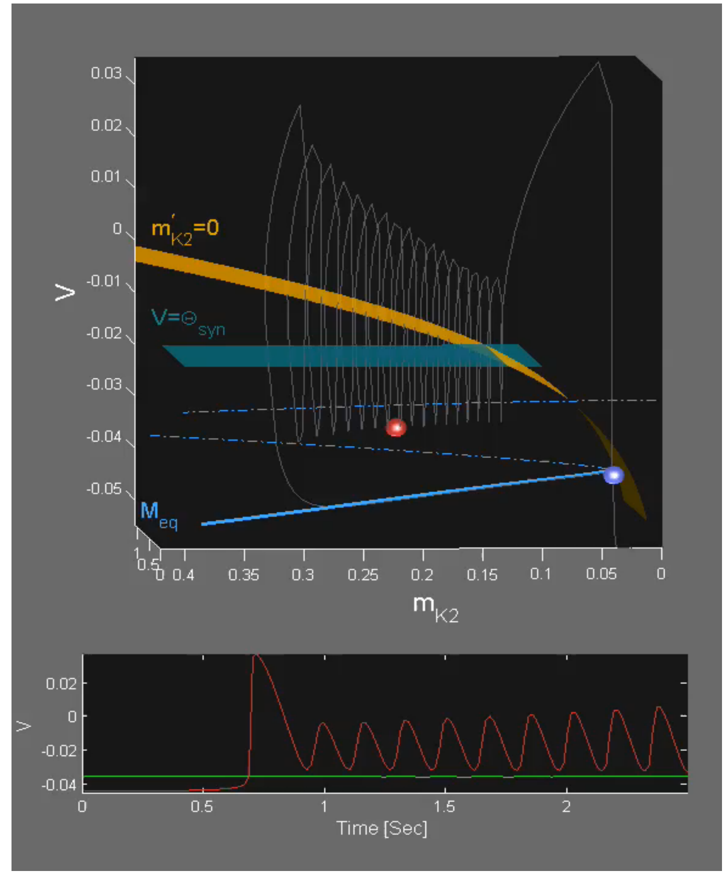


- V – Voltaj (Hizli degisken)
- h – Recovery (Yavas degisken)
- G – Sinaptik degisken

gFN Nöronlarının Özellikleri

- Fast cubic and slow sigmoidal nullclines

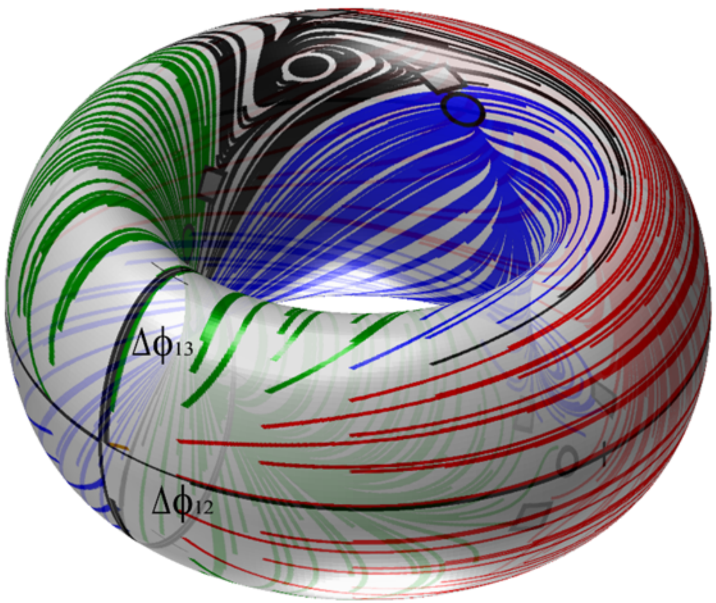




$$\dot{V}_i = m(V_i - V_i^3) - x_i + I + \Sigma G_{ij}, \quad \dot{h}_i = \epsilon\left[\frac{1}{1+e^{-k(V_i - V_0)}} - h_i\right], \quad G_{ij} = g_{ij}\left(\frac{V_{syn} - V_i}{1+e^{-k(V_i - V_0)}}\right)$$

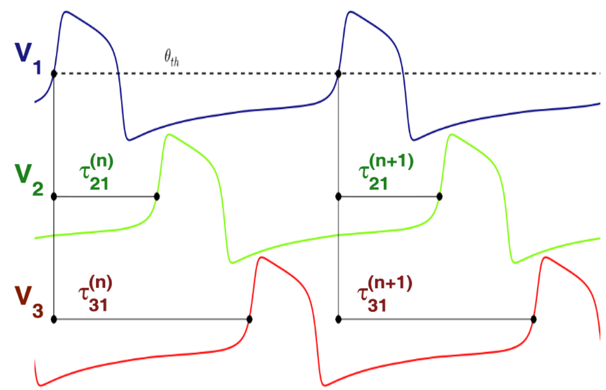
Torus ve Faz-Farklari

- ‘Donut’ surface connects cyclical rhythmic activity
- Using Cell 1 reference allows dimension reduction



Poincaré return map on a 2-D torus

gFN 3-Node Network Traces

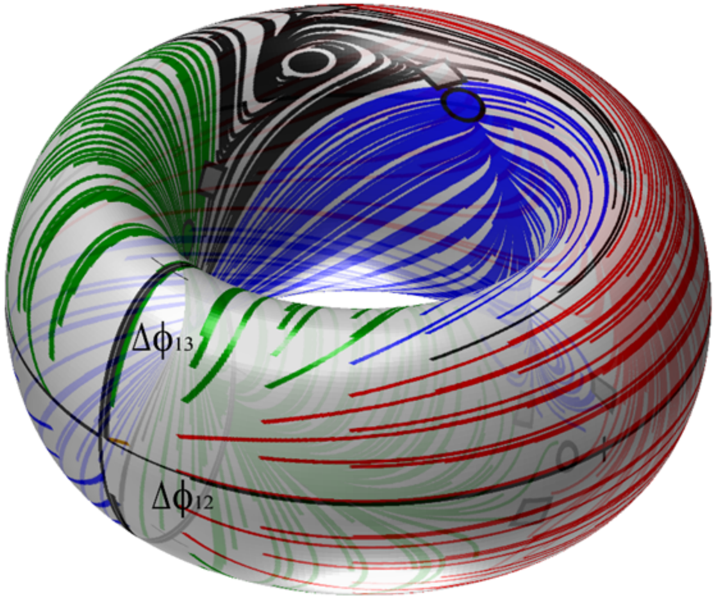


$$\Delta_{21}^{(n)} = \frac{\tau_{21}^{(n+1)} - \tau_{21}^{(n)}}{\tau_{1}^{(n+1)} - \tau_{1}^{(n)}}, \quad \text{mod } 1$$

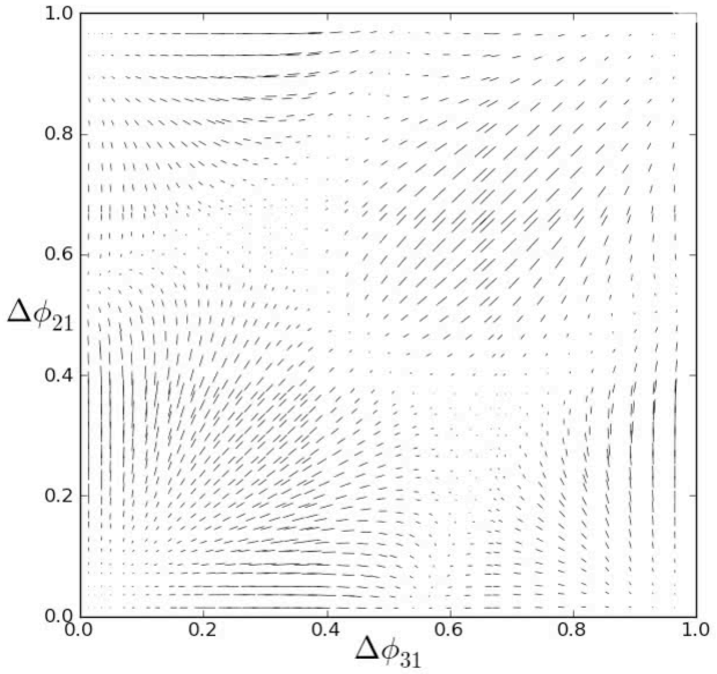
$$\Delta_{31}^{(n)} = \frac{\tau_{31}^{(n+1)} - \tau_{31}^{(n)}}{\tau_{1}^{(n+1)} - \tau_{1}^{(n)}} \quad \text{mod } 1$$

Torusun Açılımı

- Cutting the axes of the torus aids in visualization
- Spanning a grid of 900 sampled initial phase-lag conditions

