Connecting neurons

Imge: www.dana.org/article/how-does-the-brain-work/

Modeling the synapse

We have already encountered voltage-gated ion channels, e.g., in the Hodgkin-Huxley model

synaptic transmission involves

transmitter-activated ion channels

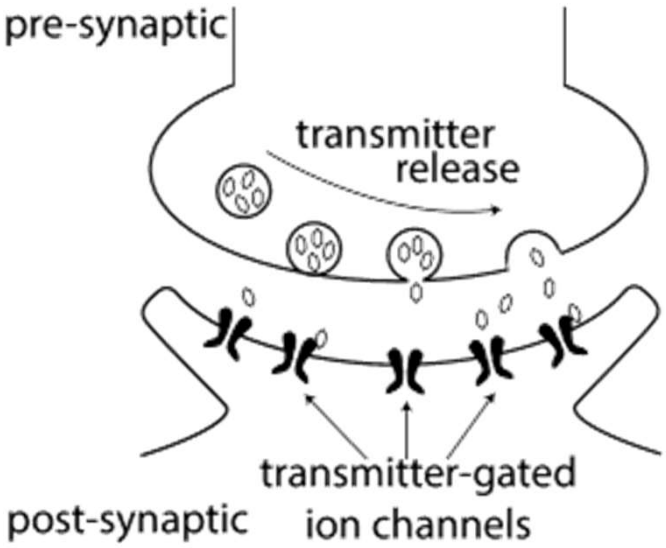


Image: neuronaldynamics.epfl.ch/online/Ch3.S1.html

The membrane potential difference now evolves as

$$C_m \, dV/dt = -I_{ion} + I_{syn}$$

where, Receptor binding gated conductance → time-varying

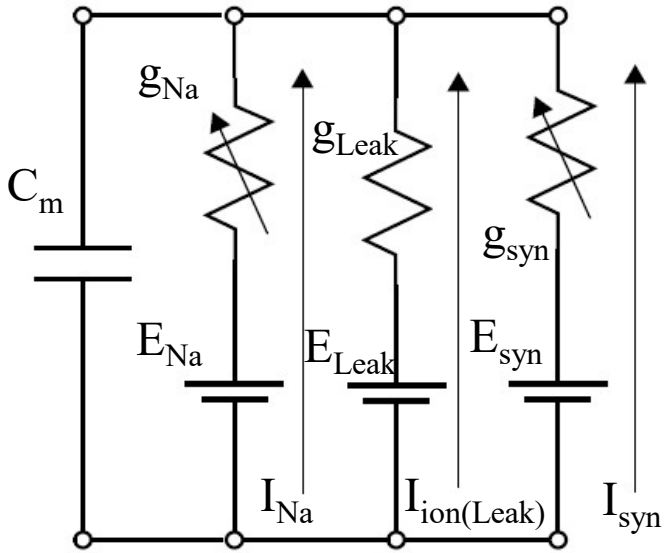
$$I_{syn} = g_{syn}(V - E_{syn})$$

with the synaptic reversal potential

E_{syn}

- $> V_{threshold}$ for excitatory synapse — Usually set to 0 mV
- $< V_{threshold}$ for inhibitory synapse — Usually set to – 75 mV

equivalent electrical circuit



Fitzhugh-Nagumo model with synapse

$$C_m\, dV/dt = -I_{ion}(V,w) + I_{syn}$$
$$dw/dt = \{w^{asymp}(V) - w\} / \tau_w$$

$w^{asymp}(V)$: kV; τ_w: $1/\varepsilon$

with $I_{syn} = \sum_i \bar{g}_{syn,i}\, s_i\, (V - E^i_{syn})$

E_{syn} { $> V_{threshold}$ (= α) for excitatory synapse; $< V_{threshold}$ (= 0) for inhibitory synapse

For each synapse, an additional dynamic variable s described by

$$ds/dt = \alpha_s(V_{pre})\,(1 - s) - \beta_s(V_{pre})\, s$$

where V_{pre}: membrane potential of pre-synaptic neuron

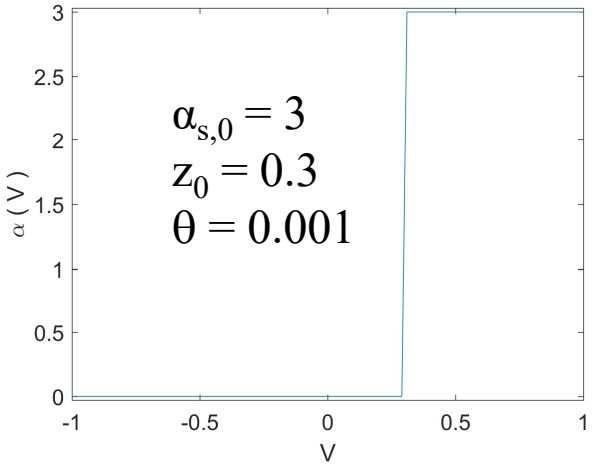
Typically

$\alpha_s(V_{pre}) = \alpha_{s,0}\, \mathcal{N}(V_{pre})$,
where $\mathcal{N}(V_{pre})$ is a sigmoid function

and $\beta_s(V_{pre}) = \beta_{s,0}\, (= \alpha_{s,0})$, a constant

For Fitzhugh-Nagumo model, a possible choice is

$\mathcal{N}(z) = \frac{1}{2}\,(\,1 + \tanh([z - z_0] / \theta\,)$



MATLAB simulations

```
> y0=zeros(6,1); %initial values
> [t,y]=ode15s(@fhnsynapsepair,[0 1000],y0);
> figure, plot(t,y(:,1),'b'), hold on, plot(t,y(:,2),'r')
```

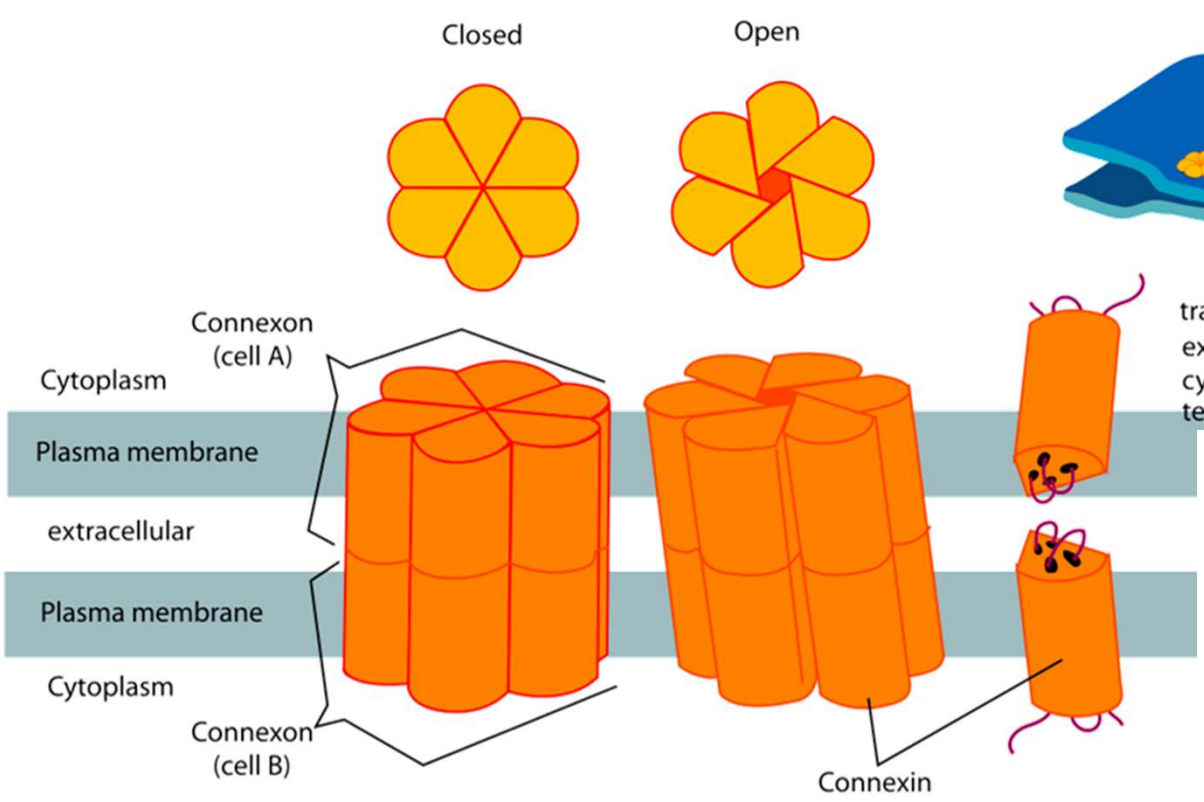
```
function dydt = fhnsynapsepair(t,y0)
E_syn=[5;-5]; %5: excitatory, -5: inhibitory
v_th = 0.3; v_sl = 0.001; %synaptic parameters
B = 3;A = 3;%synaptic parameters
g_m = 0.02; %synaptic conductance g_m can be varied in the range 0.01-1
%I=zeros(N,1); I(1)=0.2;%external current
I=[0.1;0];
W_syn=[0 1;1 0];
W_syn=sparse(W_syn);
v=y0(1:2);
w=y0(3:4);
s=y0(5:6);
dydt=[3*v.*(v-0.1).*(1-v)-w+I-g_m*((v.*(W_syn*s))-(W_syn*(E_syn.*s)));0.05*(v-w);(A*0.5*(1+tanh((v-v_th)/v_sl))).*(1-s)-B*s];
```

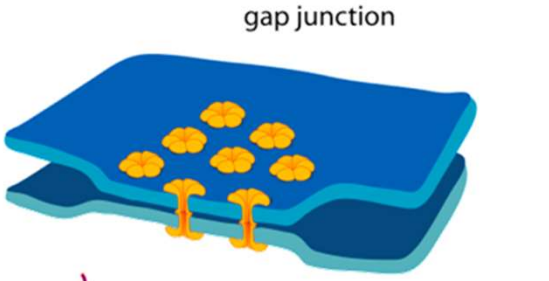
No synaptic delay

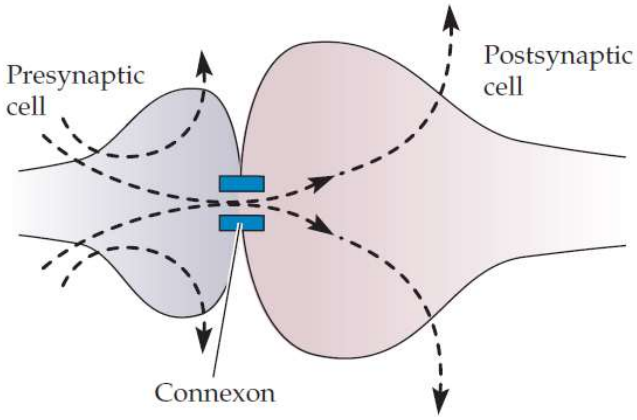
Electrical synapses ≡ gap junctions

Communication between neurons is mediated via the direct spread of electric current from one neuron to another

a connexon or a connexin hemichannel is an assembly of six connexin proteins that form the pore for a gap junction between the cytoplasm of two adjacent cells







typically dendrite-to-dendrite
or axon-to-axon

Image: Mariana Ruiz, Wikipedia

Image: Nicholls et al, From Neuron to Brain, 5th edition (2012)

How different are gap junctions from chemical synapses ?

Can gap junctions rectify ?

Gap junctions between cells of the same type usually are bidirectional, but junctions between cells of different types may show strong rectification, with depolarizations being transferred preferentially in one direction and hyperpolarizations in the other due to the two different cells contributing different protein subunits at either side of the junction

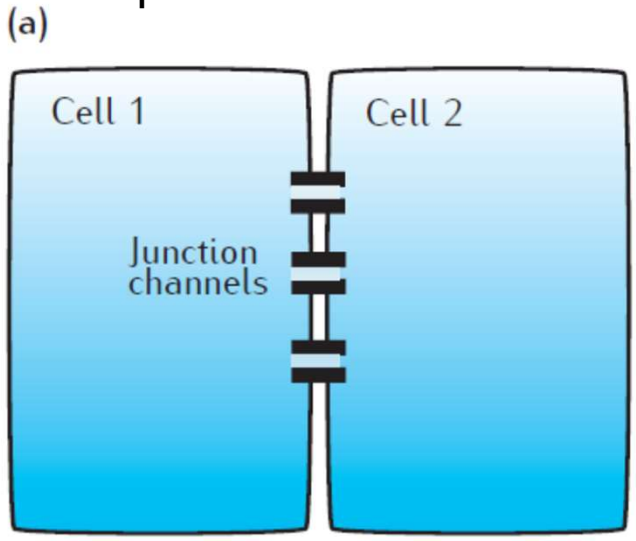
Can gap junctions adapt ?

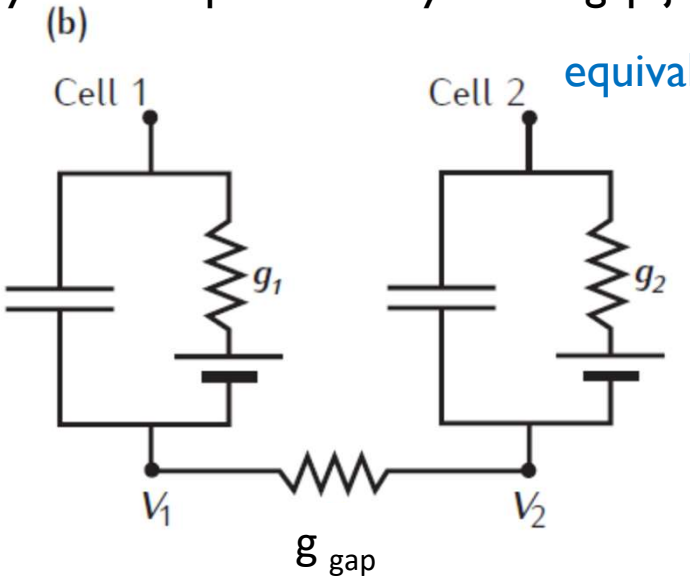
Gap junction conductance can be modulated by various G protein-coupled receptors, leading to long lasting changes in coupling strength as the result of neuronal activity, similar to long-lasting changes in chemical synapses

Non-neuronal example: In the gravid uterus, muscle cells communicate via gap junctions whose conductance can be altered over a scale of days by hormones that promote expression of connexin proteins

Modeling gap junctions

A simple model assumes a fixed, symmetric permeability of the gap junction channels





equivalent electrical circuit

The current flowing into each neuron through the gap junction is proportional to the voltage difference between the two neurons (at the junction)