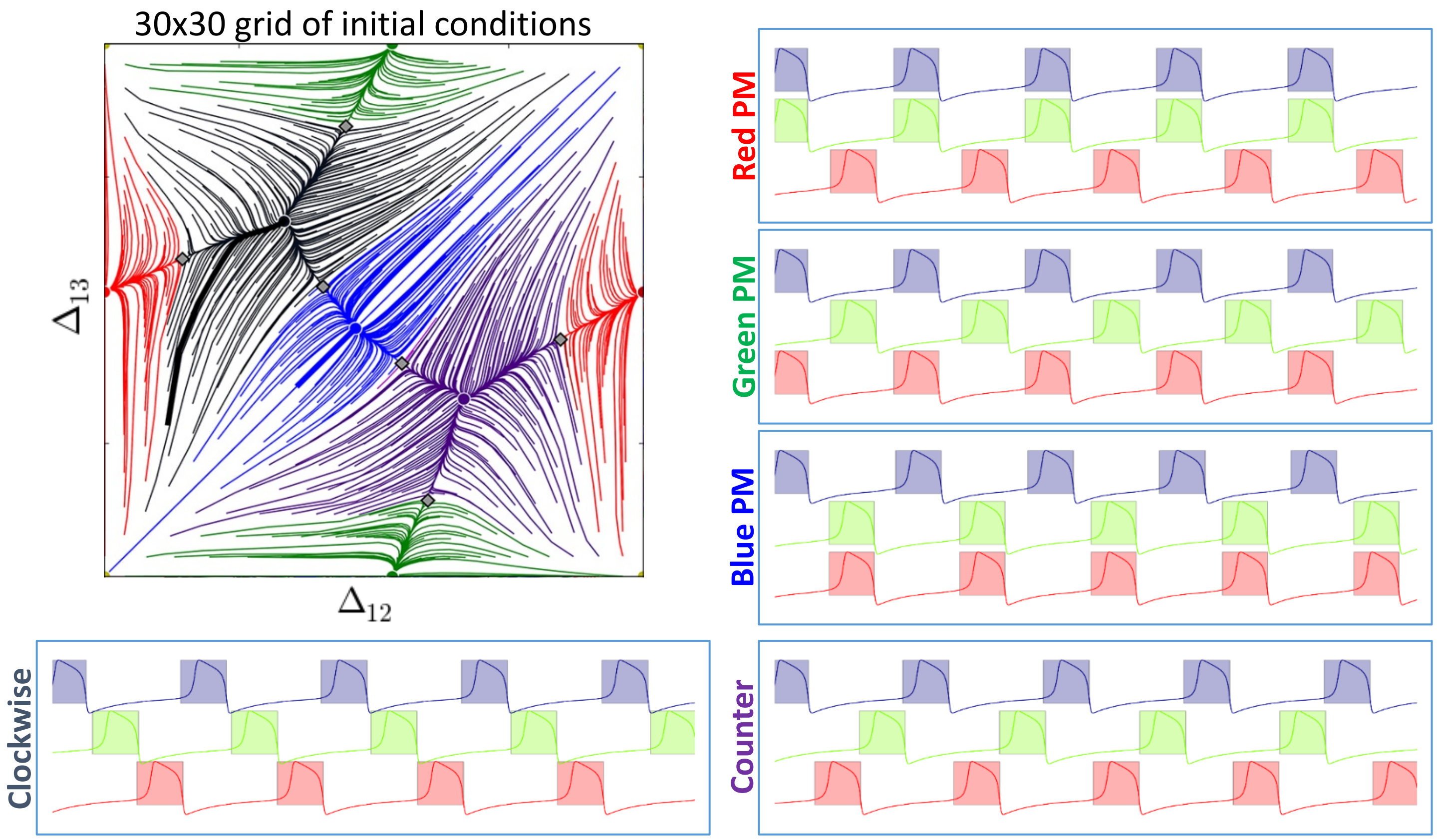


Traces converge to stable outcomes

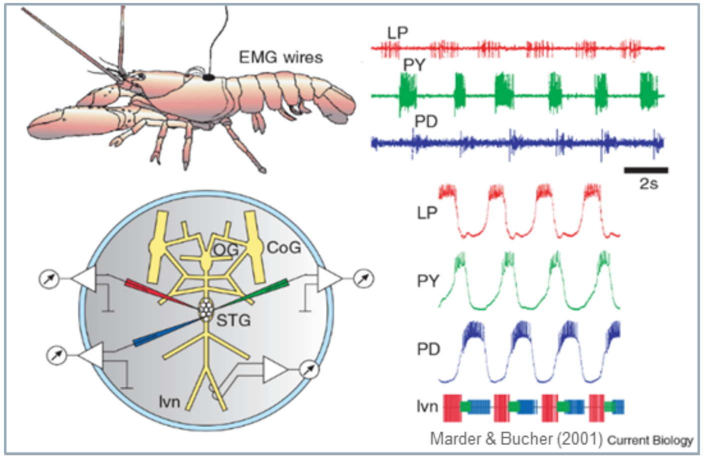


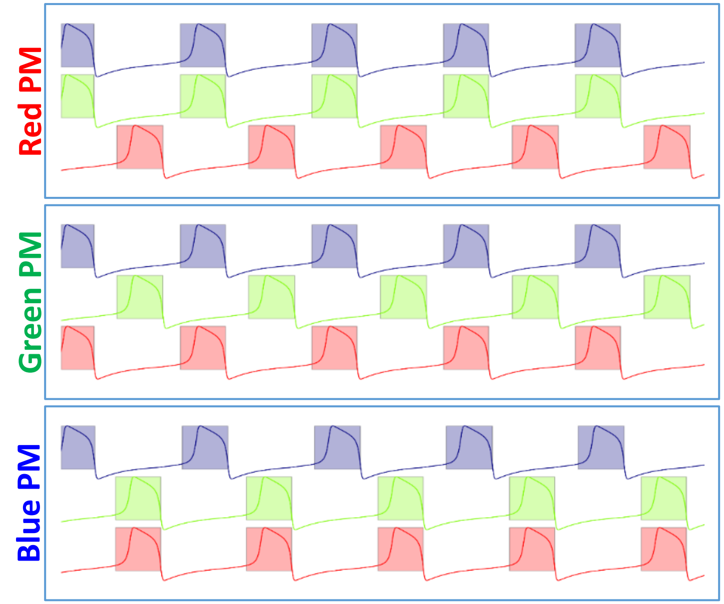
Ritim Tanımlanması

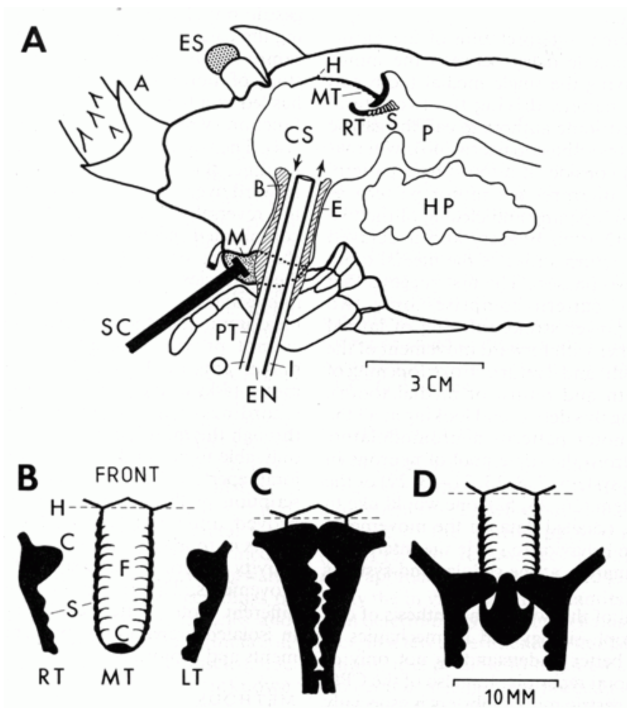
- Pentarhythmic network and basins of attraction



Ritim Tanımlanması

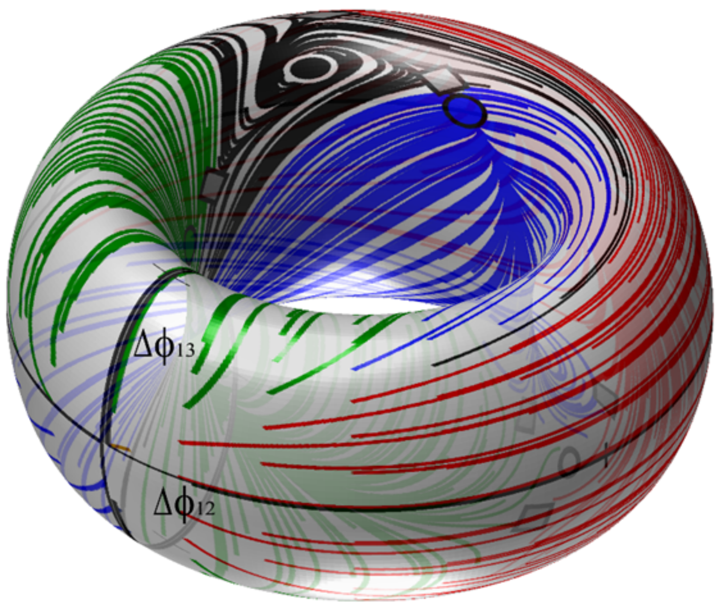




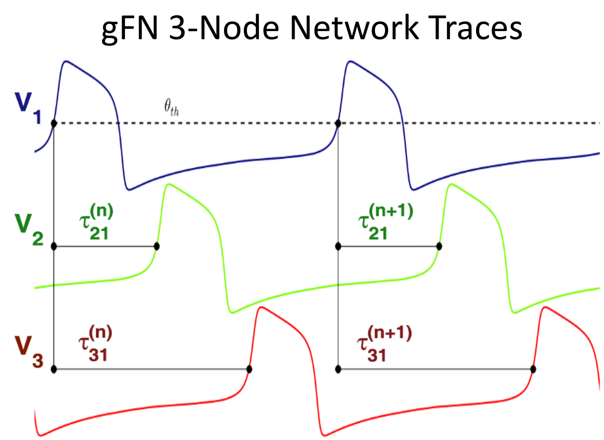


Torus ve Faz Farklari

- ‘Donut’ surface connects cyclical rhythmic activity
- Using Cell 1 reference allows dimension reduction



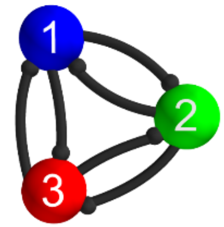
Poincaré return map on a 2-D torus



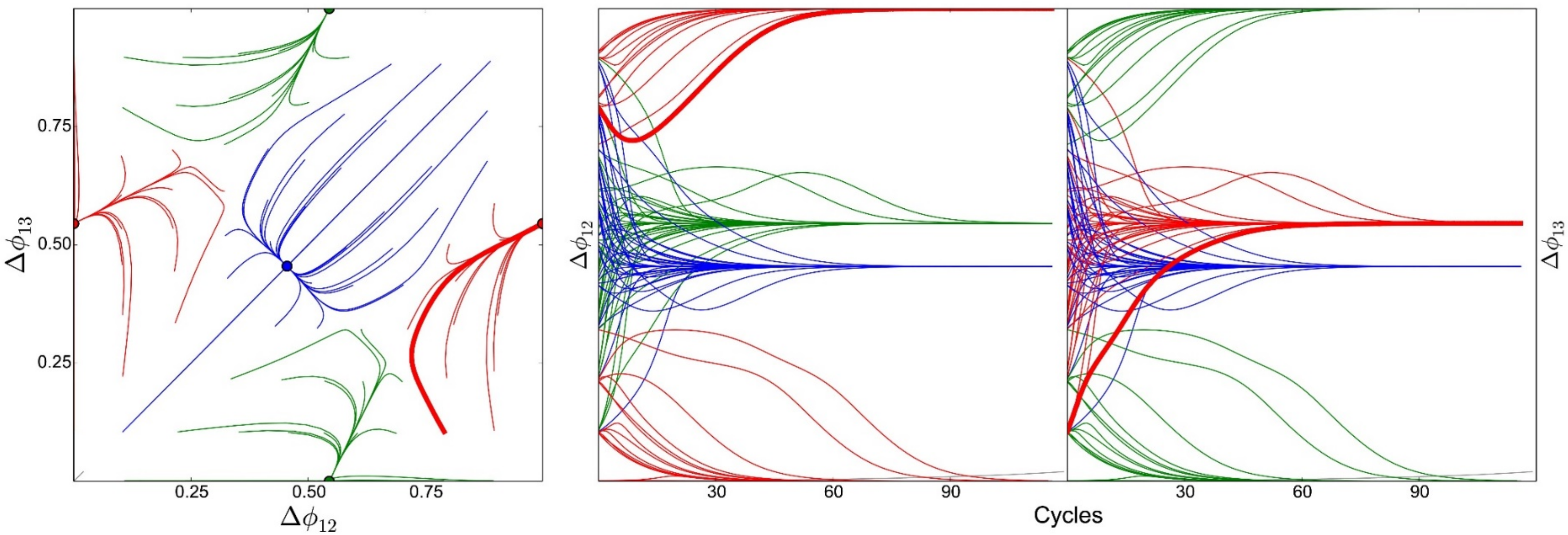
$$\Delta_{21}^{(n)} = \frac{\tau_{21}^{(n+1)} - \tau_{21}^{(n)}}{\tau_{1}^{(n+1)} - \tau_{1}^{(n)}}, \quad \text{mod } 1$$

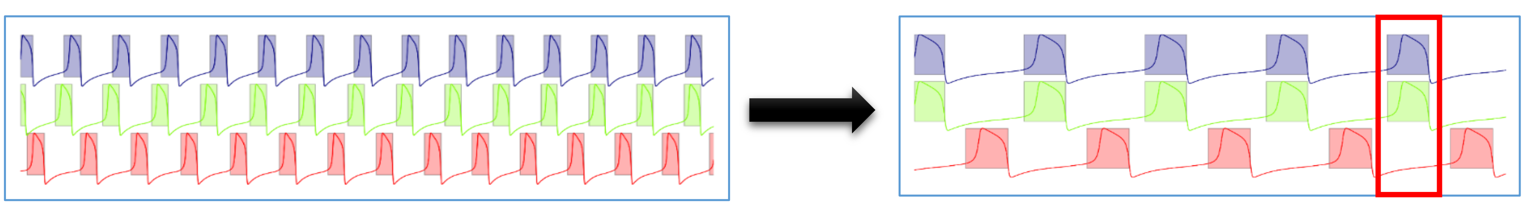
$$\Delta_{31}^{(n)} = \frac{\tau_{31}^{(n+1)} - \tau_{31}^{(n)}}{\tau_{1}^{(n+1)} - \tau_{1}^{(n)}} \quad \text{mod } 1$$

Ritim Tanımlanması



- Cutting the axes of the torus aids in visualization
- Spanning a grid of sampled initial phase-lag conditions
- Traces converge to stable outcomes

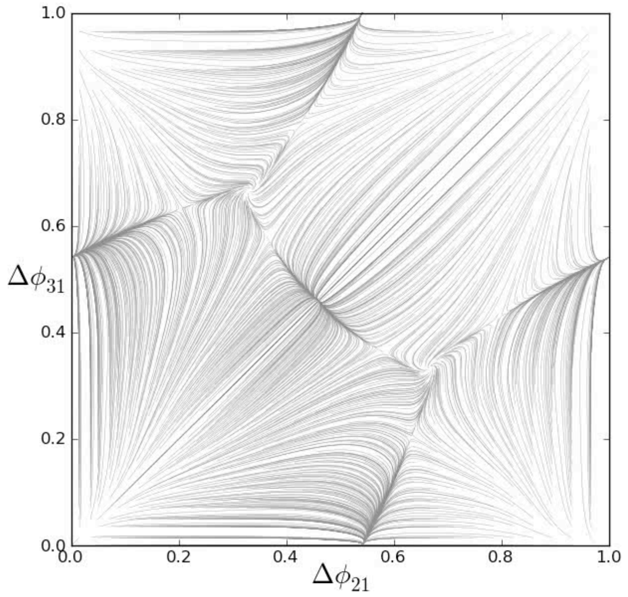


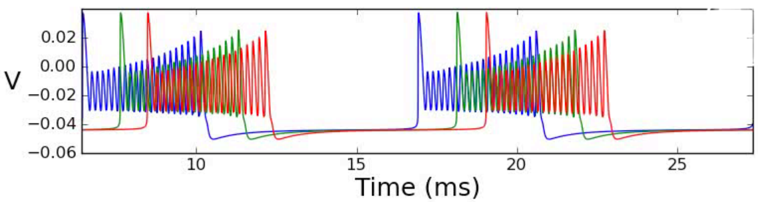


Red Pacemaker (PM)