So, the equation for transmembrane potential difference for each cell

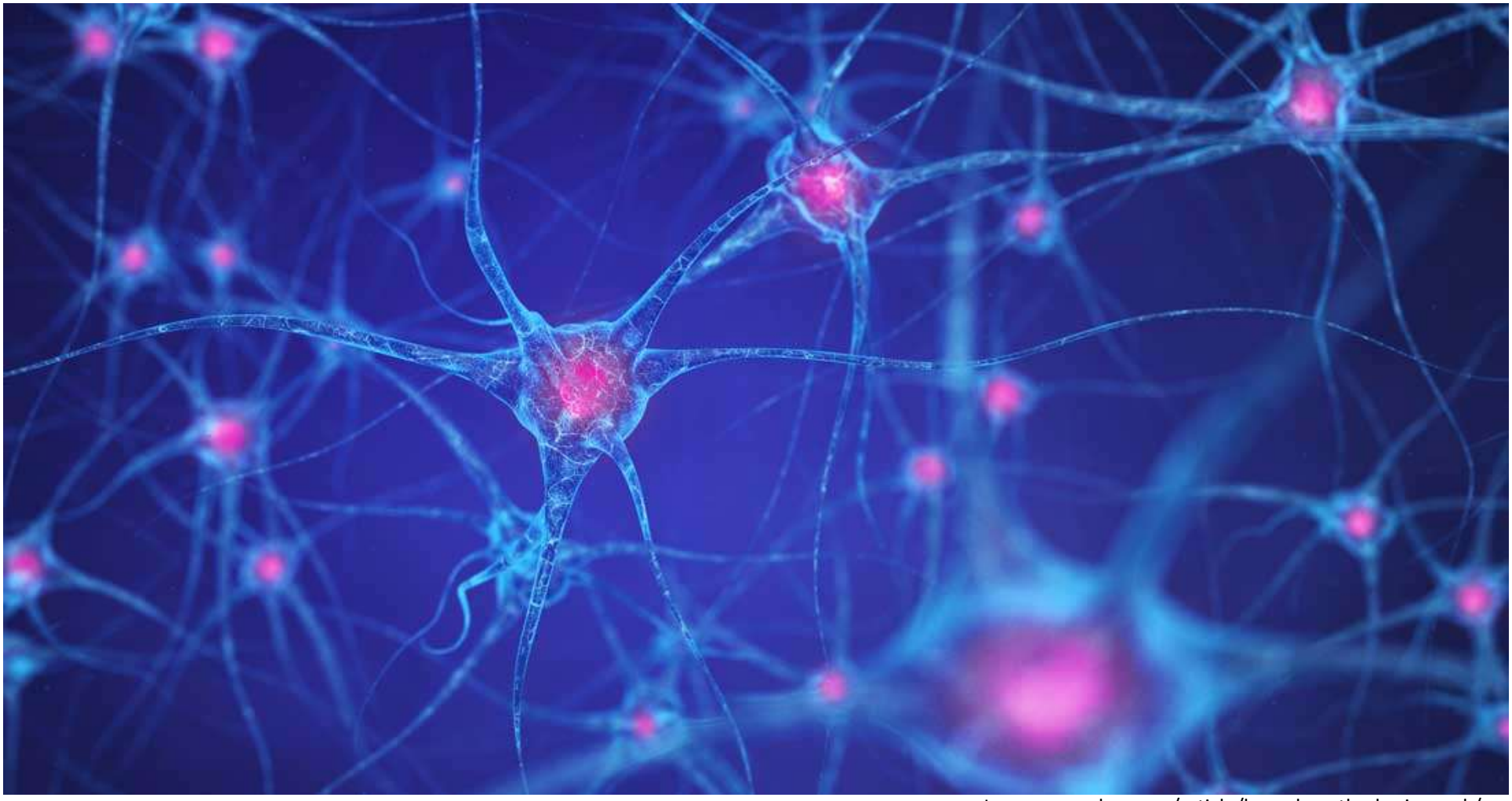
$$C_m \, dV/dt = -I_{ion} + I_{gap}$$

For Cell 1: $I_{gap} = g_{gap}(V_2 - V_1)$

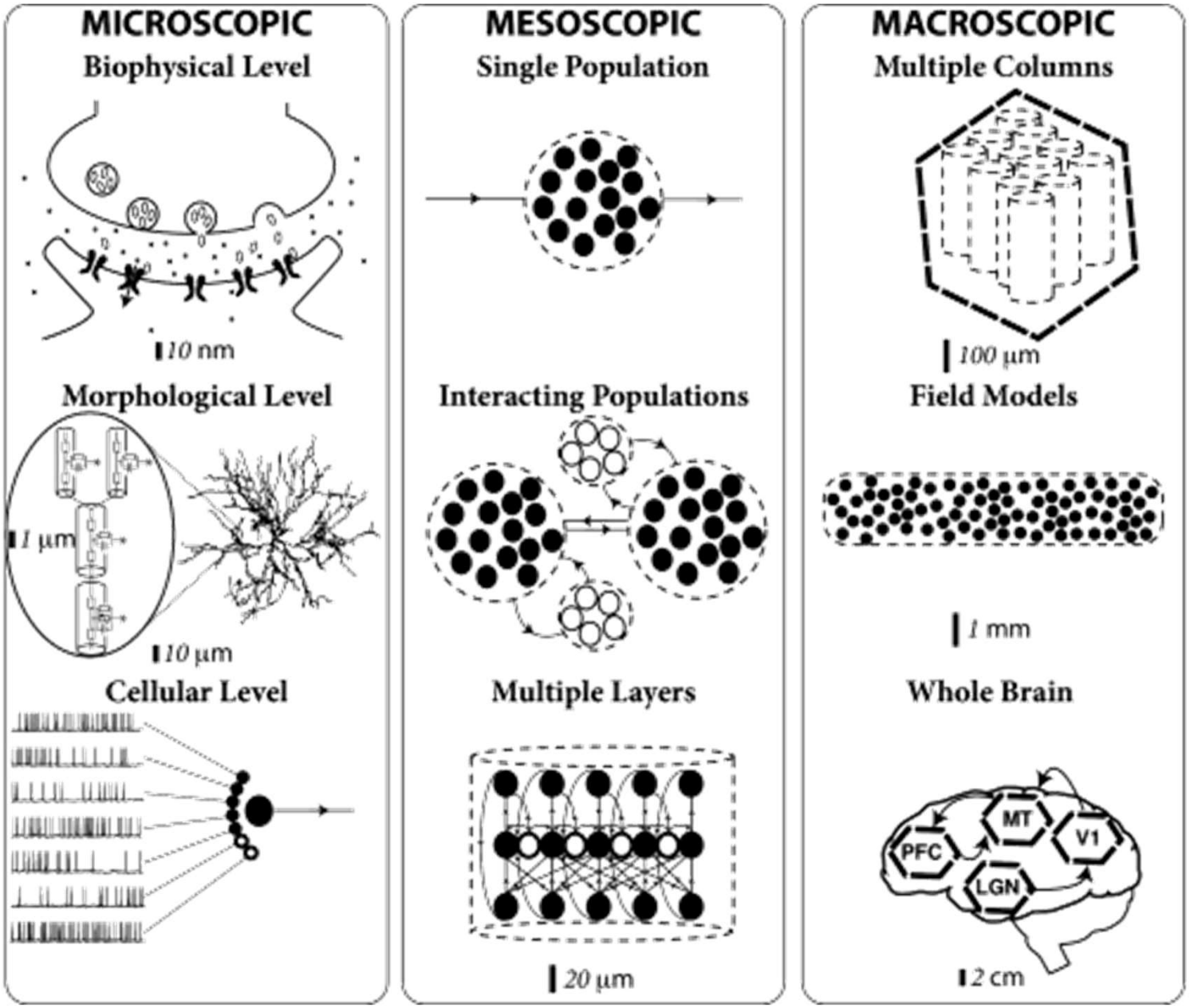
For Cell 2: $I_{gap} = g_{gap}(V_1 - V_2)$

Image: Sterratt et al, Principles of Computational Modeling in Neuroscience, Cambridge

From neurons to networks to brain



Imge: www.dana.org/article/how-does-the-brain-work/



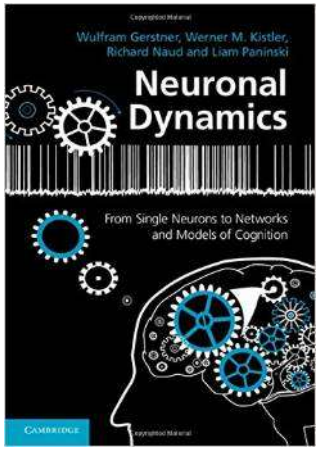


Image: neuronaldynamics.epfl.ch

Neural mass models & Neural field models

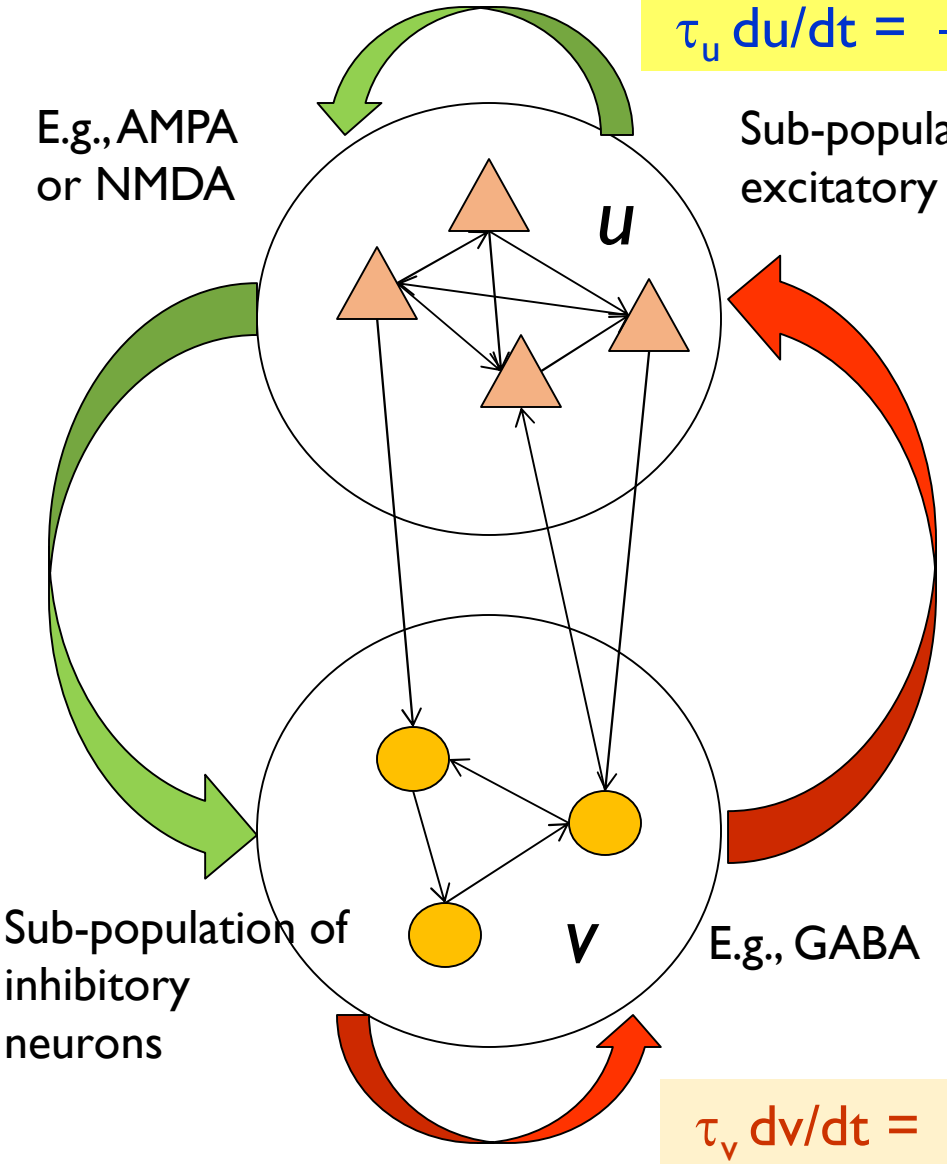
Models of brain activity can be divided into two classes:

Neural mass models : characterize activity over time only; by assuming that all neurons in a population are located at (approximately) the same point.

Neural field models: prescribe how a quantity characterizing neural activity (such as average depolarization of a neural population) evolves over both space and time.

Modeling the Dynamics of a Local Brain Region

$$\tau_u \, du/dt = -u + (1-u)\, S\,(w_{uu}\, u - w_{uv}\, v + I_u^{ext})$$



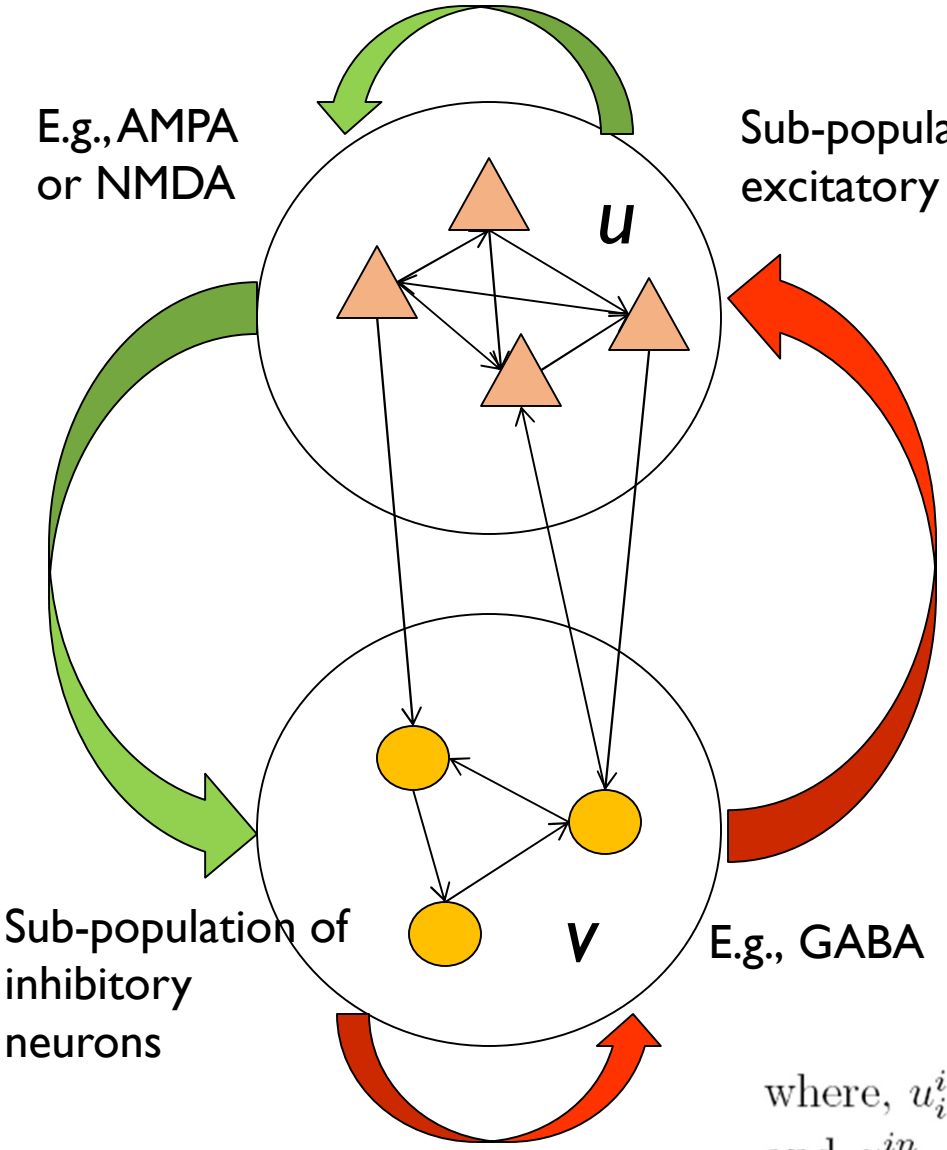
u: fraction of active excitatory neurons

v: fraction of active inhibitory neurons

S: input-output function, usually of sigmoidal nature

$$\tau_v \, dv/dt = -v + (1-v)\, S\,(w_{vu}\, u - w_{vv}\, v + I_v^{ext})$$

Modeling the Dynamics of a Local Brain Region



Wilson-Cowan Model (1972)

Phenomenological description of activity in a system of coupled subpopulations of excitatory & inhibitory neurons

$$\tau_u \dot{u}_i = -u_i + (\kappa_u - r_u u_i)\ \mathcal{S}_u(u_i^{in}),$$
$$\tau_v \dot{v}_i = -v_i + (\kappa_v - r_v v_i)\ \mathcal{S}_v(v_i^{in}),$$

$$\text{where, } u_i^{in} = c_{uu}u_i - c_{uv}v_i + \sum{}'(w_{ij}^{uu}u_j - w_{ij}^{uv}v_j) + I_u^{ext}$$
$$\text{and } v_i^{in} = c_{vu}u_i - c_{vv}v_i + \sum{}'(w_{ij}^{vu}u_j - w_{ij}^{vv}v_j) + I_v^{ext}$$