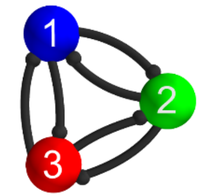
Ritim Tanımlanması

- Penta-ritmik network and basins of attraction

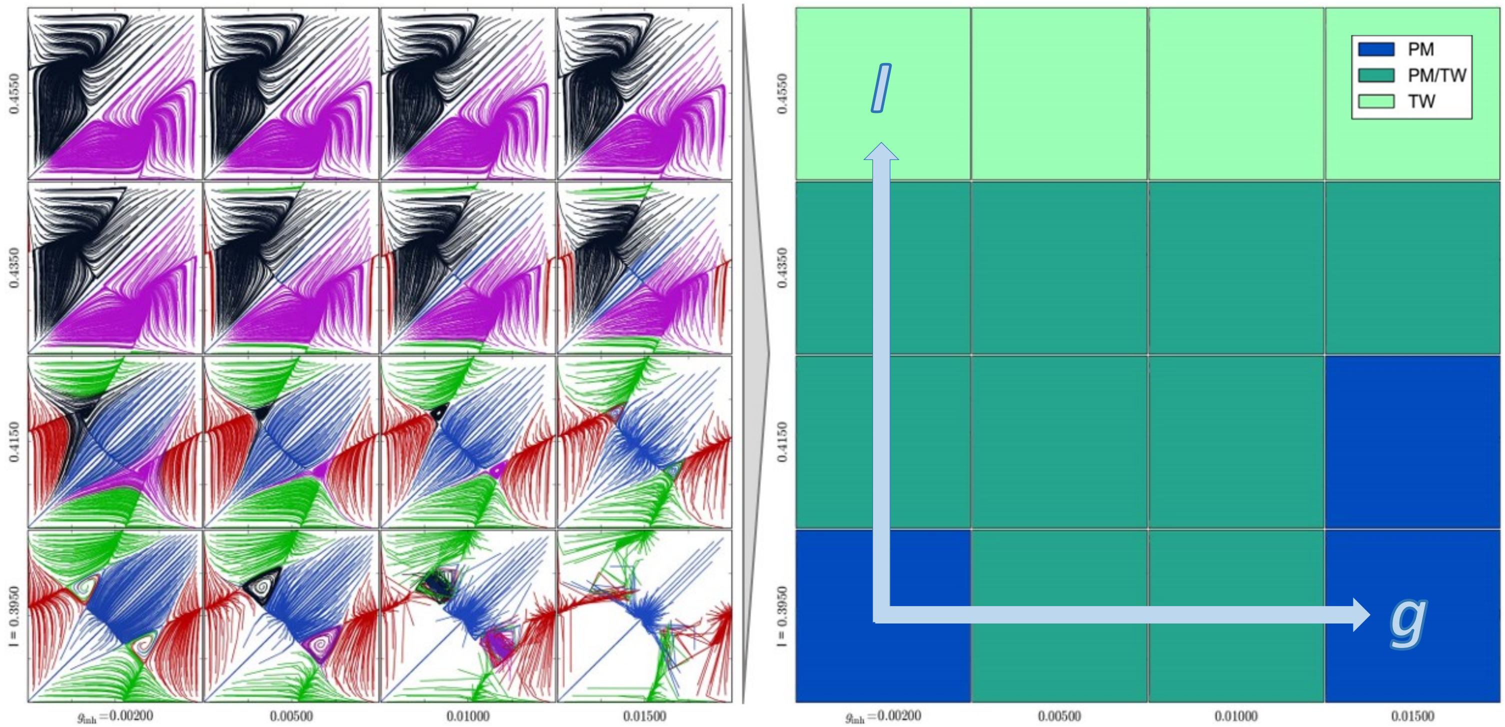




Poincare Maplerinin Çatallanma Analizi

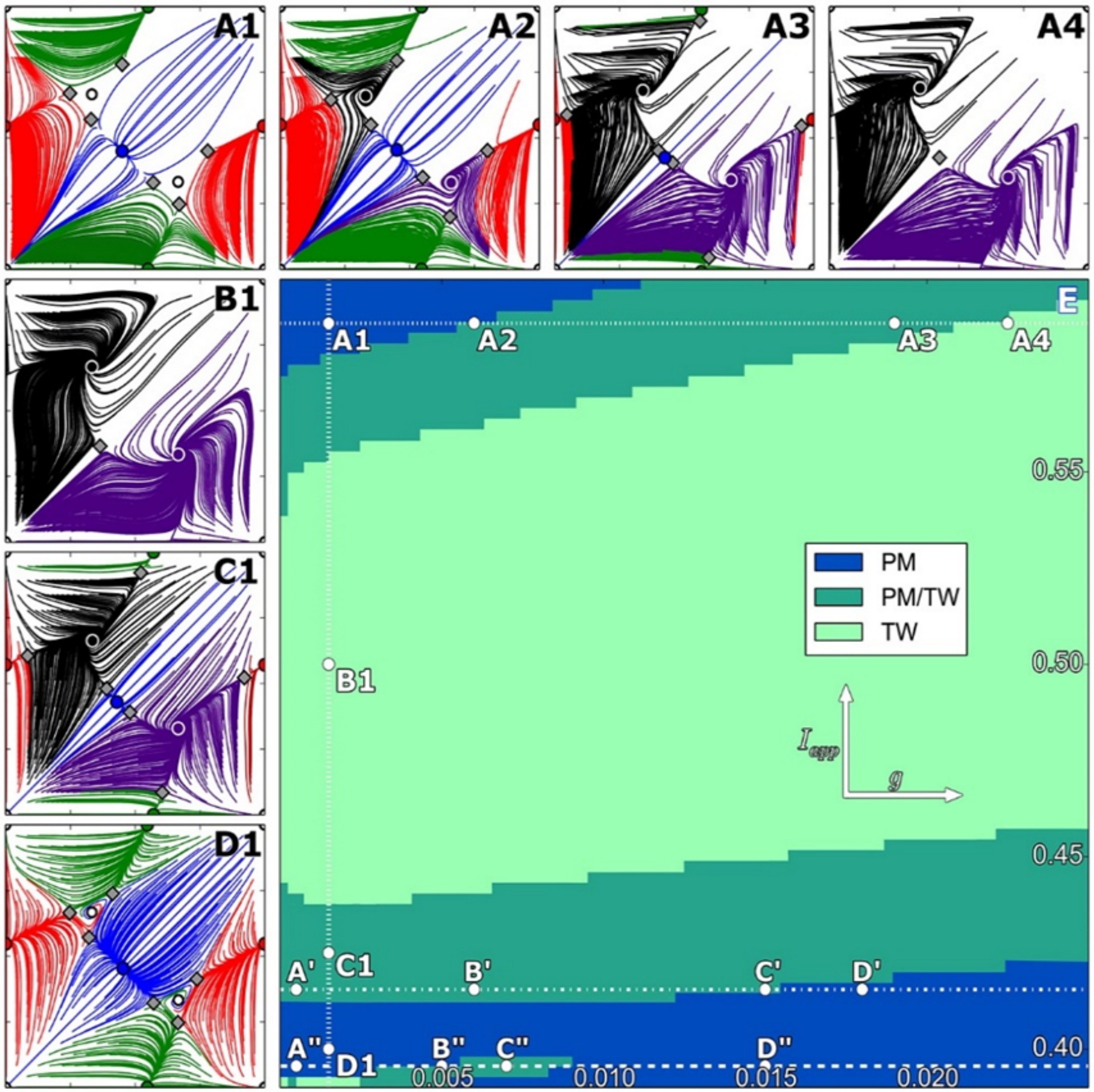


- Bi-parametric (*g*, *I*) sweep for regions of similar rhythm outcomes
- Color-coding by rhythms observed



$$\dot{V}_i = m(V_i - V_i^3) - x_i + I + \Sigma G_{ij}, \; \dot{h}_i = \epsilon[\frac{1}{1+e^{-k(V_i - V_0)}} - h_i], \; G_{ij} = g_{ij}(\frac{V_{syn} - V_i}{1+e^{-k(V_i - V_0)}})$$

Çatallanma Diyagrami



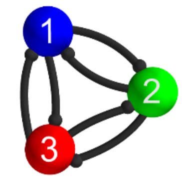
75x75 grid of (g_{ij}, I_{app})-space

Synaptic Escape

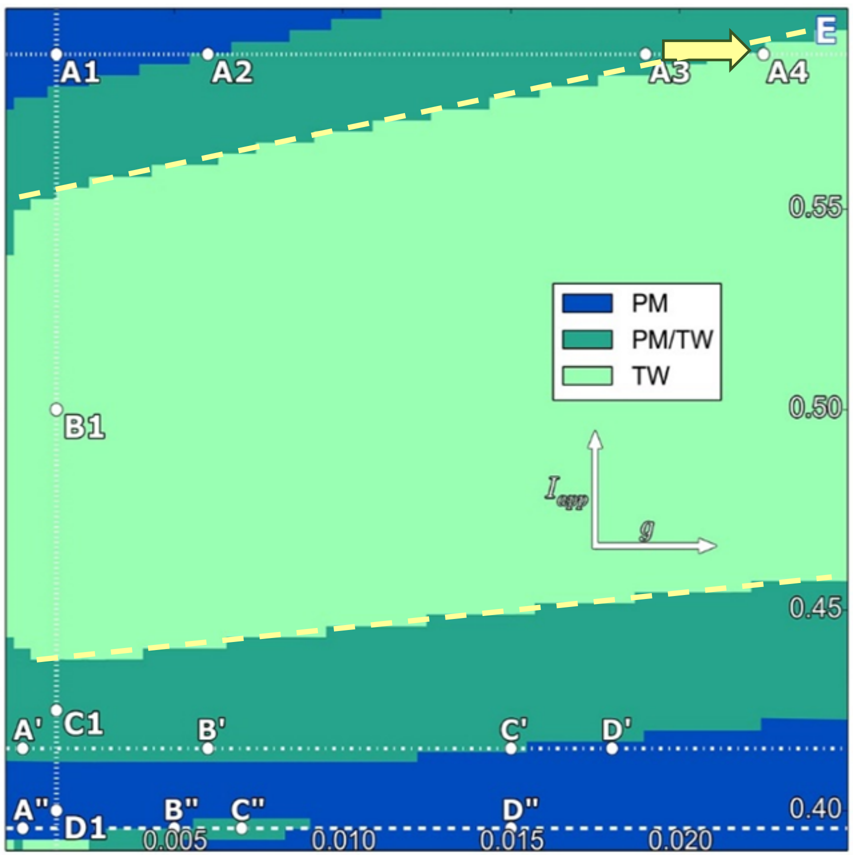
- 5,625 return maps evaluated
- 5,062,500 trace outcomes

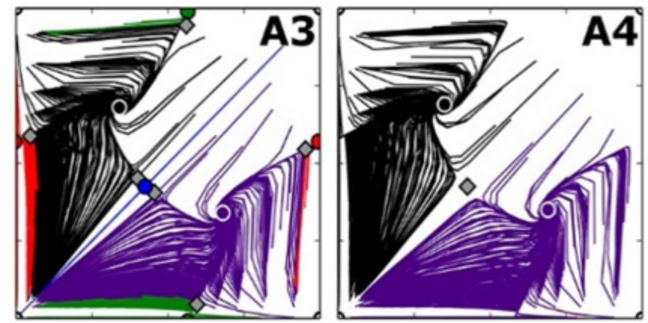
Synaptic Release

Symmetric - Pitchfork Bifurcation

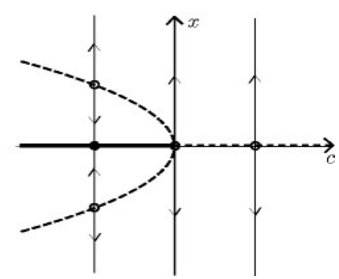


- Pacemakers lose stability via pitchfork bifurcation
- Dashed yellow lines indicate PM stability change



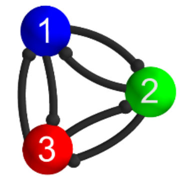


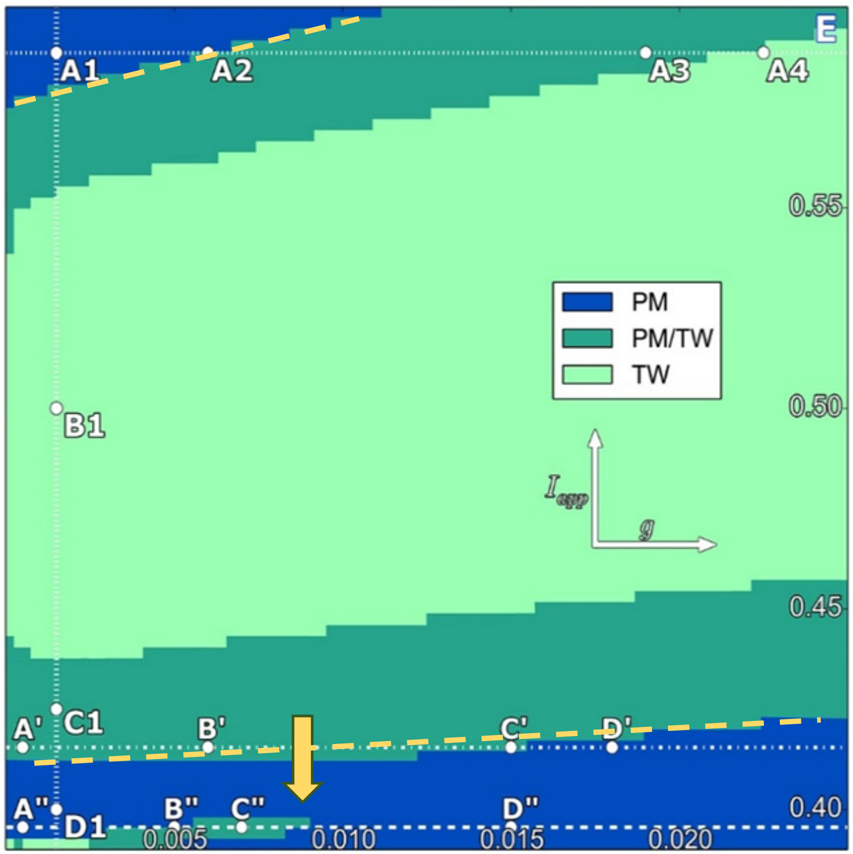
Unstable saddles collapse onto stable PM node, which then loses stability

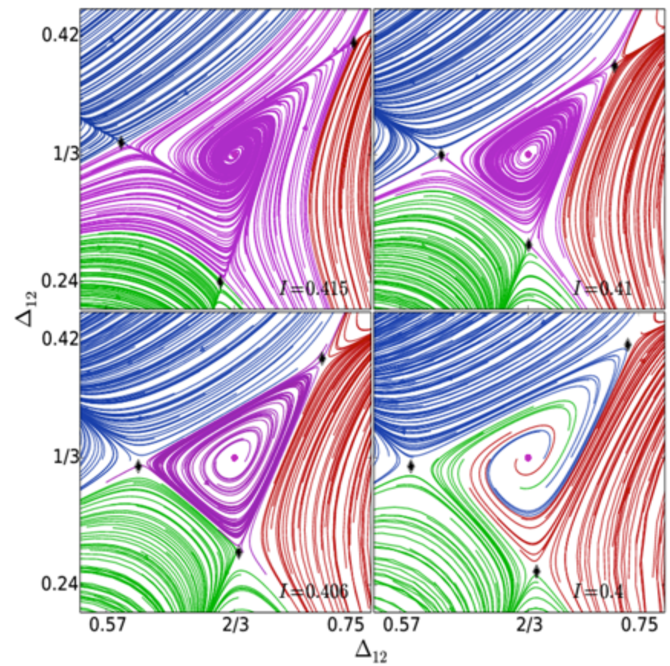


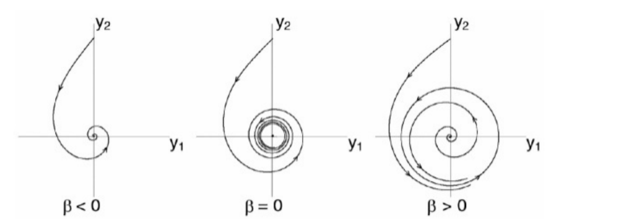
Symmetric – Andronov-Hoph Bifurcation

- Traveling wave fixed points gain or lose stability via 'Andronov-Hopf' or torus bifurcation



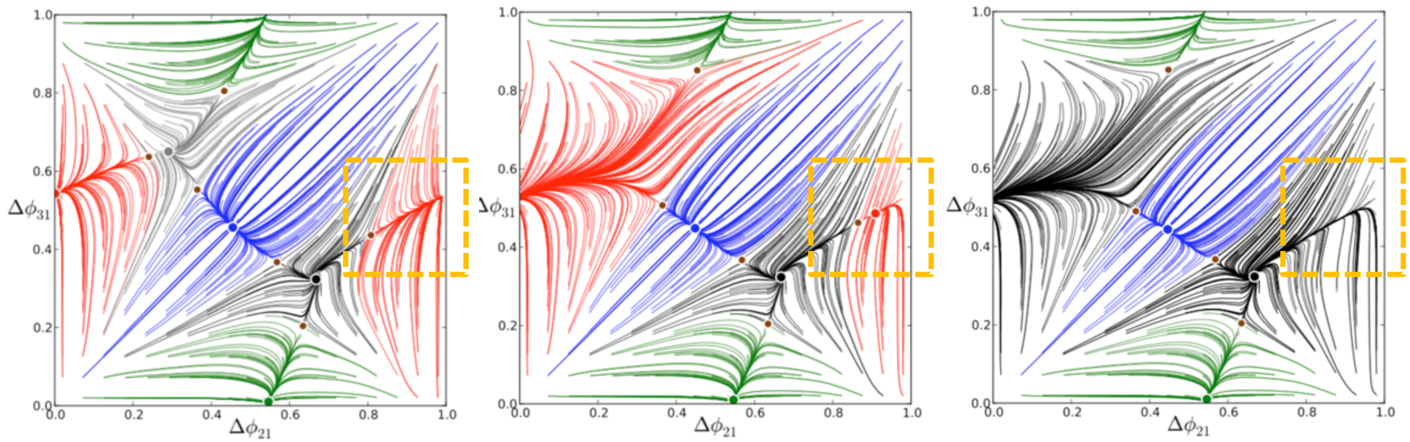


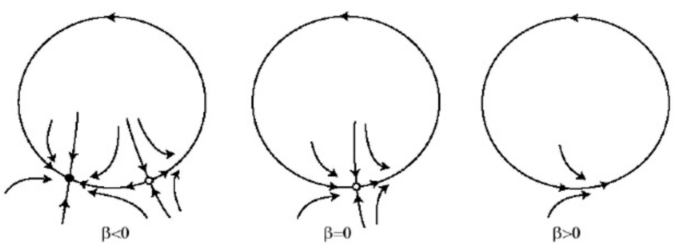




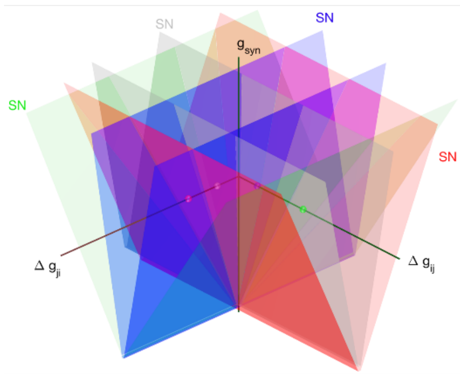
Saddle-node Bifurcations

- Saddle-node bifurcation occurs when a repelling saddle and attracting node collide and obliterate one another





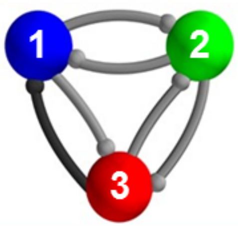
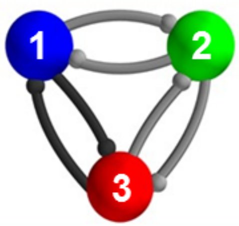
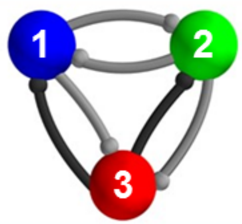
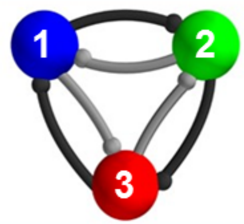
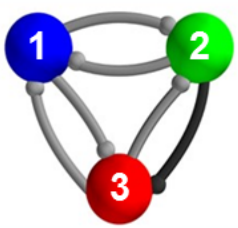
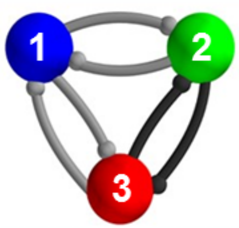
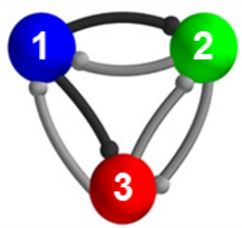
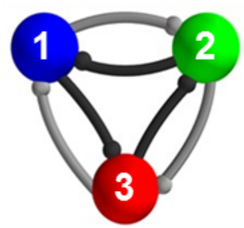
Example of saddle-node on an invariant circle (SNIC)



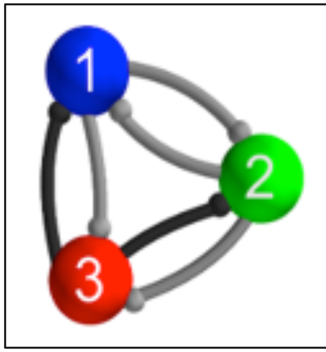
Arnold's Tongue can represent potential bifurcations with multiple parameter shifts