Oscillations in the Wilson-Cowan model

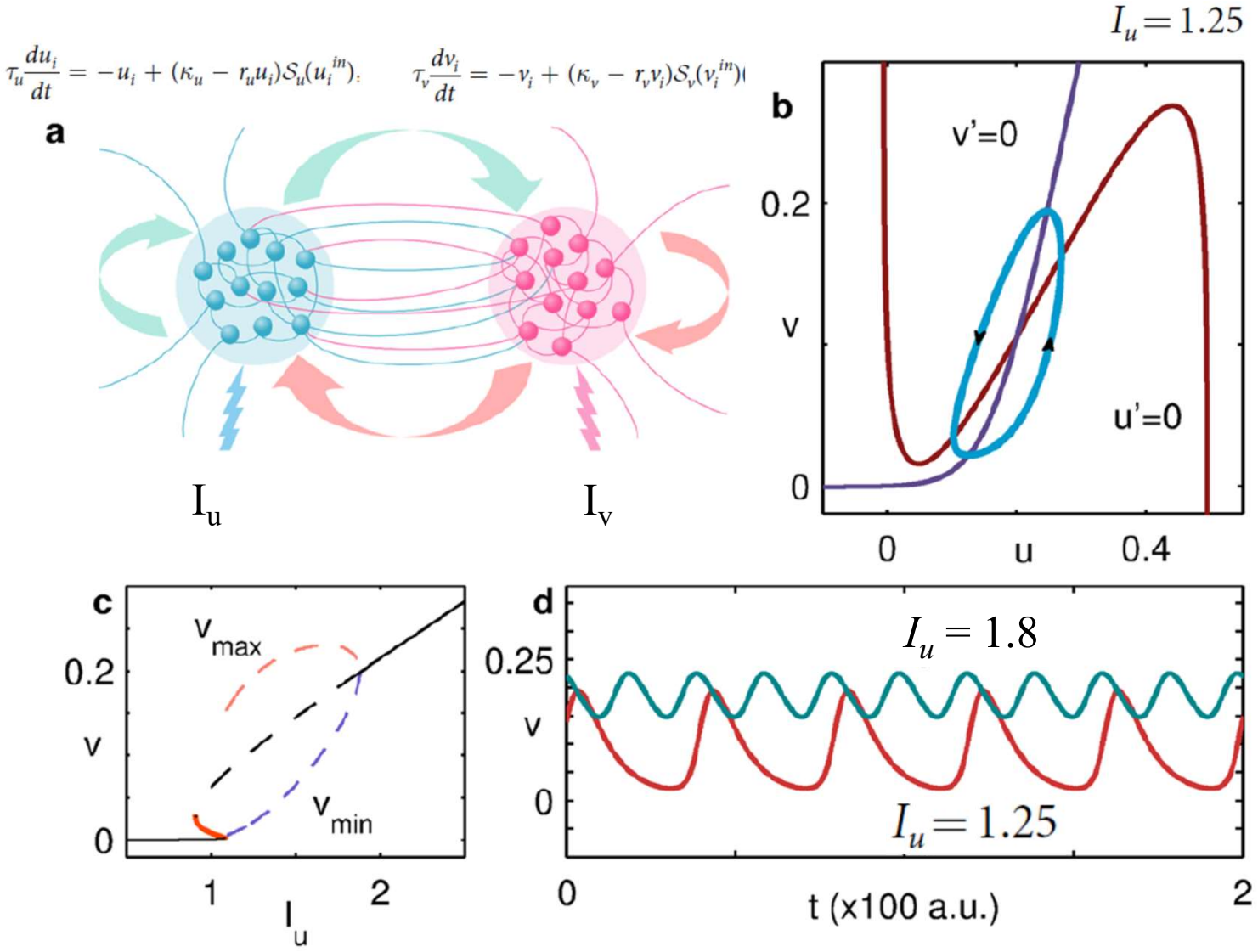
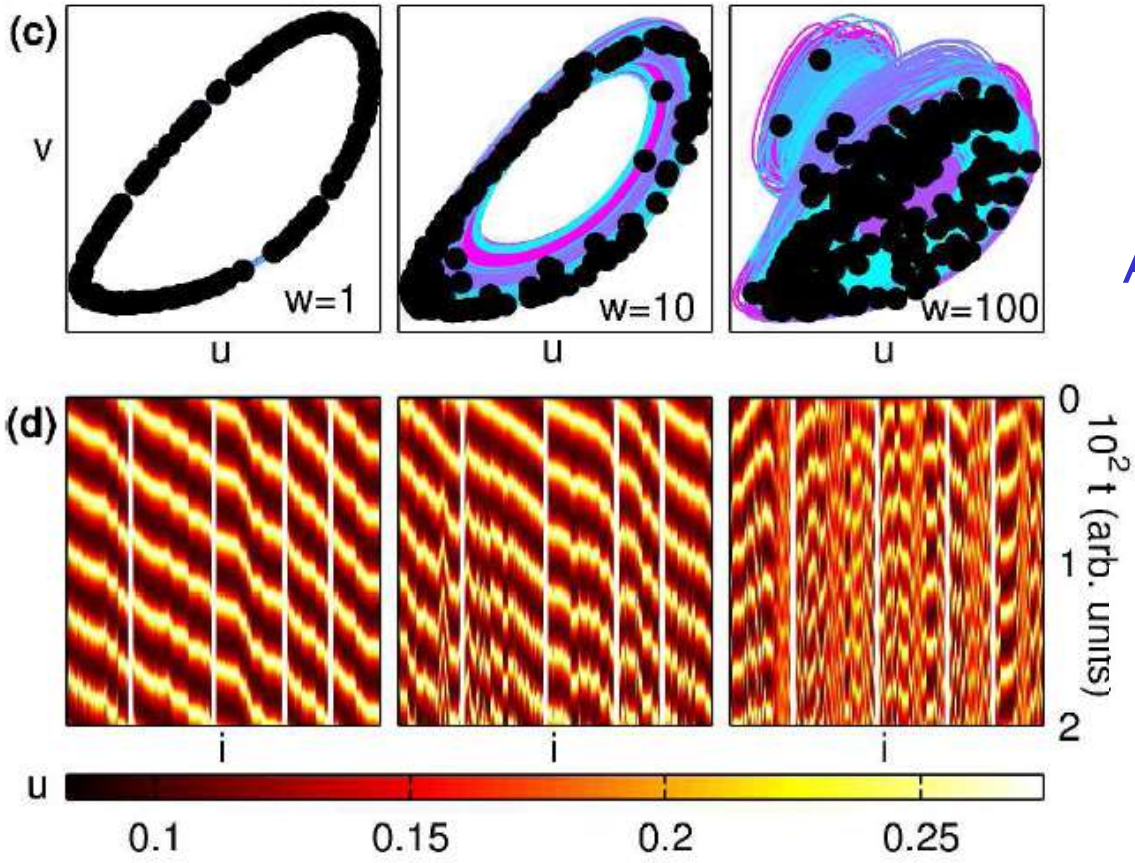


Image: V Sreenivasan, S N Menon & SS, Sci. Rep. 7 (2017)

Collective Dynamics of WC Networks

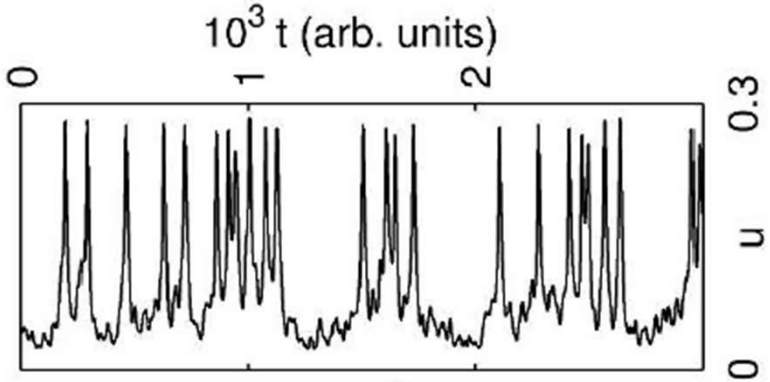
Increasing connection strength →



Images: R Singh, S N Menon & SS. Sci. Rep. **6** (2016).

Parameters of WC model chosen so that each isolated node has limit cycle dynamics: Relaxation oscillations

Activity in each node of a Macaque monkey cortico-cortical network is simulated using WC model



Resulting time-series of node activity are qualitatively similar to experimentally recorded activity in Macaque brain regions

Neural field models:

Reaction-diffusion equation

$$C_m \frac{\partial V}{\partial t} = g_{gap} \frac{\partial^2 V}{\partial x^2} - I_{ion}$$

Diffusion

Reaction (Nonlinear dynamics)

For neural **oscillators**, we can define a complex amplitude

$$W = R \exp (i\varphi)$$

For SHO, Amplitude R : $dR/dt = 0$
Phase φ : $d\varphi/dt = \omega_0$

W(x,t) at each point represents the dynamical state of the system

Reaction (Nonlinear dynamics) Diffusion

$$\partial W/\partial t = \mu (\sigma_l + i\, \omega_l) W - (g_r + i\, g_i) |W|^2 W + D\, \partial^2 W/\partial x^2$$

where $D = d_r + i\, d_i$ is a complex diffusion coefficient

This is the **Complex Ginzburg-Landau Equation**

Complex Ginzburg-Landau Equation

Describes spatiotemporal pattern formation

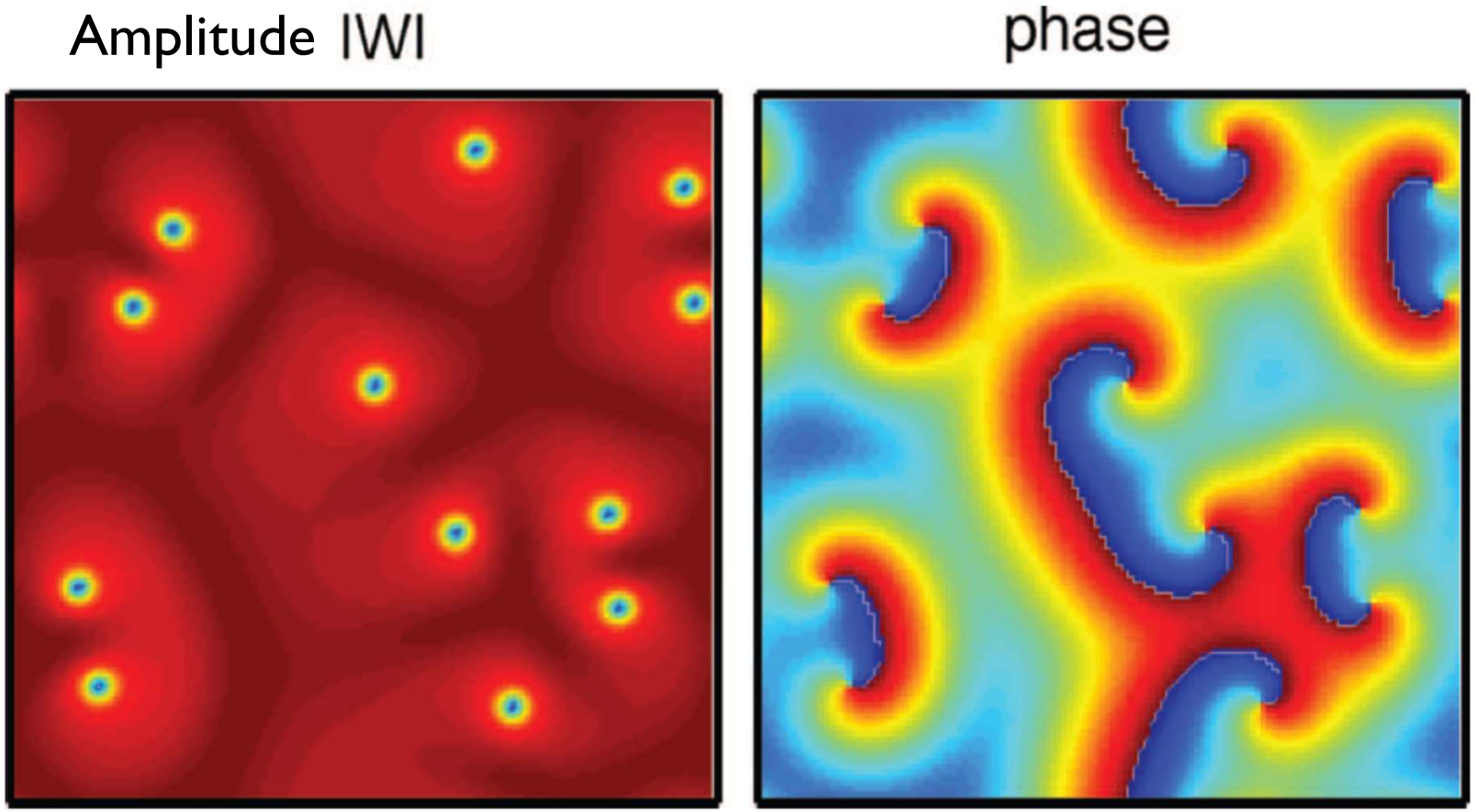


Image: Garcia-Morales & Krischer, Contemp Phys (2012)

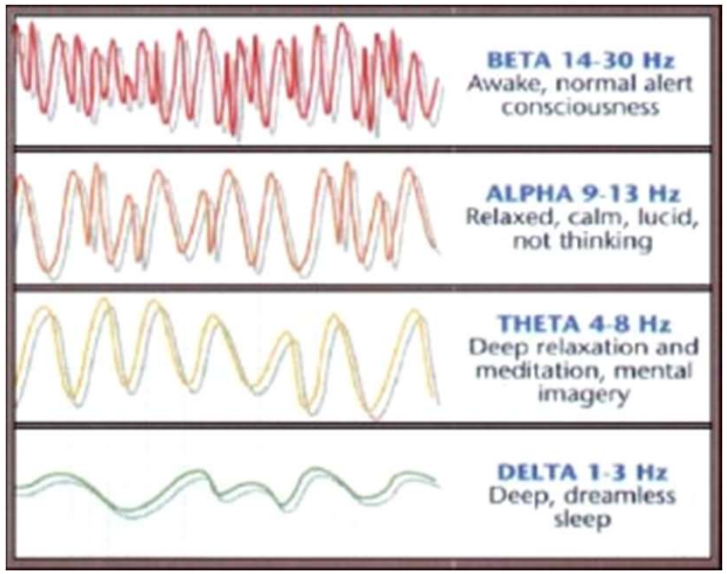
2-Dimensional CGLE on a square domain

Mean-field models of the brain

When simulating a large number of interacting neurons, it maybe easier to approximate the population dynamics of interconnected neurons by mean-field models.

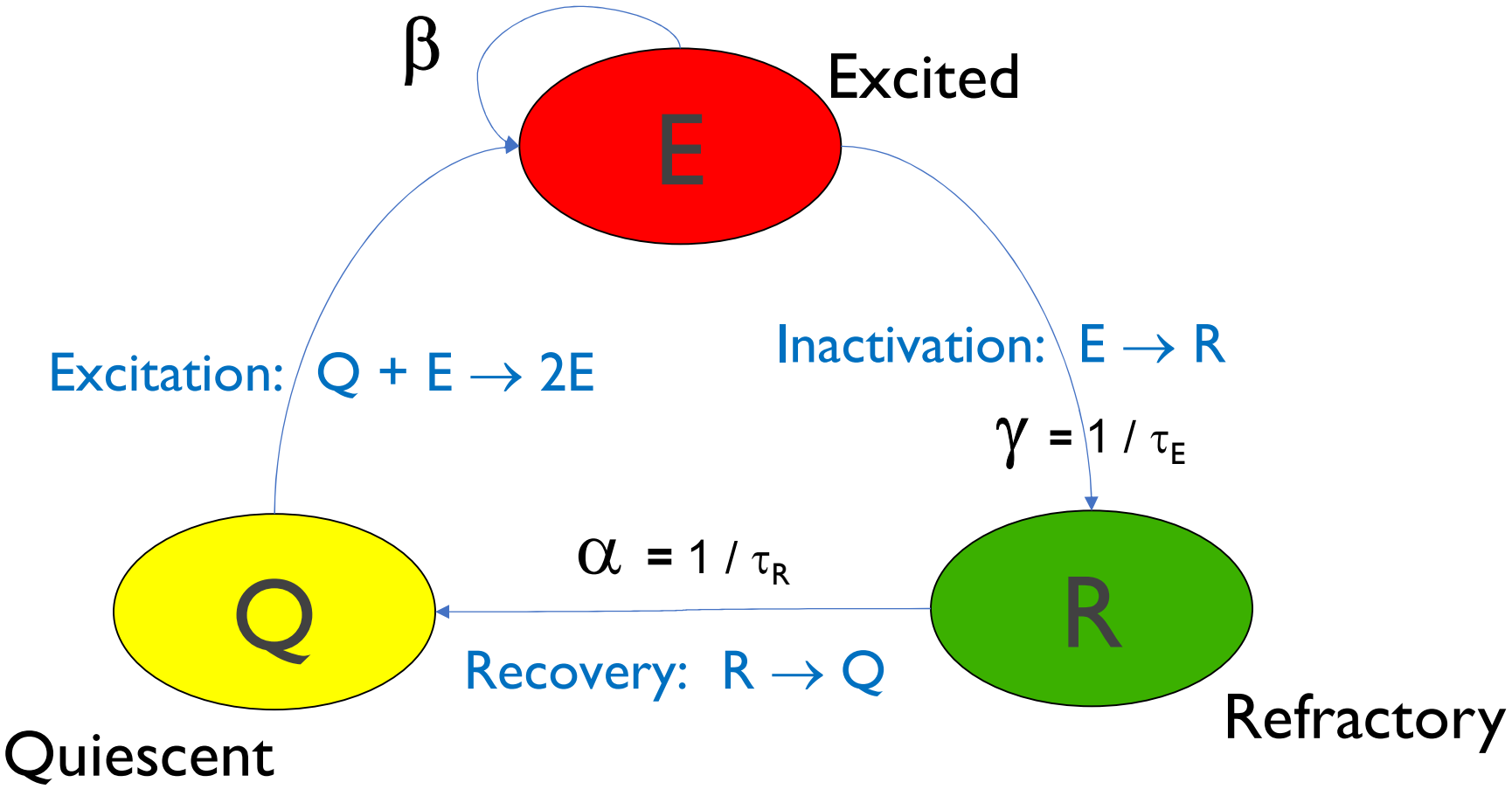
By ignoring details of individual neurons, it is possible to describe the macroscopic behavior of large networks, e.g., the mean firing rate of the population

To arrive at a deeper understanding of neural activity as measured by fMRI or electrophysiology.