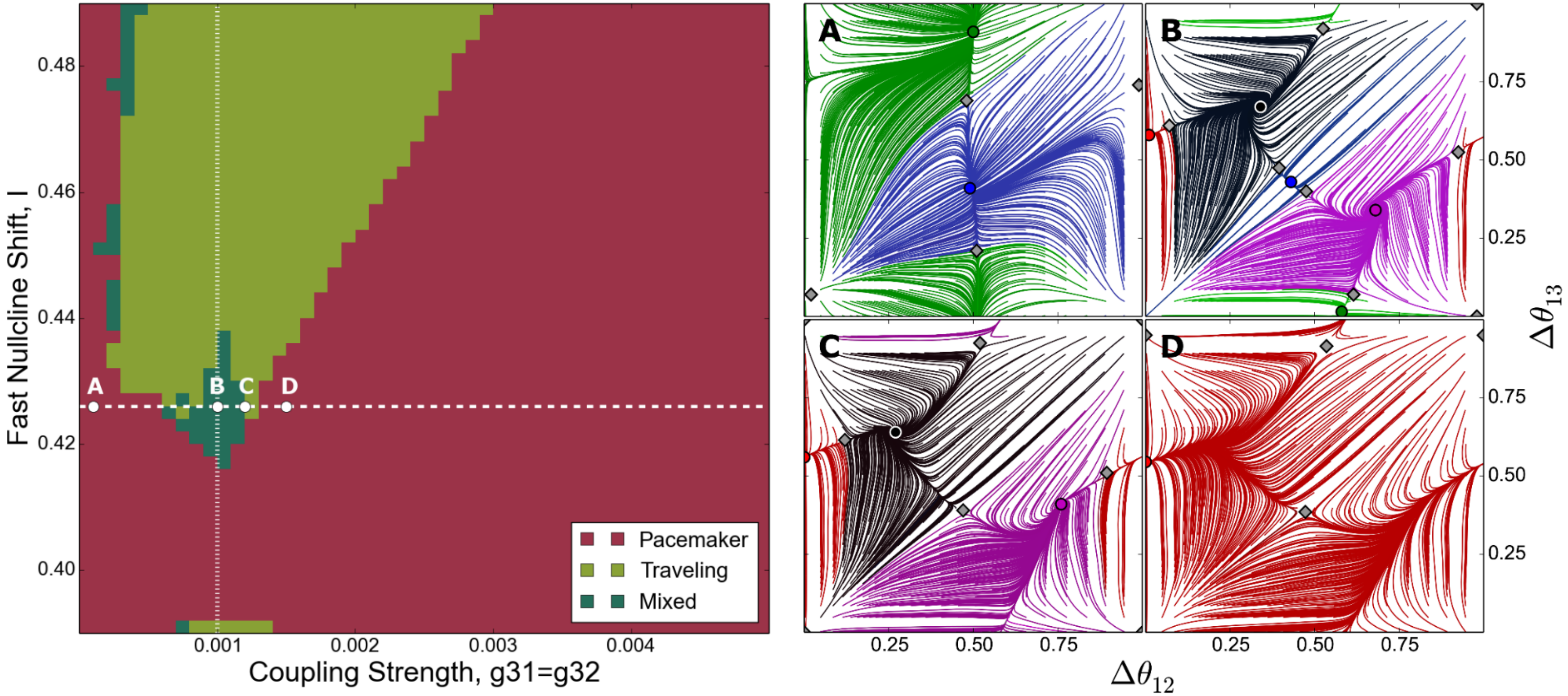
Key 3-Cell Motifs

- Results extend to networks with identical internal dynamics

Motif	Mono-biased	Pairwise-Biased	King-of-Mountain	Clockwise
Base Case				
Alternate Example				
Symmetrically Equivalent List	$\mathbf{g_{31}}$, g_{32}, g_{12}, g_{21}, g_{23}*, g_{32}	$\mathbf{g_{31}=g_{13}}$, $g_{12}=g_{21}$, $g_{23}=g_{32}$*	$\mathbf{g_{31}=g_{32}}$, $g_{12}=g_{13}$*, $g_{21}=g_{23}$	$\mathbf{g_{31}=g_{12}=g_{23}}$, $g_{13}=g_{32}=g_{21}$*

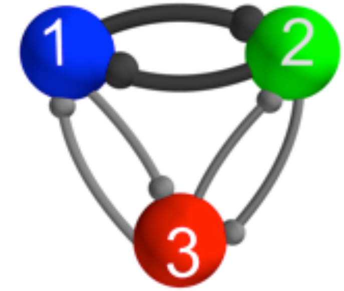
King-of-the-Mountain Bifurcations

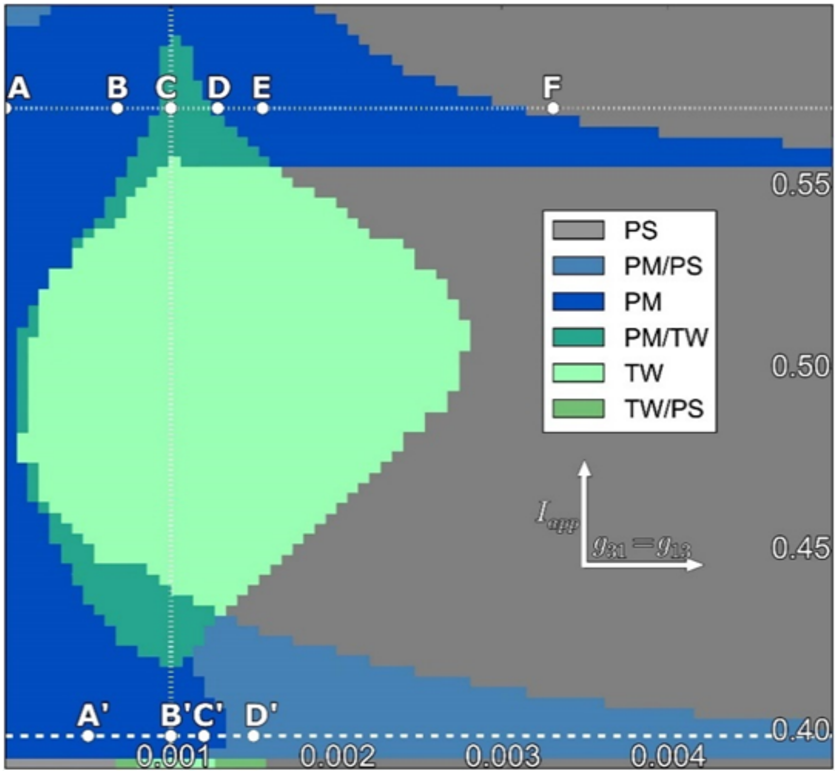


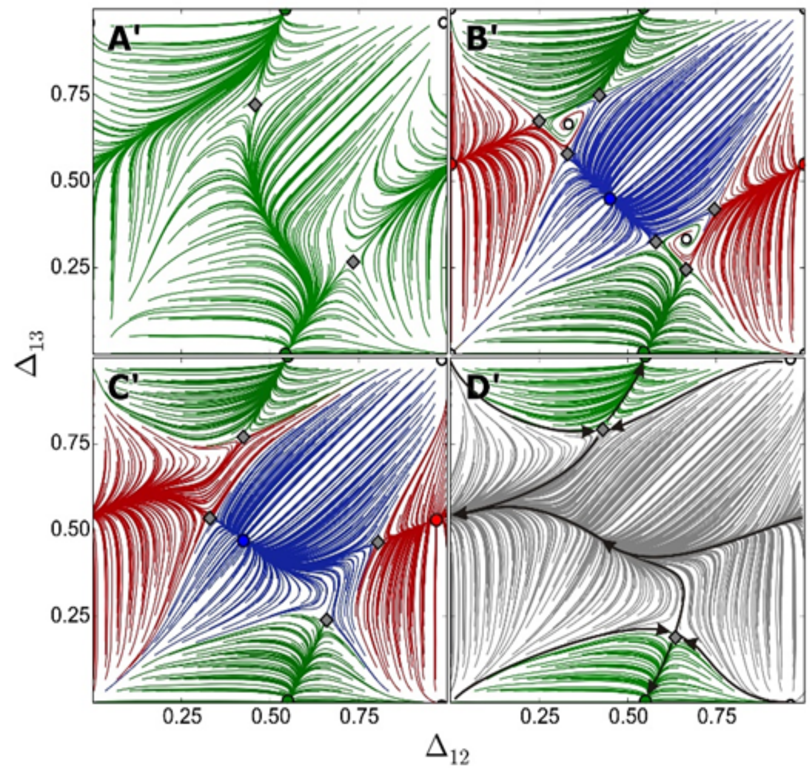


- Fixed points and saddle-nodes help identify bifurcation dynamics
- Interesting, unanticipated behavior occurs near symmetry