A simple model of activity in a homogeneous population of excitatory neurons

Q-E-R-Q model



Dynamics of the QERQ model

Change in quiescent population, dQ/dt = Gain from neurons recovering from refractory state – Loss through new excitations

= $(1 / \tau_R)$ x Current refractory population – β x mean number of connections of a neuron x fraction of excited neighbours per neuron x current quiescent population

$$dQ/dt = (1 / \tau_R)\, R - \beta\, k\, (E/N)\, Q = (1 / \tau_R)\, R - \beta\, k\, (E/N)\, [N - E - R]$$

Dividing by N, fractional change $dq/dt = (1 / \tau_R)\, r - \beta\, k\, e\, [1 - e - r]$

Change in excited population, dE/dt =

Growth through new excitations – Loss via passage to refractory state

$$dE/dt = \beta\, k\, (E/N)\, [N - E - R] - (1 / \tau_E)\, E$$

Dividing by N, $de/dt = \beta\, k\, e\, [1 - e - r] - (1 / \tau_E)\, e$

Change in refractory population, dR/dt = Growth by passage of excitatory neurons to refractory state – loss from neurons recovering to quiescent state

$$dR/dt = (1 / \tau_E)\, E - (1 / \tau_R)\, R$$

Dividing by N, $dr/dt = (1 / \tau_E)\, e - (1 / \tau_R)\, r$

Dynamics of the QERQ model

The mean-field dynamics reduces to 2 coupled ODEs

$$de/dt = e \{ \beta k [1 - e - r] - (1 / \tau_E) \}$$

$$dr/dt = (1 / \tau_E) e - (1 / \tau_R) r$$

The nullclines for e are $e=0$ and $e= 1 - r - [1/(\tau_E \beta k)]$

The nullcline for r is $e = (\tau_E / \tau_R)r$

$\Rightarrow$ Two equilibria are

- $e_1^*=r_1^*=0$, and
- $e_2^*= (\tau_E \beta k - 1)/(\beta k\{\tau_E + \tau_R \})]$, $r_2^*= (\tau_E - \{1/ \beta k\})/(1 + \{\tau_E / \tau_R\})$

$\Rightarrow$ How about stability ?

The $e_1^*=r_1^*=0$ is stable if $\tau_E \beta k < 1$

In other words, if $\tau_E \beta k > 1$, the network will show persistent excitation (i.e., a finite fraction will always be excited)

Analogous to the basic reproduction number R_0 in epidemiology

And hence to binary state neurons…

Quiescent, i.e., resting state ≡ 0

Active, i.e., firing action potentials ≡ 1

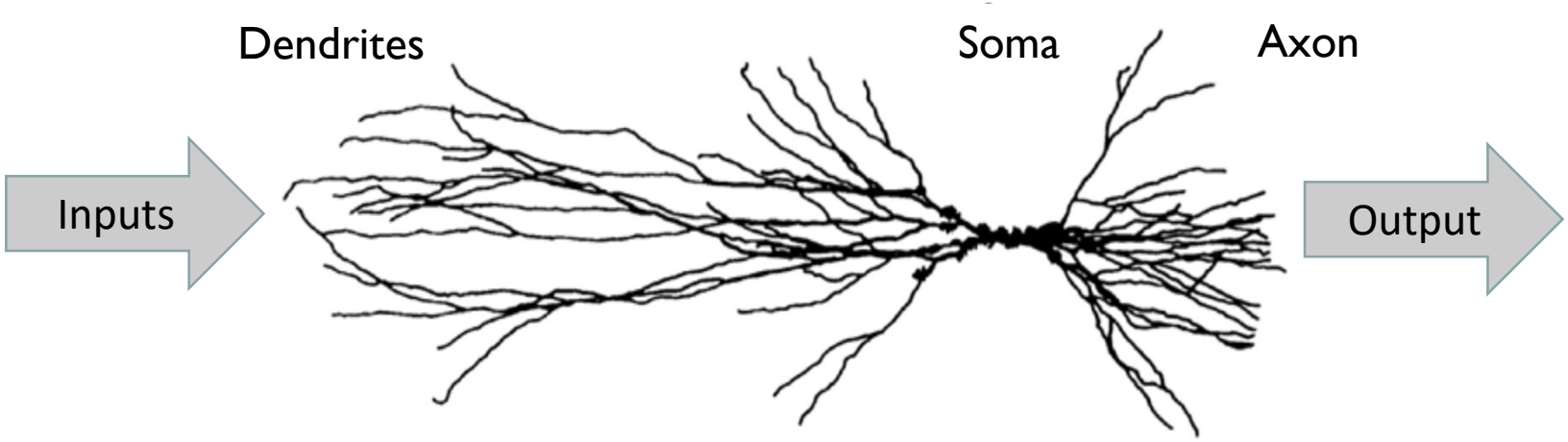


Image: Current Biology

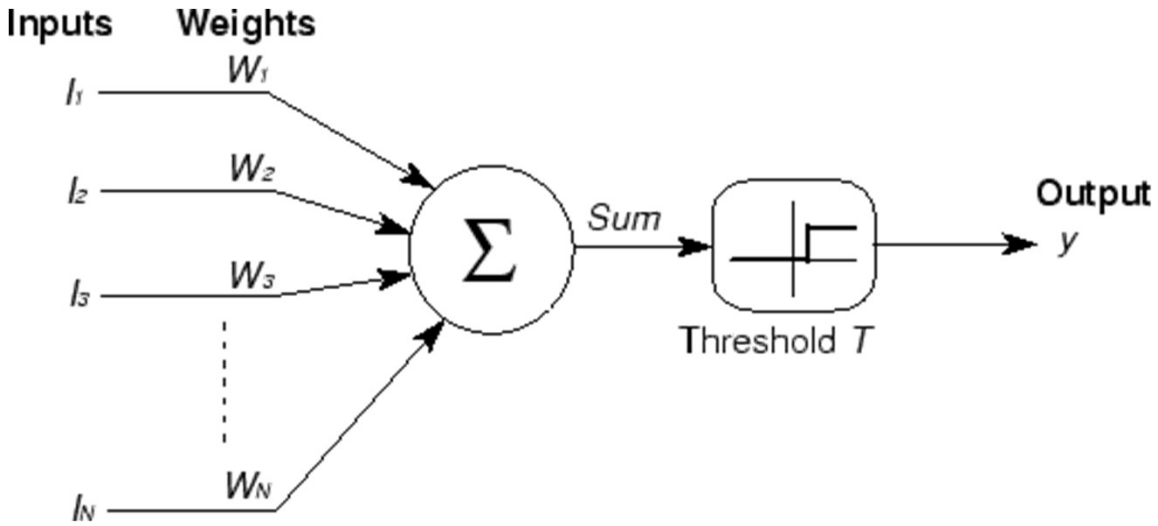


Image: chatbotslife.com/keras-in-a-single-mcculloch-pitts-neuron-317397cccd45

Spin models as a paradigm for Complex Systems

The McCulloch-Pitts neuron

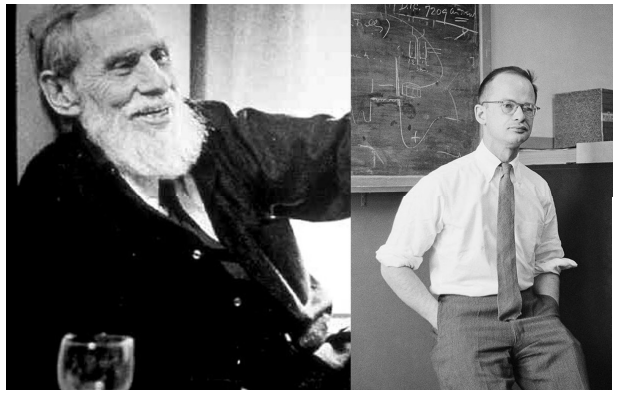


Image:infonintelli.blogspot.com

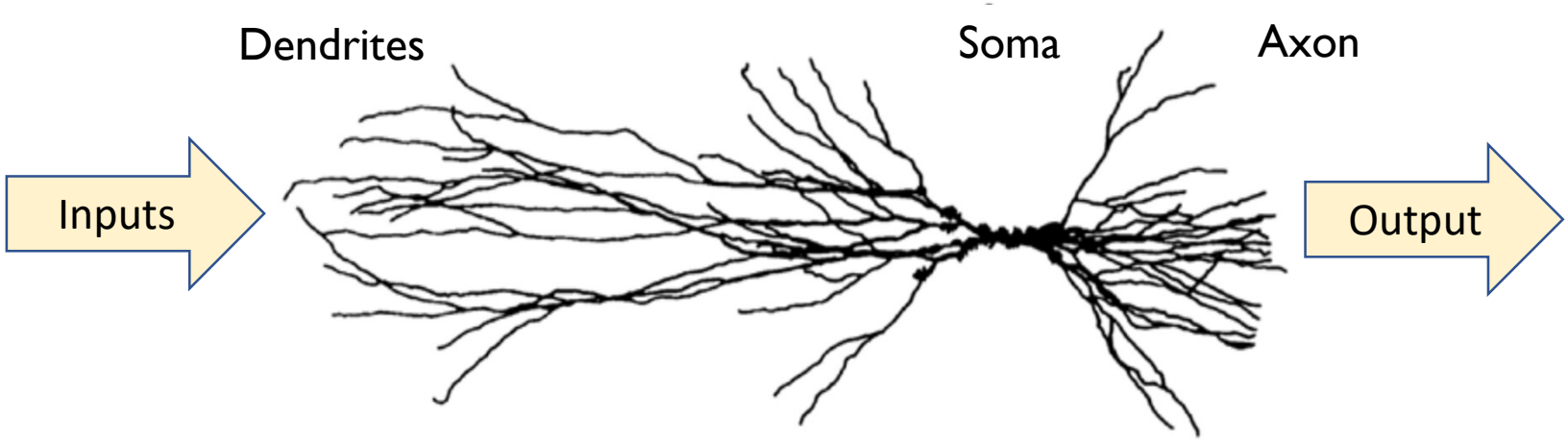


Image: Current Biology

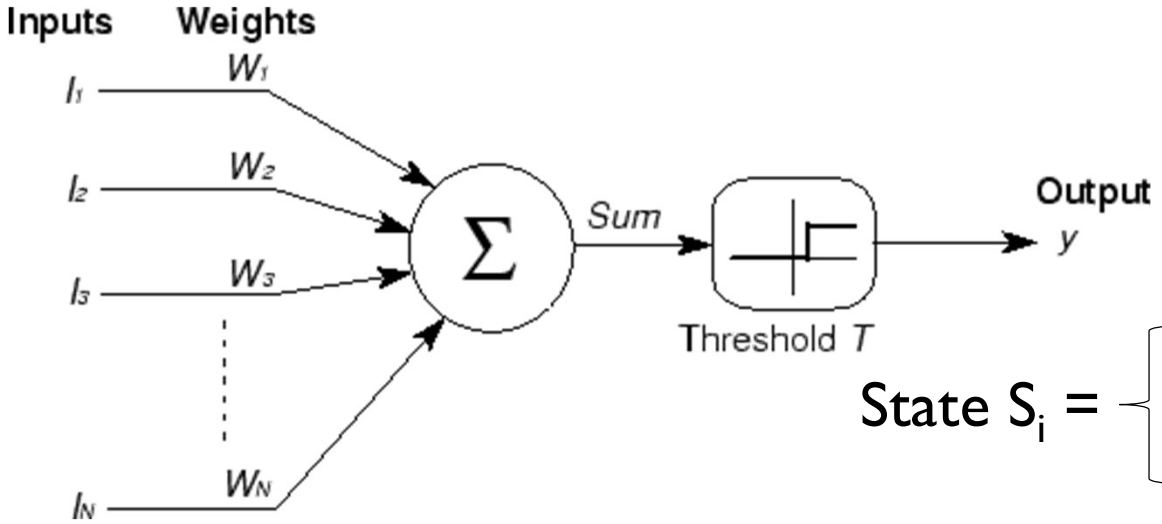
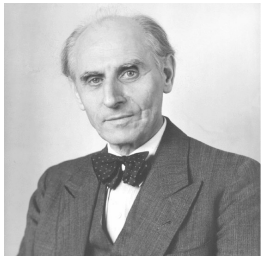


Image: chatbotslife.com/keras-in-a-single-mcculloch-pitts-neuron-317397cccd45

State S_i = { −1 Resting ; +1 Firing

The Lenz-Ising model (1920-5)

A highly simplified model for explaining spontaneous magnetization



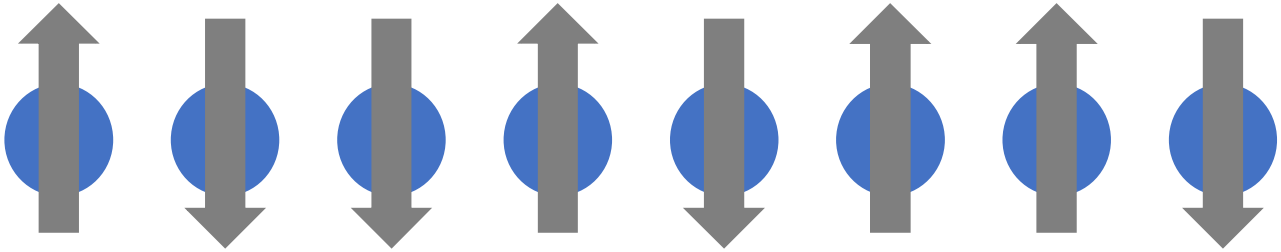
Wilhelm Lenz

Ernst Ising

Image: wikipedia

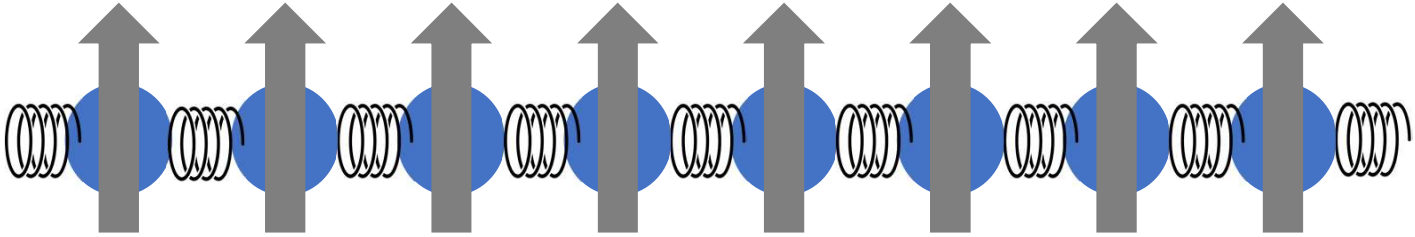
No order

In absence of interactions



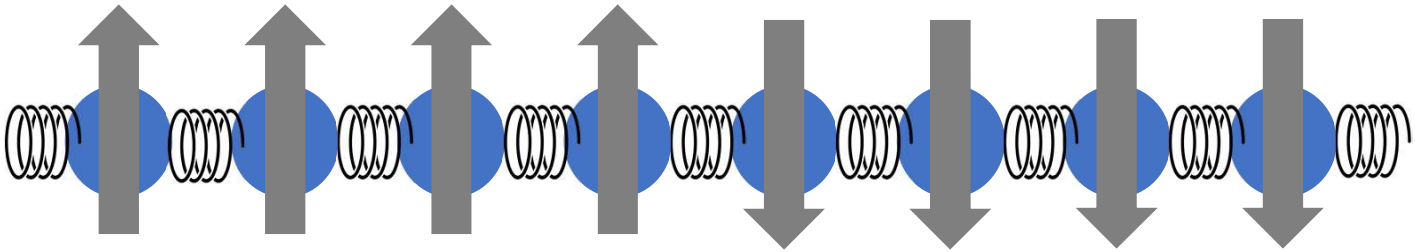
Order

T=0, with interactions



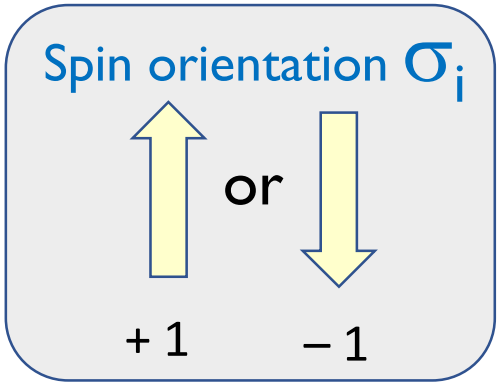
Disorder

T>0, with interactions



Magnetic moments of atoms reduced to a single (z) component, allowed to be only in 1 of 2 states and interact only with nearest neighbors

The Ising model is described by



spin-orientation coupling

external field

$$H = -\sum_{ij} J_{ij}\,\sigma_i\,\sigma_j - \sum_i h\,\sigma_i$$

interaction

environment

For spontaneous ordering in a ferromagnet, $J_{ij} = J > 0$ and $h = 0$

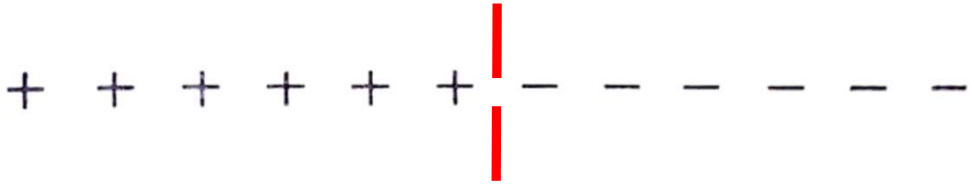
Once we introduce thermal fluctuations (at finite temperature T>0) system behavior is governed by

$$\text{Free energy } F = U - T\,.\,S$$

Disorder at any finite temperature in a 1-dimensional array of Ising spins

Let there be a perfectly ordered arrangement of N+1 Ising spins (all spins parallel)

Can disorder by introducing a single boundary in the array where neighboring spins are not in parallel orientation – has an energy cost of 2 J



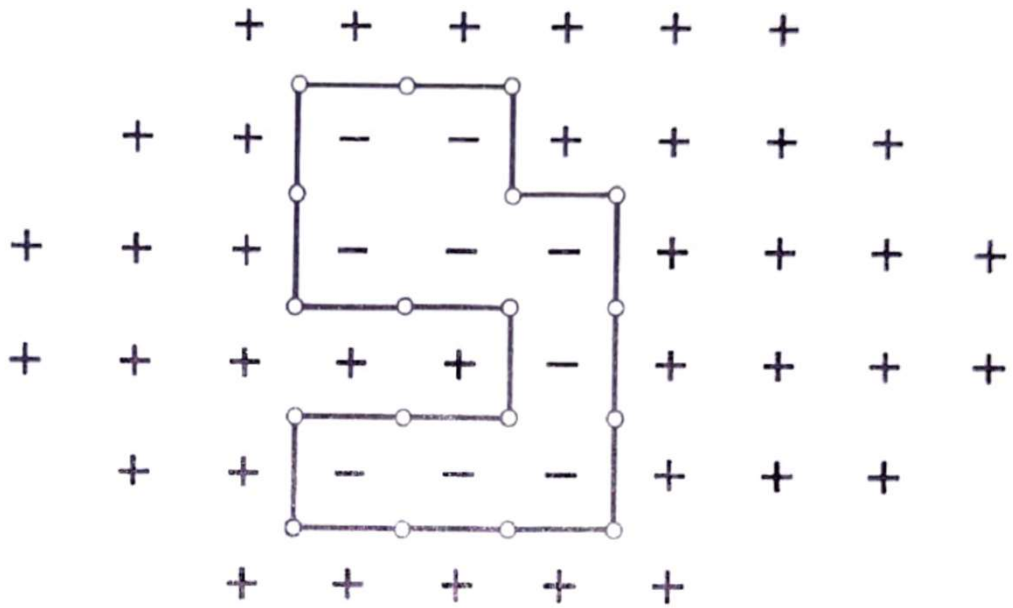
The boundary can be placed in any of N positions in the array
$\Rightarrow$ Entropy gain of k log N

Change in Free Energy is 2 J – k log N
$\Rightarrow$ For large N, free energy is always lower for disordered state when T > 0

So no order in 1D for finite temperature

The Peierls argument (1936)

Can there be order in 2D for T>0 ?



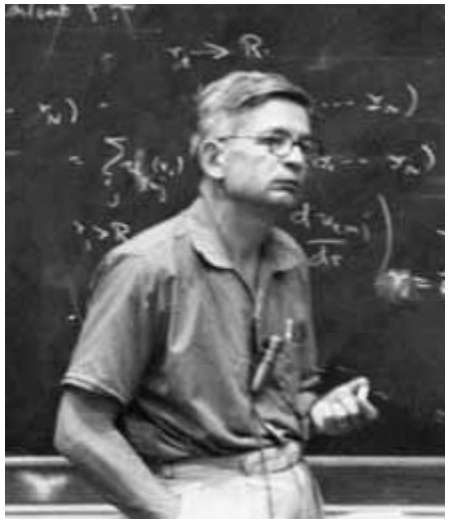


Image: American Institute of Physics

Rudolf Peierls

Energy cost as well as entropy varies with N

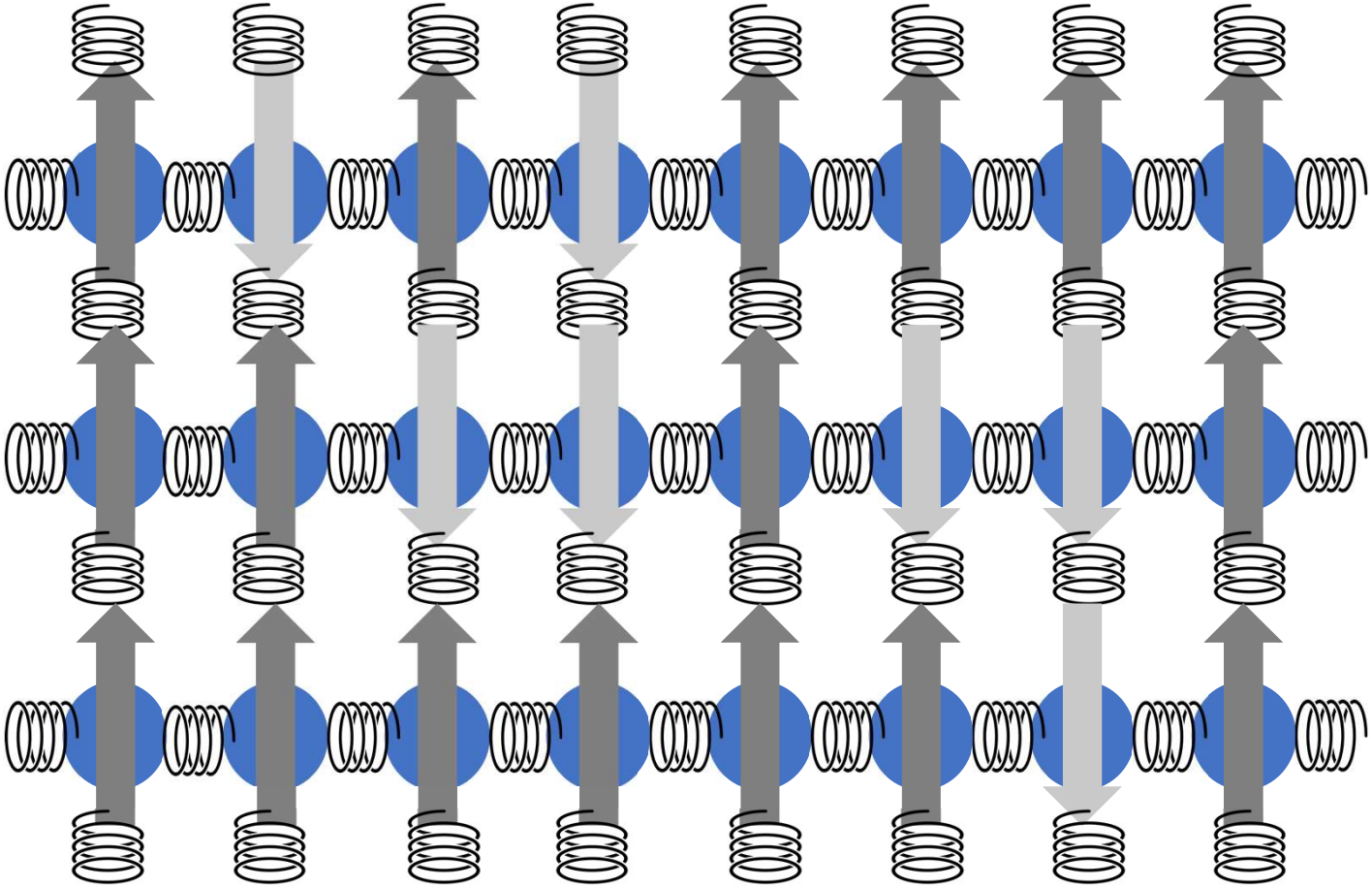
A similar chain of argument will show that disorder does not have a lower free energy at a low but finite temperature

$\Rightarrow$ The array will show spontaneous ordering below a critical temperature T_c

The 2-dimensional Ising model (1944)

A model for self-organized coordination

The system spontaneously orders at $T < T_c$



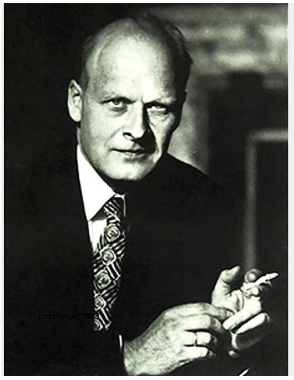


Image: wikipedia

Lars Onsager

The 2-dimensional Ising model (1944)

A model for self-organized coordination

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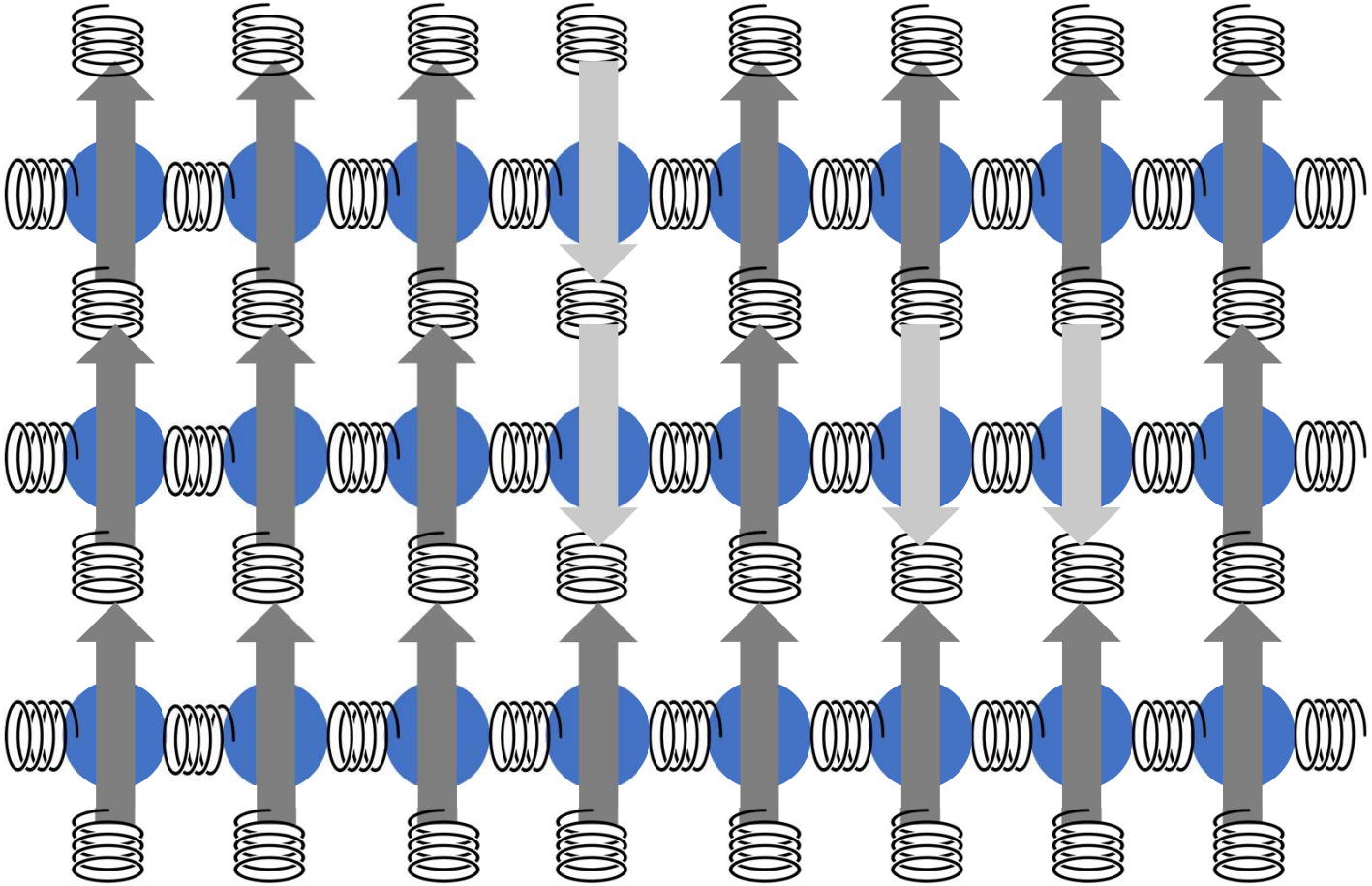

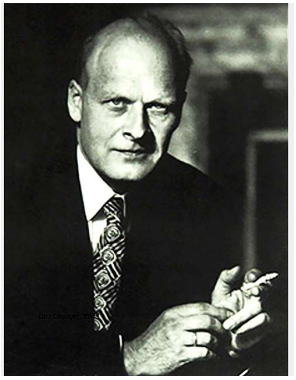

Image: wikipedia

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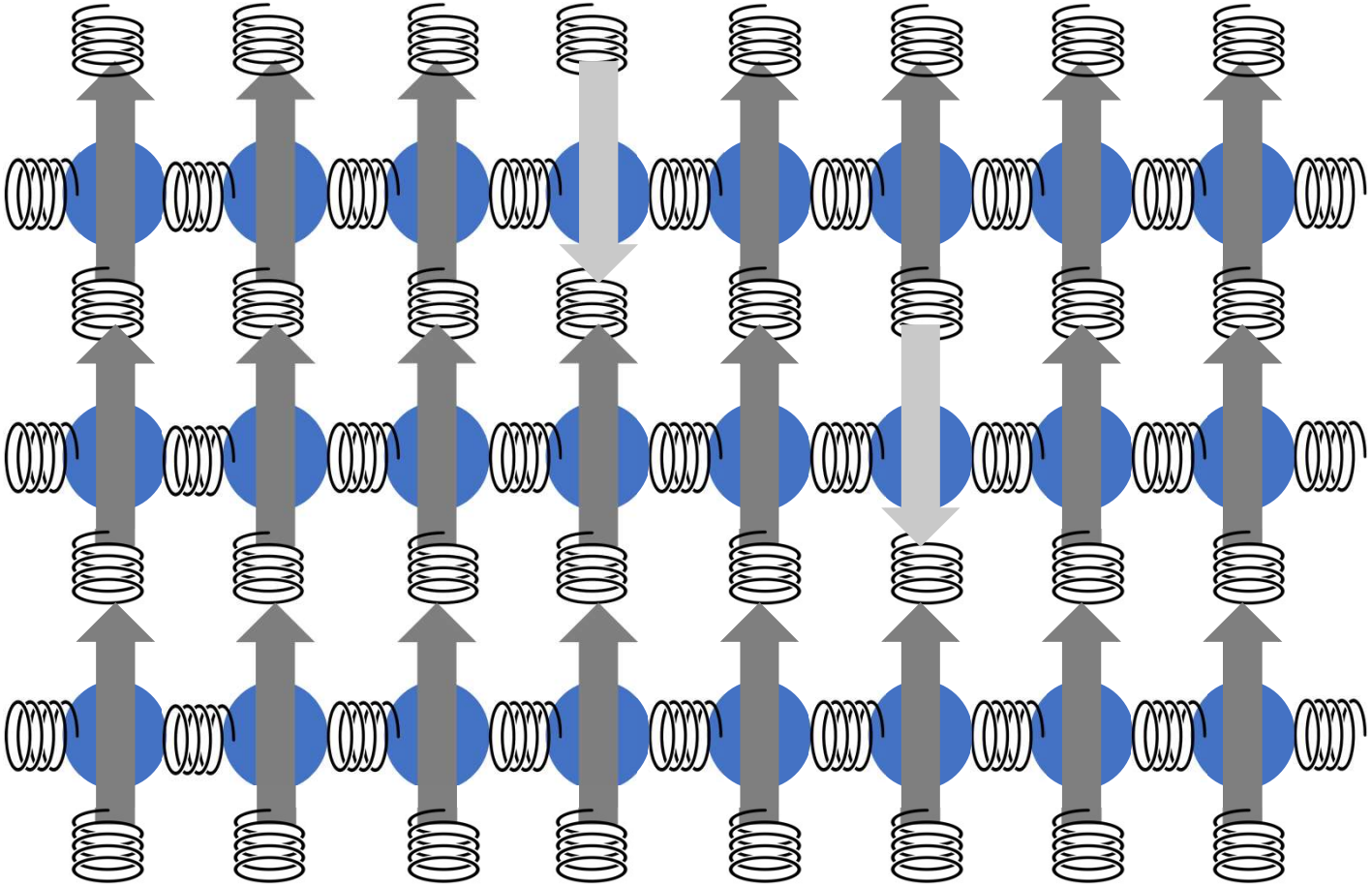