Pair-wise Biased Bifurcations

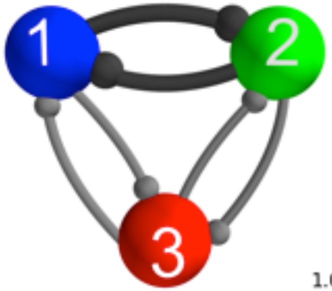


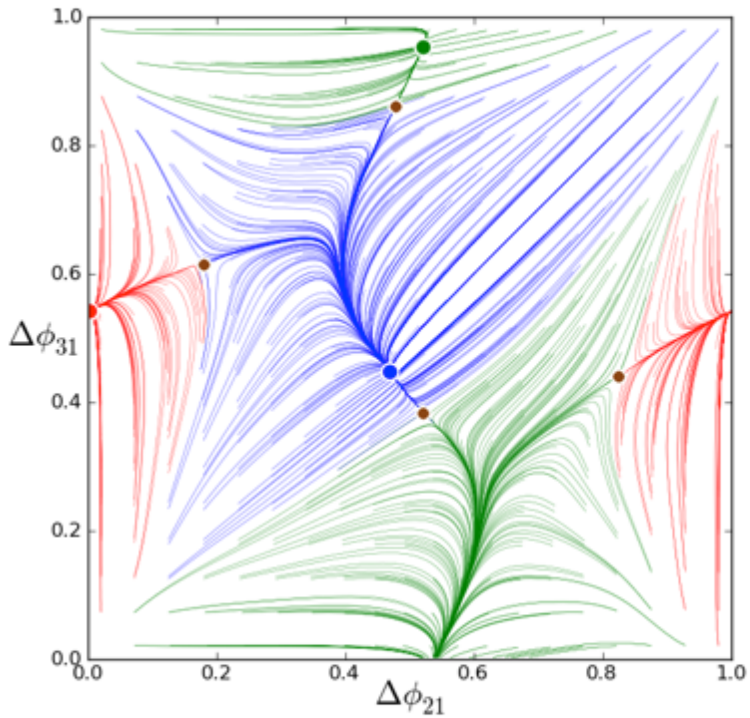


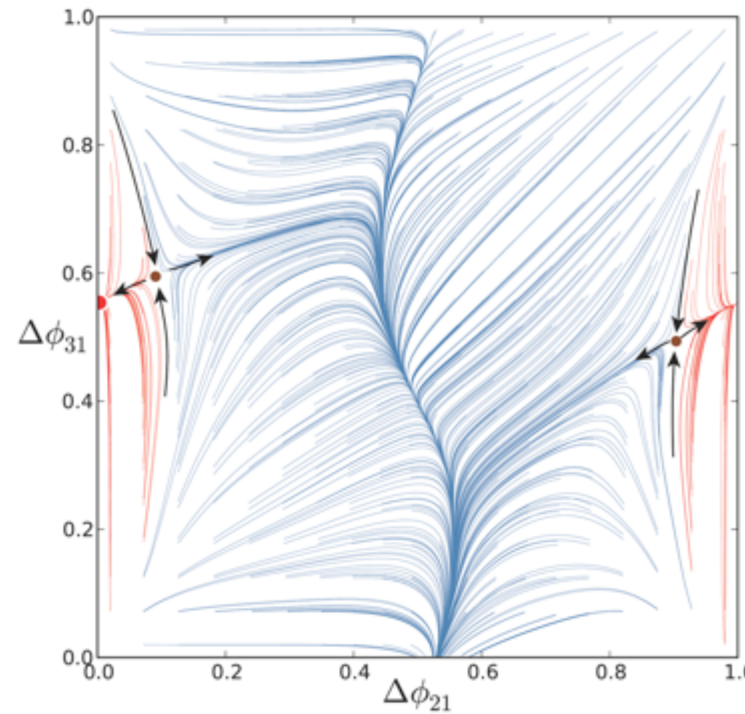


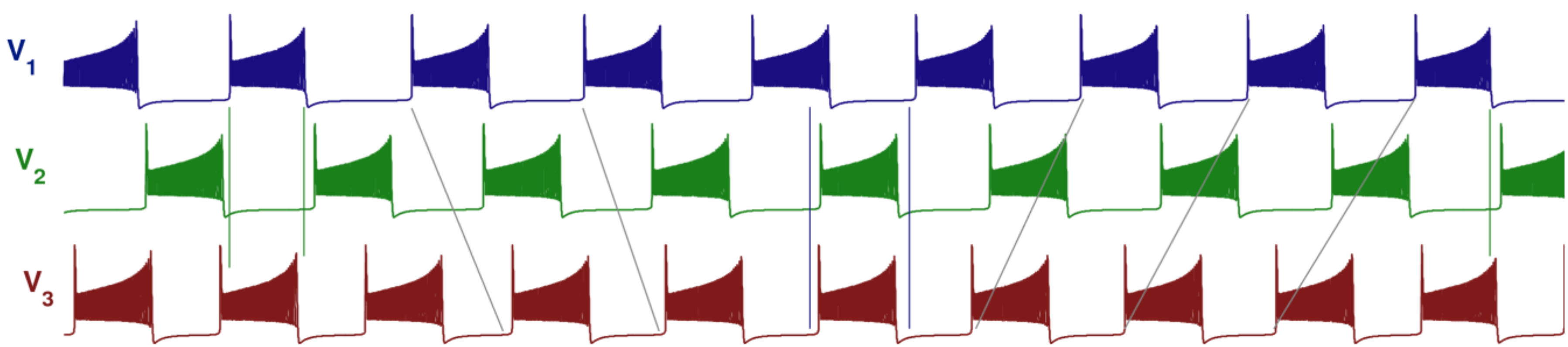
- ‘Rivers’ of phase-varying lags permit an additional layer of rhythm dynamics where two cells may remain near anti-phase