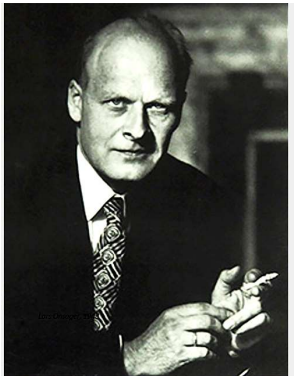

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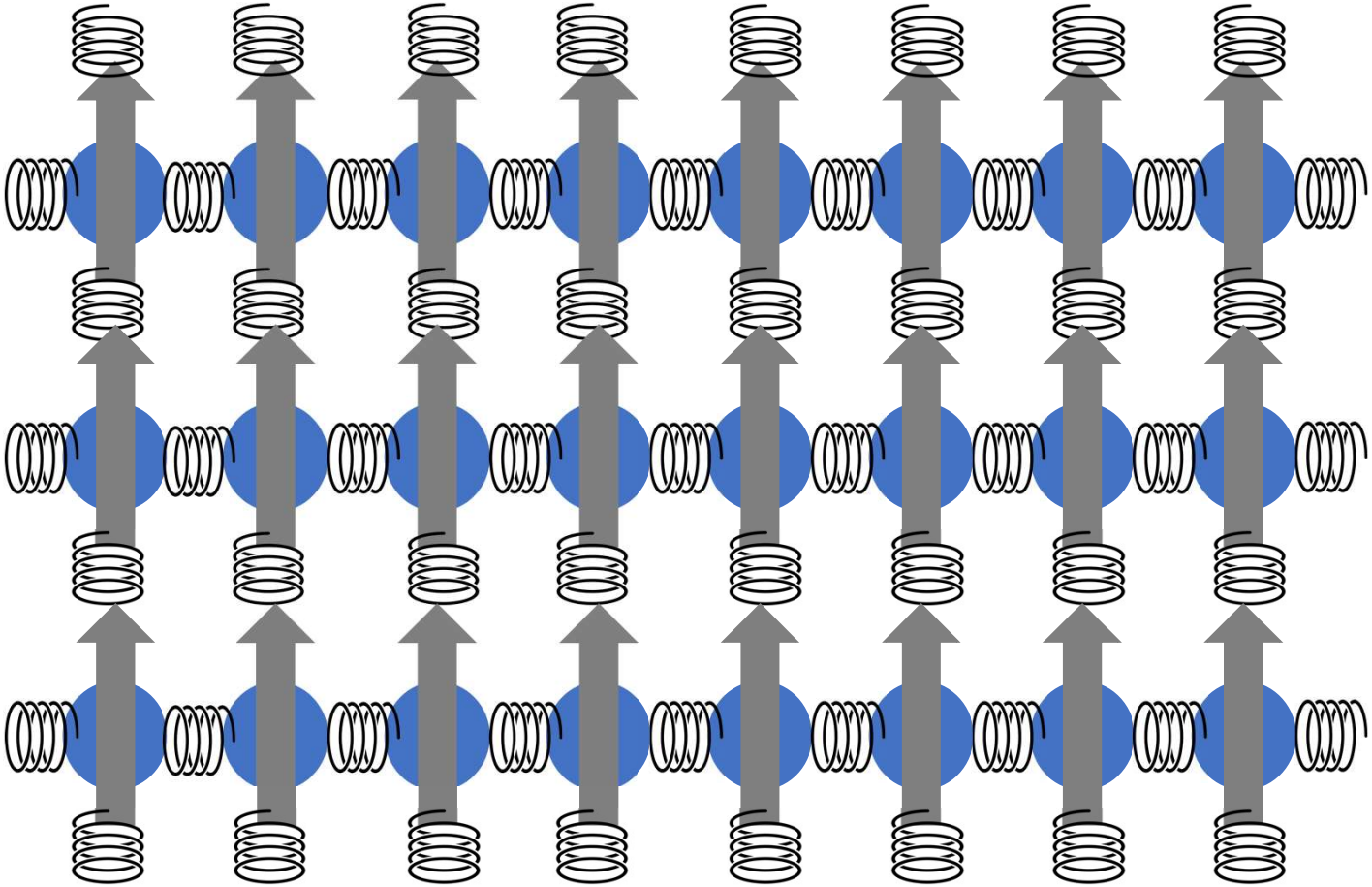


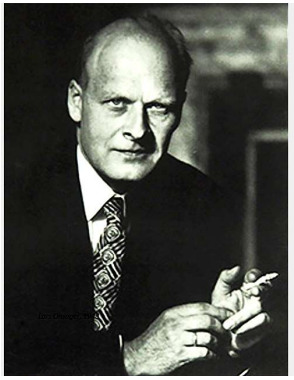
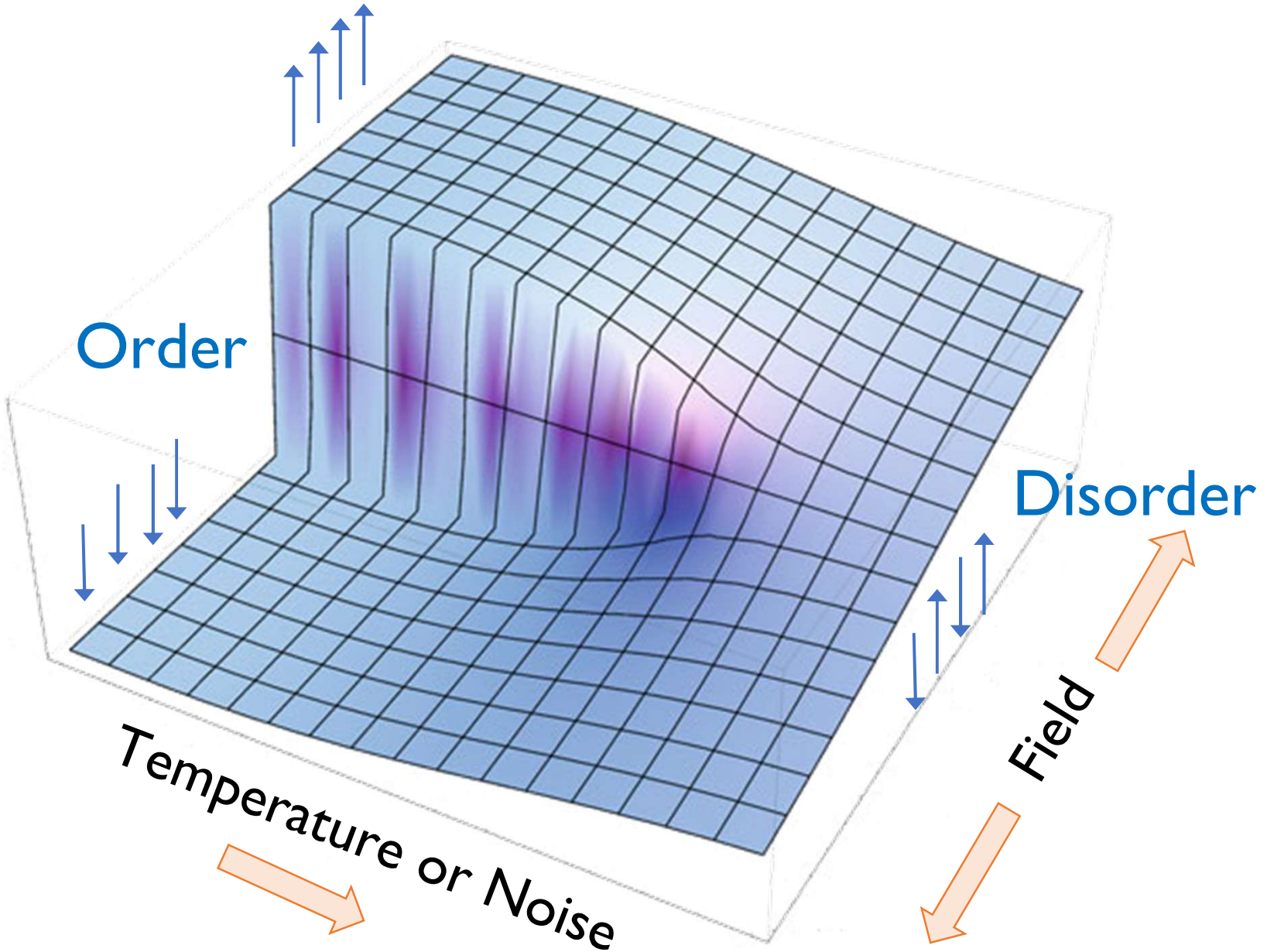


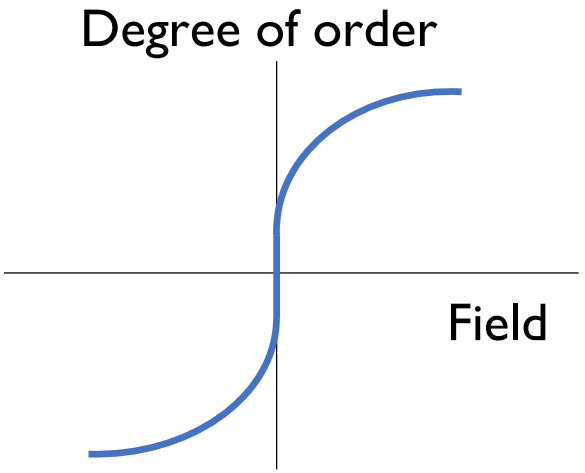
Image: wikipedia

Lars Onsager



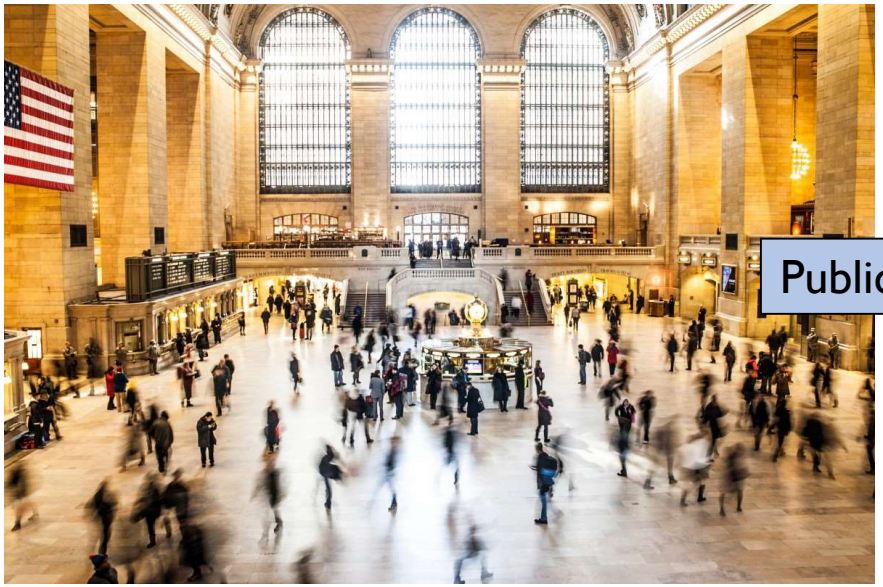
Selinger, Introduction to the Theory of Soft Matter, Springer

Order-disorder transition



"Field" induced transition from

"Disorder"



Creative Commons

Public announcement

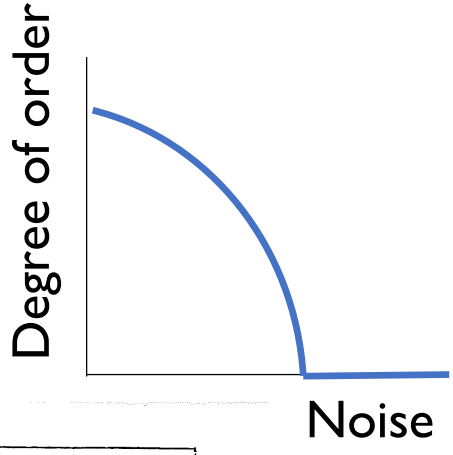
"Order"

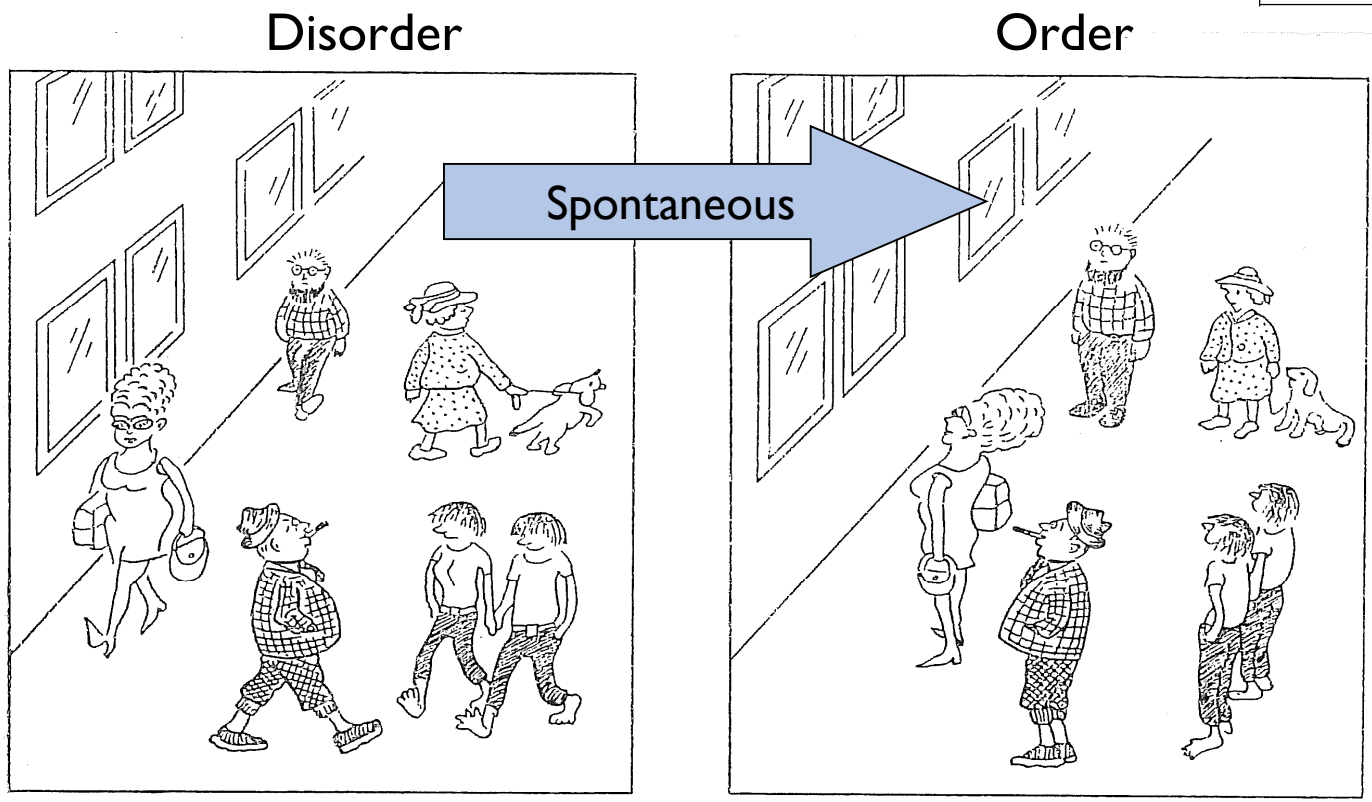
Jake Wyman/Corbis

Discontinuous or First-order phase transition

Cooperative phenomenon

Self-organized transition from





Kikoin & Kikoin, Molecular Physics, Mir

Continuous phase transition

Hopfield Model

Attractor Network Model for Associative Memory

Image: bulletin.swarthmore.edu

John J Hopfield

Globally connected system of "neurons" (spins)

State S_i = $\begin{cases} -1 \text{ Resting} \\ +1 \text{ Firing} \end{cases}$

T=0 or deterministic dynamics

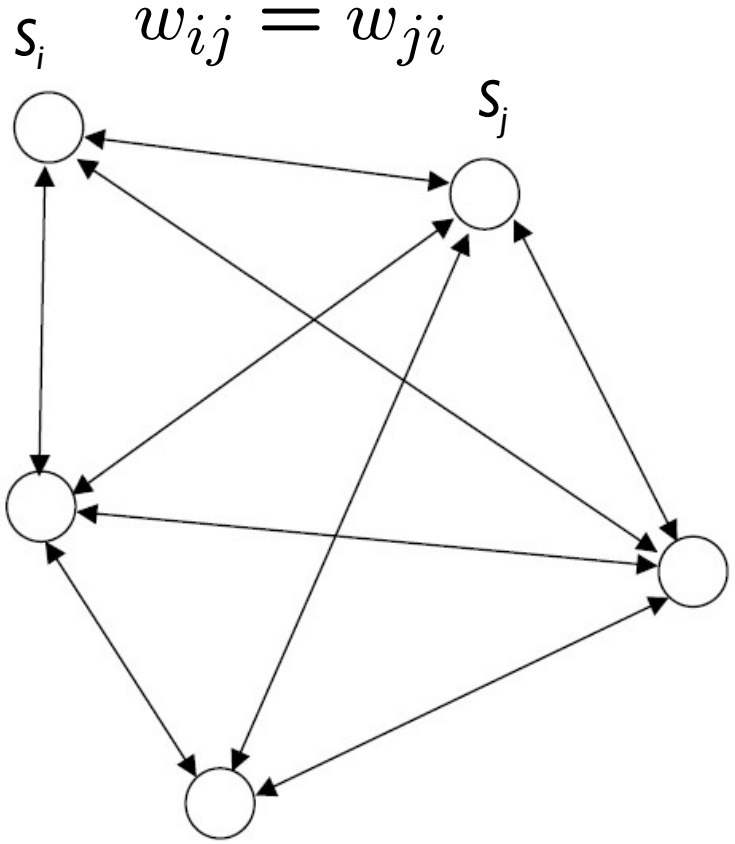
Time-evolution $S_i = \text{sgn}(\sum_j w_{ij} S_j)$

- sgn (q) = -1, if q < 0;
- sgn (q) = $+1$ otherwise

❑ Symmetric connection weights $w_{ij} = w_{ji}$

A brilliant step backwards (Amit)

❑ w_{ii}=0 (No self connections)



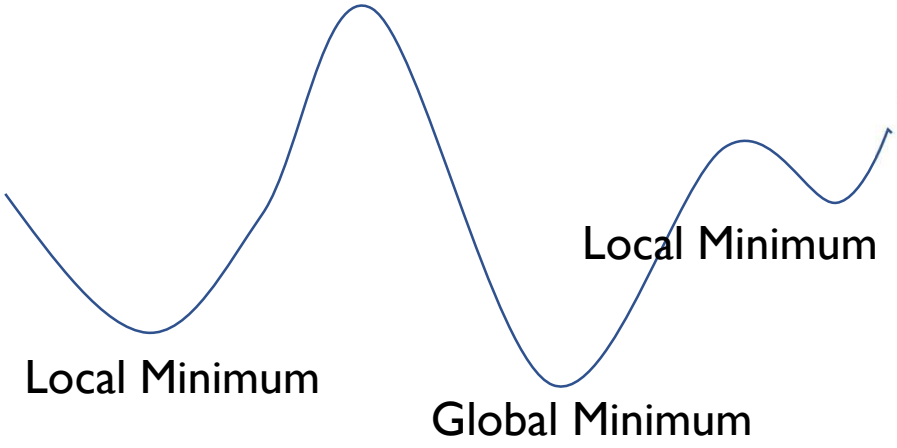
Memory Recall in Hopfield Network

- Start from arbitrary initial configuration of {x}
- What final state does the network converge ?
- Evaluate an 'energy' value associated with the network state:

$$E = -\frac{1}{2}\sum_{j}\sum_{\substack{i=1 \\ i\neq j}}^{N} w_{j,i}x_i\ x_j$$

- System converges to an attractor

  a local/global minimum of *E*



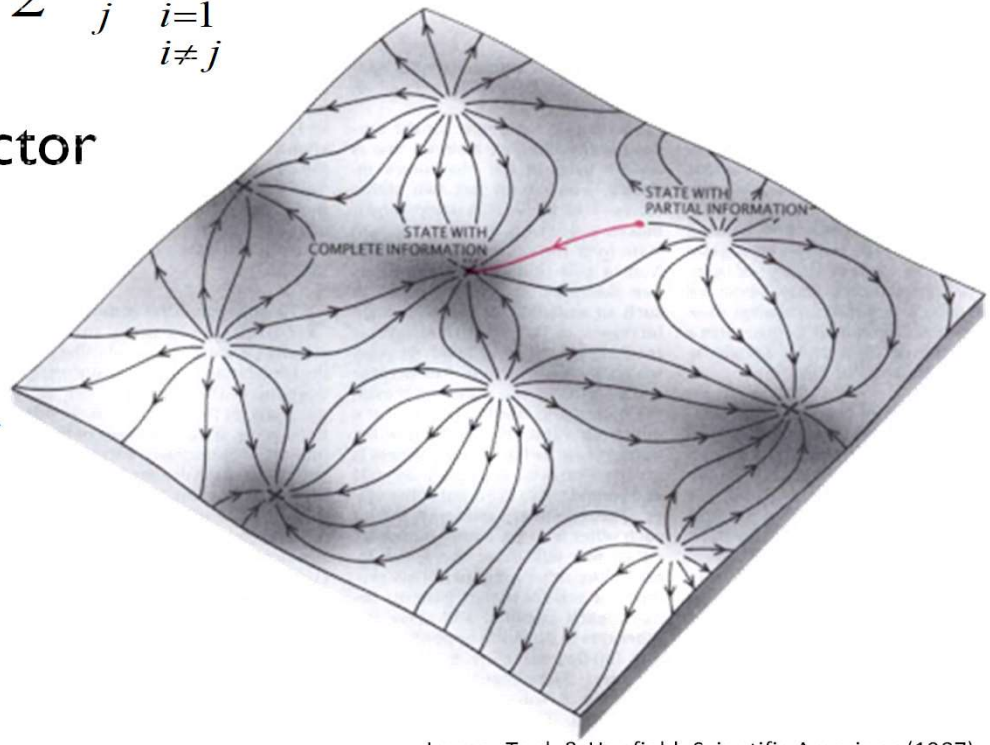


Image: Tank & Hopfield, *Scientific American* (1987)

T>0 or Stochastic dynamics

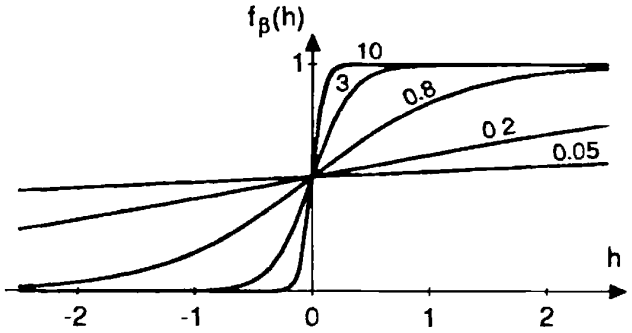
In neurons, fluctuations in the release of neurotransmitters in discrete vesicles
$\Rightarrow$ neurons may fire even when weighted input < threshold or not fire when input > threshold

Noise $\rightarrow$ Stochasticity in neuronal firing

Amount of noise quantified by "pseudo temperature" T
T=0 $\rightarrow$ deterministic dynamics

For T>0

$$\text{Prob}\,(S_i = +1) = f_T\left(\sum_j w_{ij} S_j\right)$$



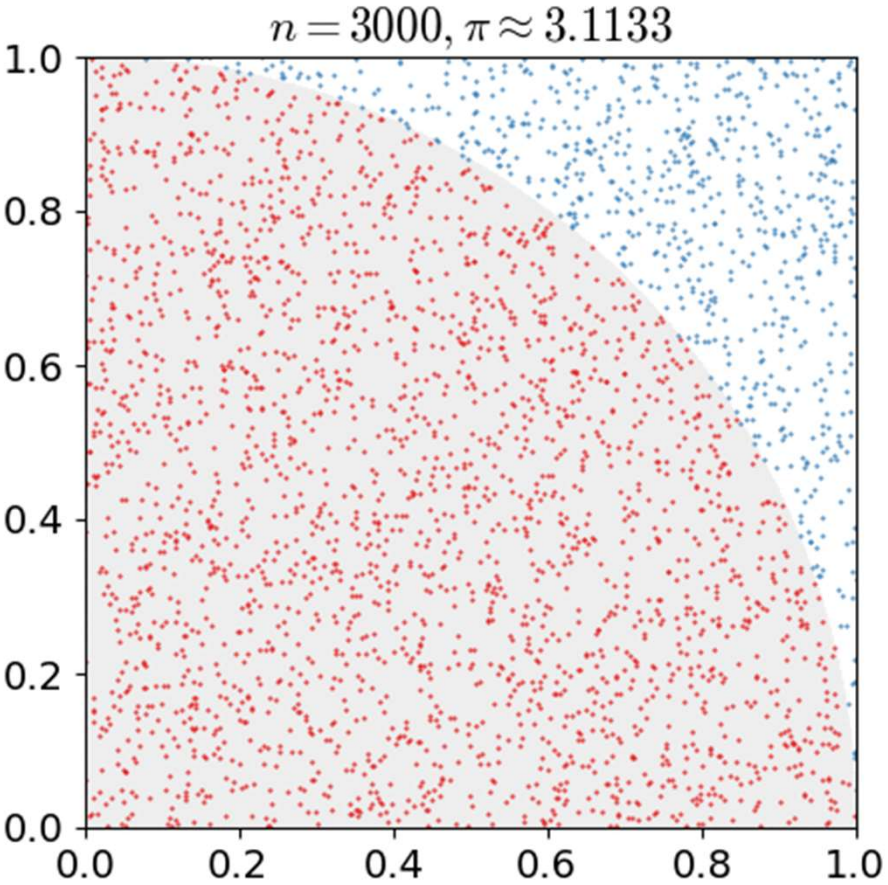
$$= 1/[1 - \exp(2 \textstyle\sum_j w_{ij} S_j / T)]$$

T>0 or Stochastic dynamics

The Monte Carlo Method

Using repeated random sampling to solve problems

Stanislaw Ulam



Estimating $\pi/4$

Image: Wikipedia

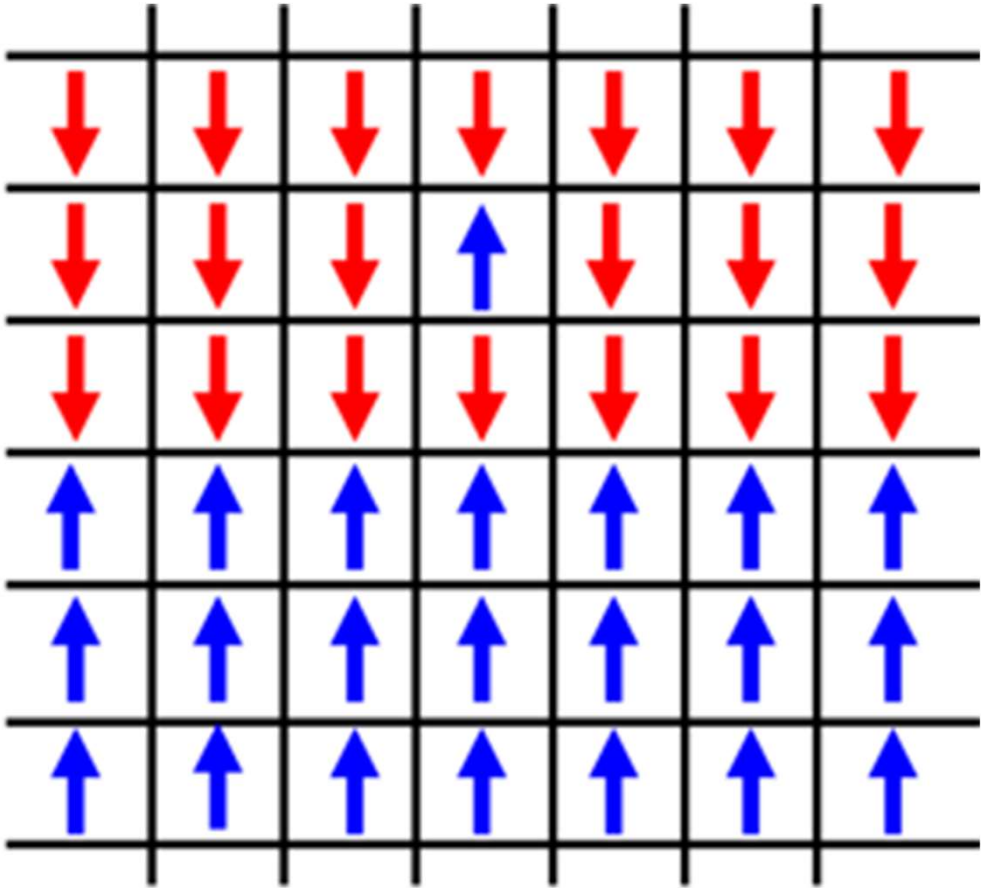
Stan Ulam got the idea while recovering from surgery, playing solitaire to estimate the odds of a successful game.
Realized that, instead of doing combinatorics, a more practical method to estimate is to lay out the game hundreds of times and count the number of successful plays.

Named Monte Carlo Method because of its association with chance and gambling by

Nicholas Metropolis

T>0 or Stochastic dynamics

The Monte Carlo Method

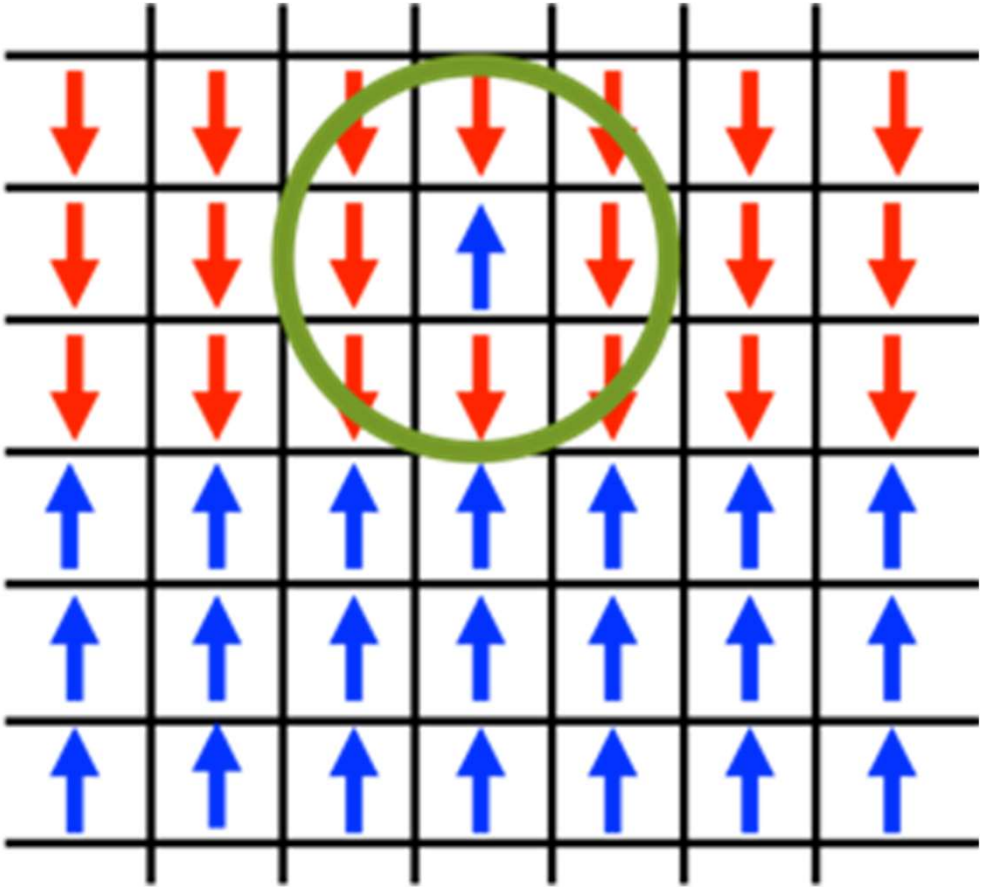


Let's consider a particular spin configuration in a 2-dimensional Ising model with each spin interacting with strength J with its 4 nearest neighbours