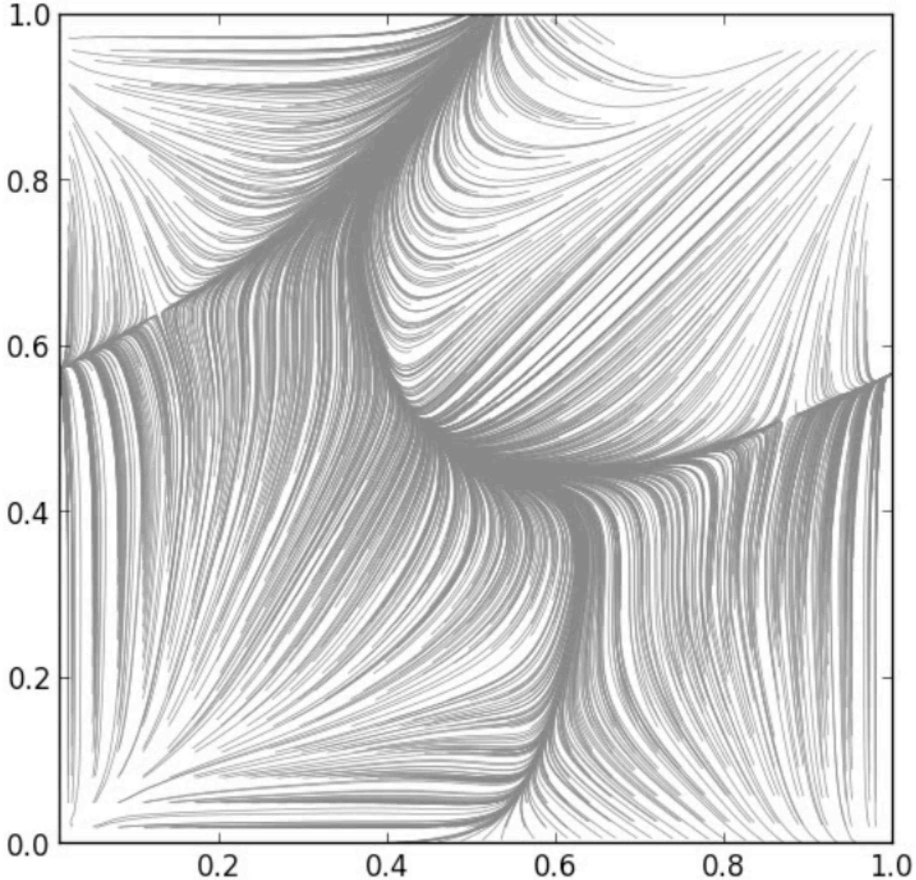
Phase slipping – invariant circles

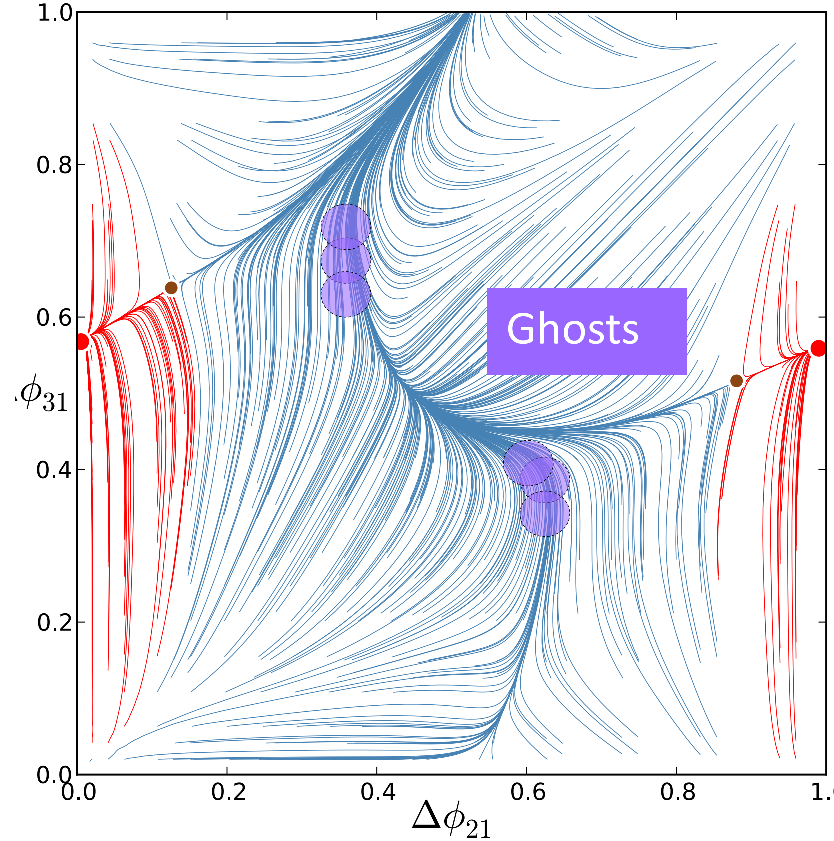


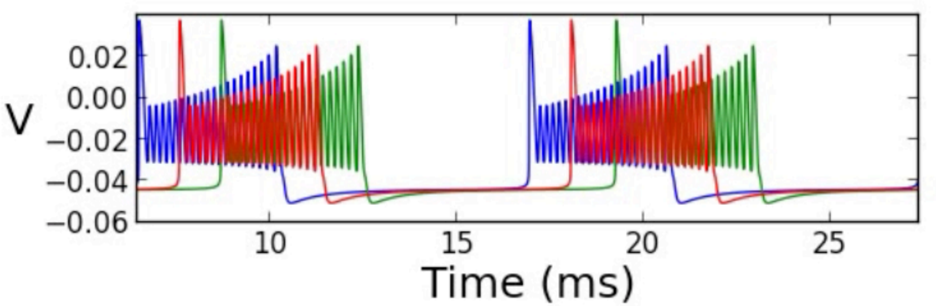


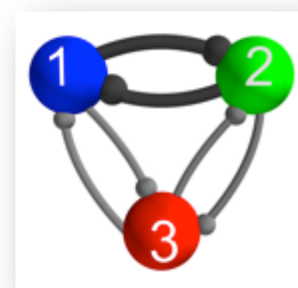






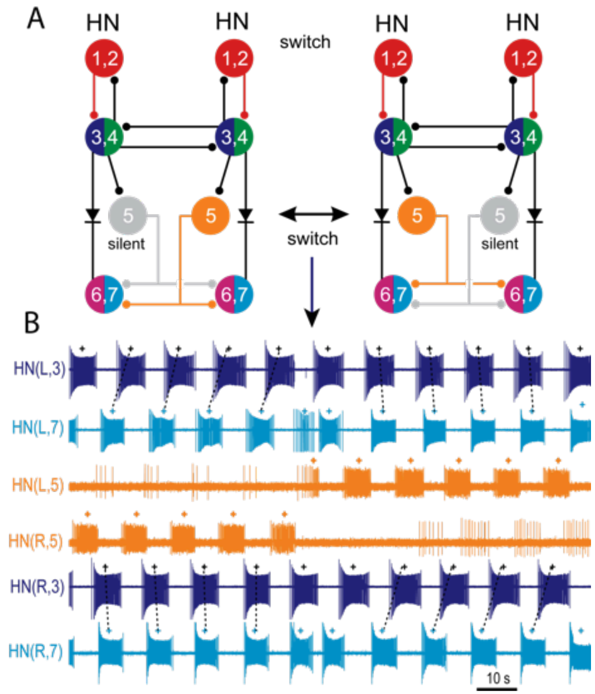


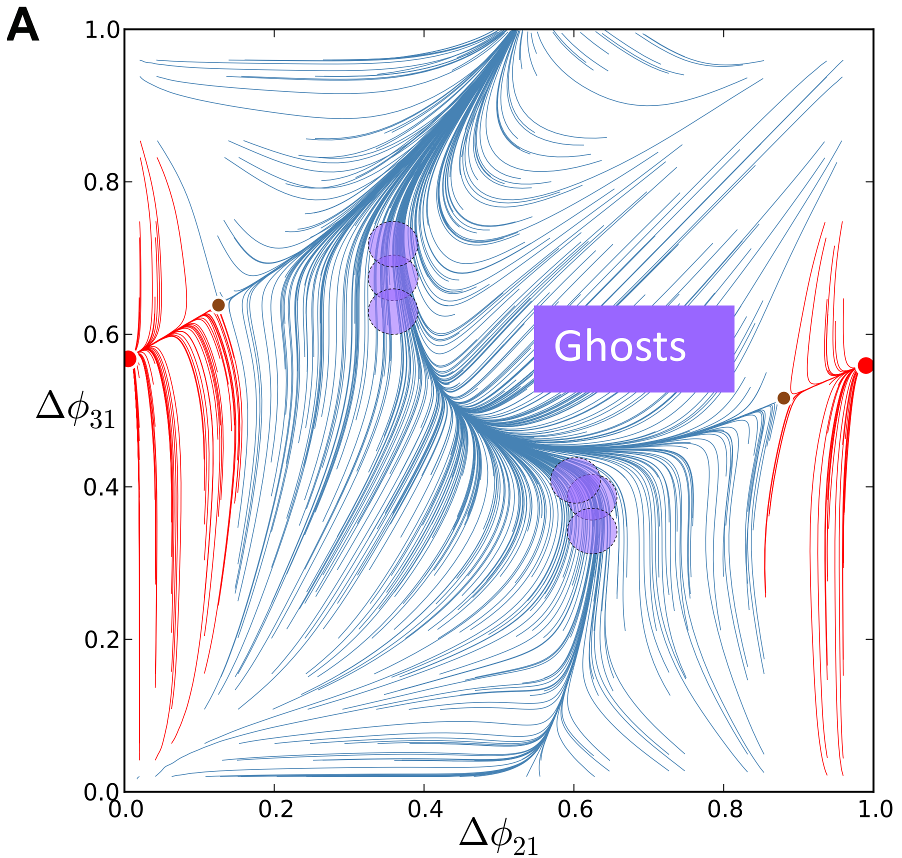


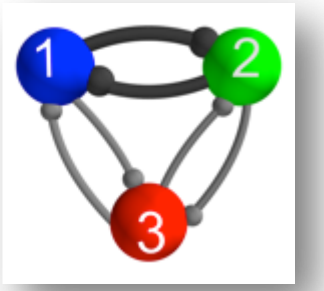


Phase slipping:

invariant curve on 2D torus





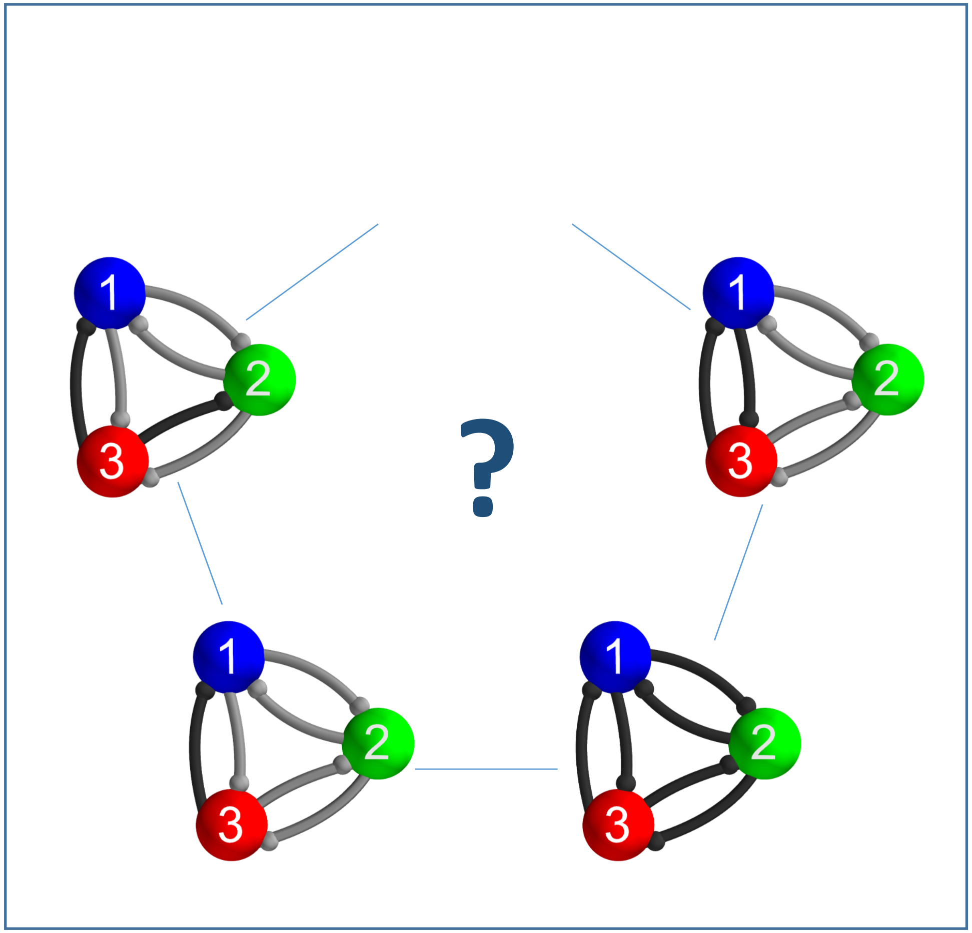


Phase slipping:

invariant curve on 2D torus

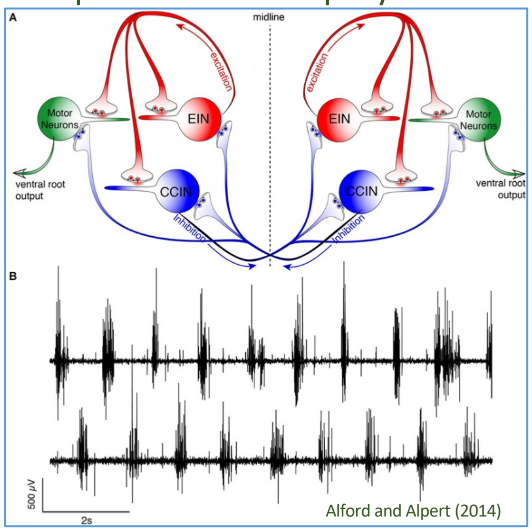
6-Nodlu ve Daha Büyük Networkler

- 3-cell motifs may be used as building blocks for larger networks
- Characterization of motifs permits hypotheses regarding 6-cell rhythm generation
- Applications in 4, 5, and much larger networks

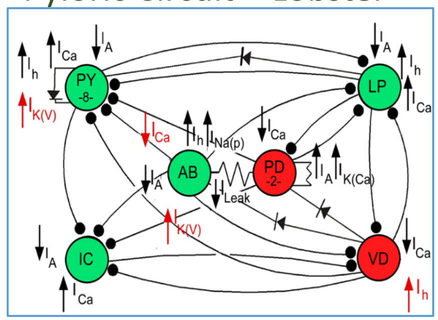


Dogada 6-Nodlu in

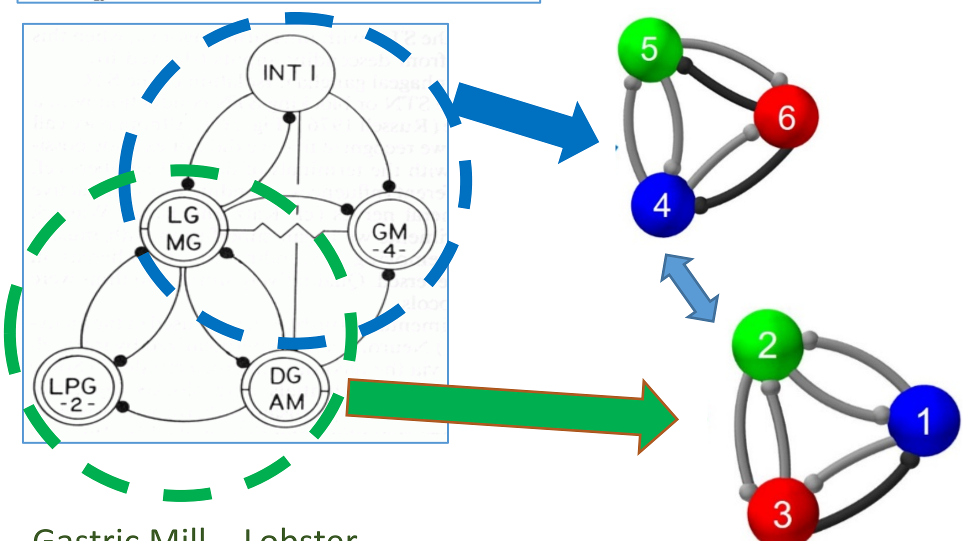
Spinal CPG – Lamprey



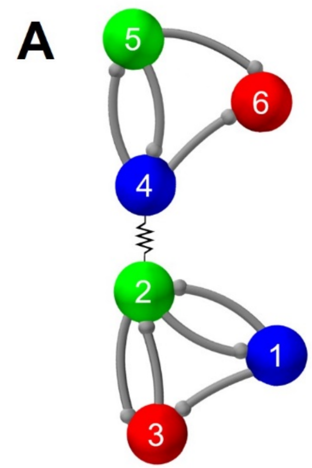
Pyloric Circuit – Lobster

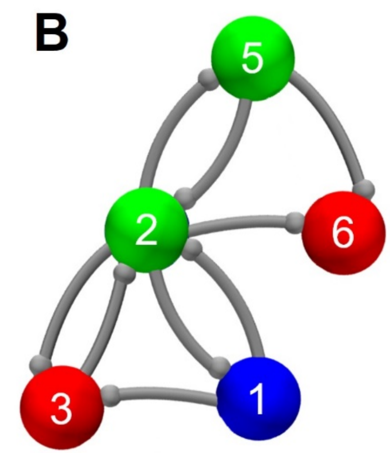


Harris-Warrick and Johnson (2010)



Gastric Mill – Lobster





- Known networks can be built from characterized motif libraries
- Predictions can be made from 3- and 6-Node simulations
- These predictions can be tested in-vitro

TESEKKÜRLER!