Image: www.bdhammel.com

T>0 or Stochastic dynamics

The Monte Carlo Method



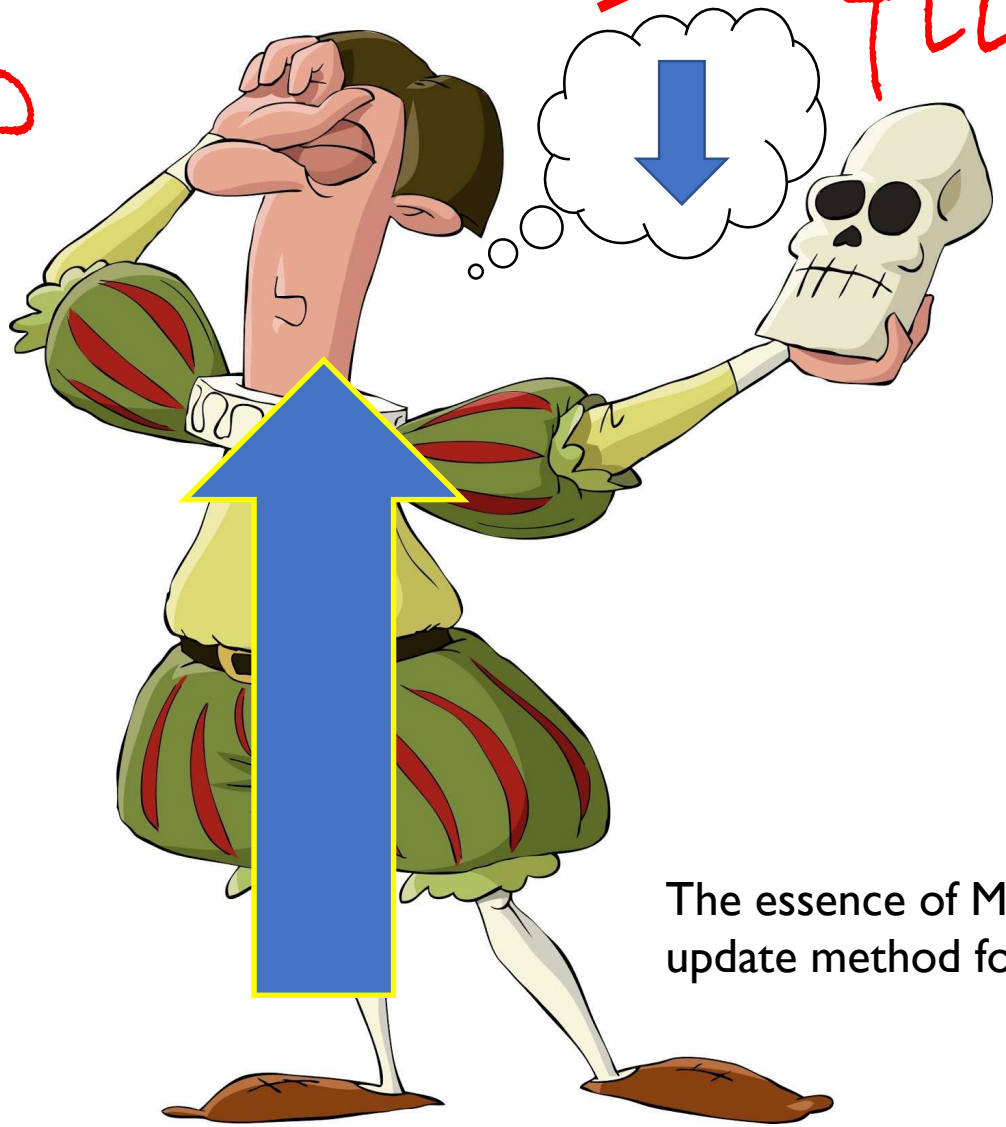
Let's randomly select a particular spin whose new state will be decided

How much will the energy of the system change if we flip the spin to its opposite orientation ?

$$\Delta E = -\{\sum_j J(-1)(-1)\} - \{-\sum_j J(+1)(-1)\} = -8J$$

Image: www.bdhammel.com

To ~~be~~ or not to ~~be~~

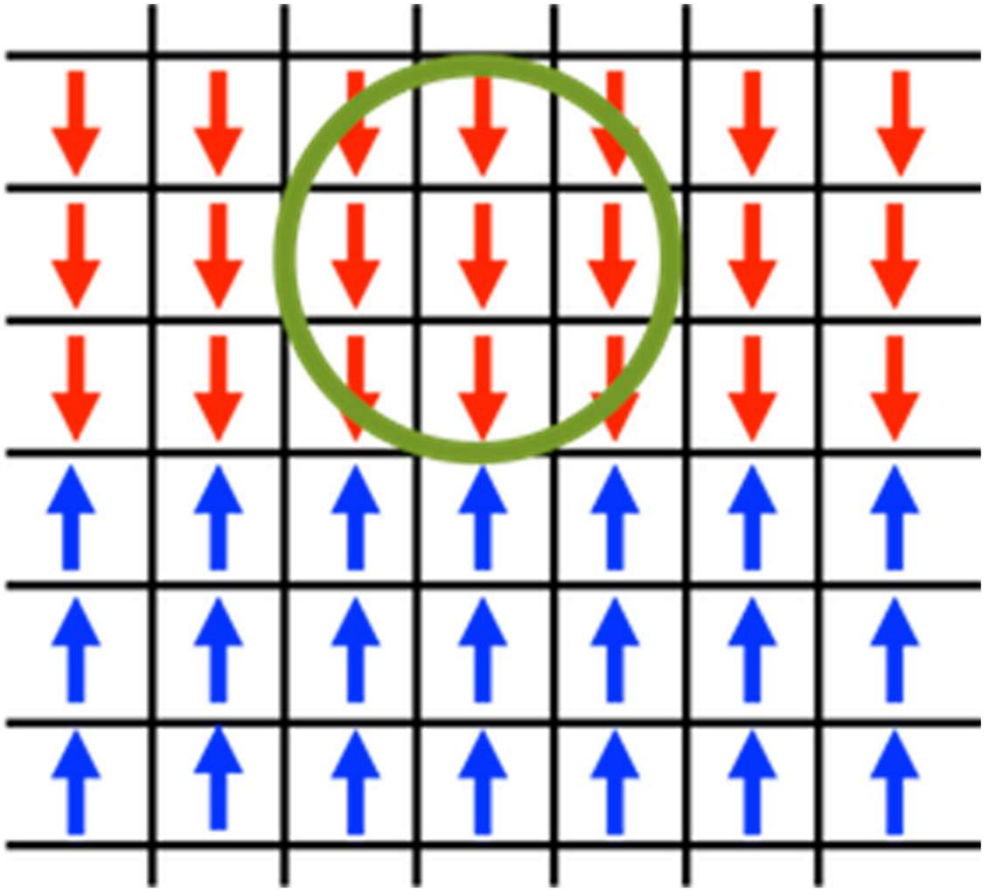


The essence of Monte Carlo update method for the Ising model

Image: adapted from queenelizabethsfantasy.blogspot.com

T>0 or Stochastic dynamics

The Monte Carlo Method

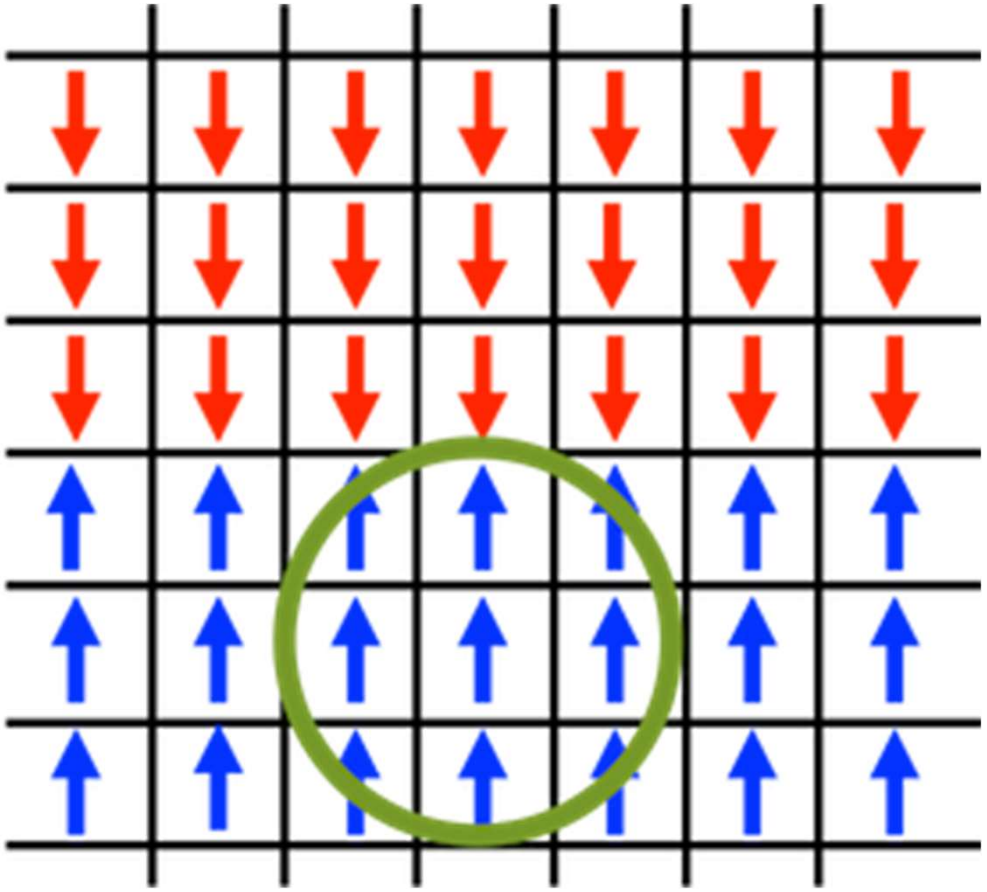


As the energy decreases as a result of the flip, this change is accepted and the new state will be

Image: www.bdhammel.com

T>0 or Stochastic dynamics

The Monte Carlo Method



Next, randomly choose another spin

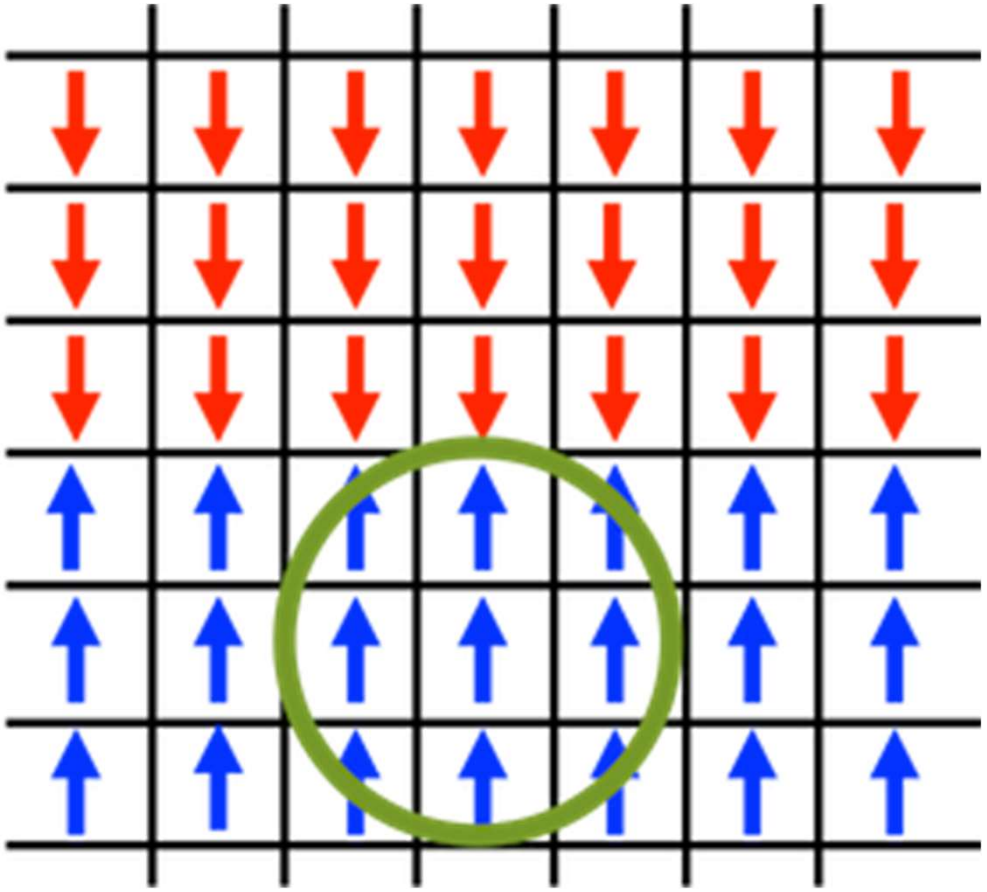
… and ask what will be the energy change if we flip it ?

$$\Delta E = -\{\sum_j J(-1)(+1)\} - \{-\sum_j J(+1)(+1)\} = 8J$$

Image: www.bdhammel.com

T>0 or Stochastic dynamics

The Monte Carlo Method



As the energy increases, we don't immediately accept the change but ask:
can this additional energy cost be obtained from thermal fluctuations (~ $k_B T$ at temperature T) ?

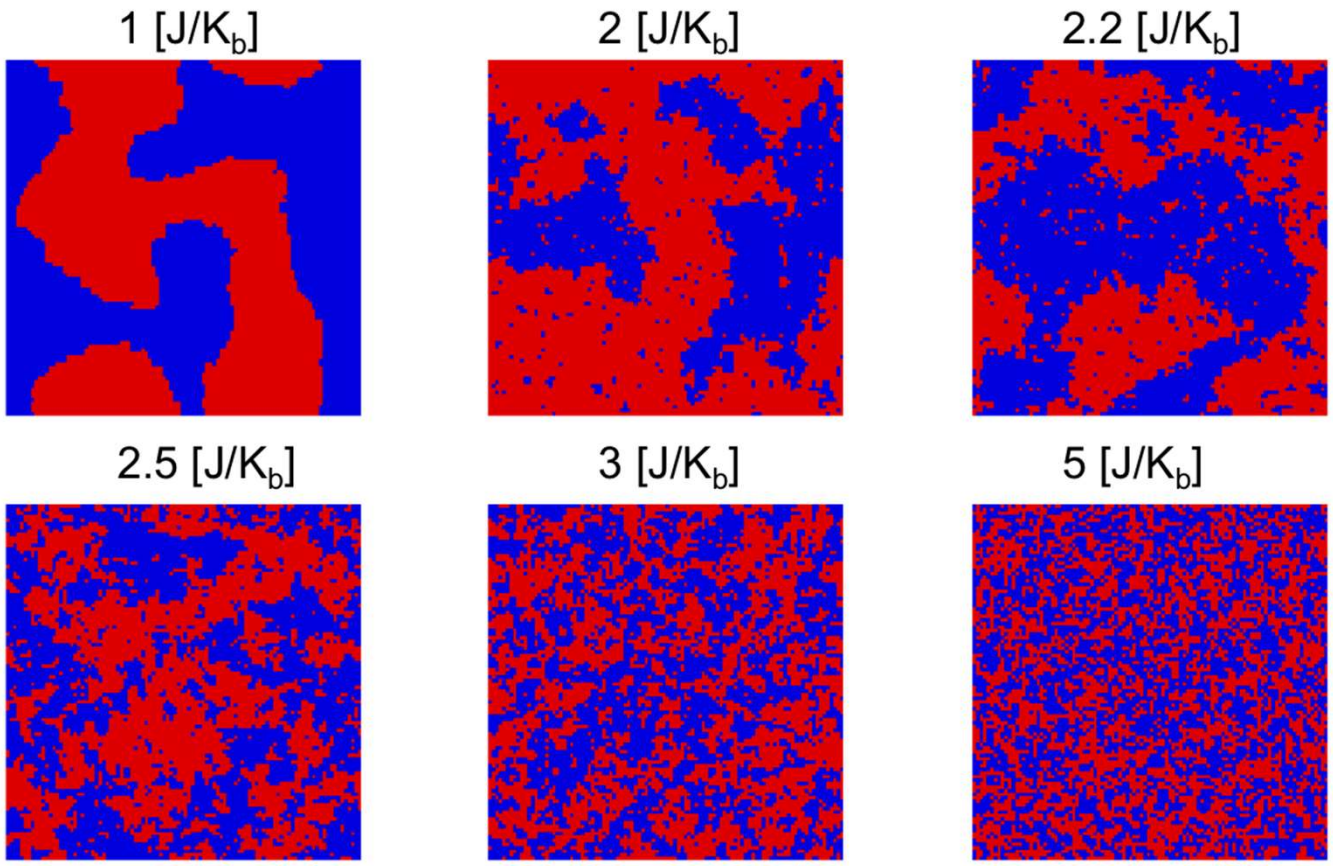
Probability of accepting the move:
$P (+ \rightarrow -) \sim \exp (-\Delta E / k_B T)$

Image: www.bdhammel.com

T>0 or Stochastic dynamics

The Monte Carlo Method

Continue to repeat this process by randomly selecting a spin at successive rounds and deciding what its state will be (i.e., to flip or not to flip)



At higher temperatures, Ising system more likely to get disordered as the updates are continued

Image: www.bdhammel.com