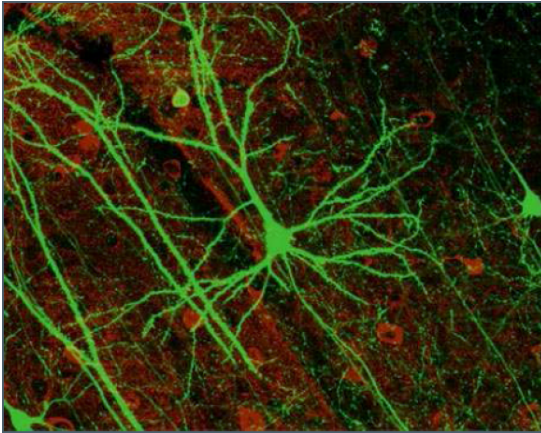


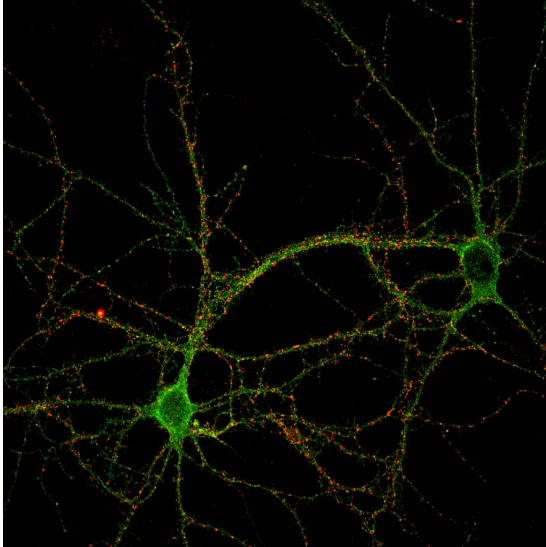
# Outline

- The Neuron
- The Synaps
  - Binding Scheme
  - Synaptic current
- Reduced Neuron Models
  - $I_{Na^+ - K^+}$ -model
  - SNIC bifurcation
  - Hopf bifurcation
- Mean Field Approach
  - Spike rate models
  - 1D tissue model
  - 1D Neural Field with dendrites and axons
- Traveling Waves
  - waves in neural media
  - integrate and fire model
  - wavespeed
- literature
- projects

# Neuron



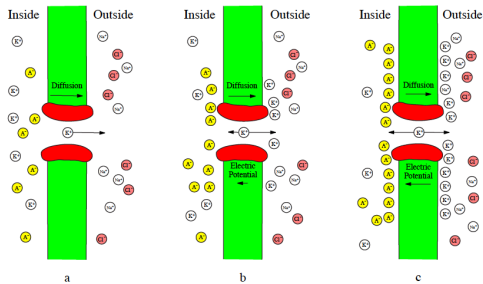
From the lab of Wytse Wadman



# The Neuron

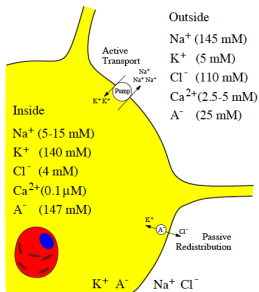
- Nernst potential
- Single Compartment
- Hodgkin-Huxley formalism
- Voltage dependent conductance
- Giant squid axon
- Reduced models
- Leaky integrate and fire neurons

# Balancing diffusion and electric potential



Taken from Izhikevich

# Membrane



## Equilibrium Potentials

$$\text{Na}^+ \quad 62 \log \frac{145}{5} = 90 \text{ mV}$$

$$62 \log \frac{145}{15} = 61 \text{ mV}$$

$$\text{K}^+ \quad 62 \log \frac{5}{140} = -90 \text{ mV}$$

$$\text{Cl}^- \quad -62 \log \frac{110}{4} = -89 \text{ mV}$$

$$\text{Ca}^{2+} \quad 31 \log \frac{2.5}{10^{-4}} = 136 \text{ mV}$$

$$31 \log \frac{5}{10^{-4}} = 146 \text{ mV}$$

Taken from Izhikevich

## The Neuron - Nernst Potential

The Nernst Potential is the electric potential force over the cell membrane that balances diffusion. Ion pumps are responsible for differences in concentration of ions across the membrane.

$$E_{\text{ion}} = \frac{RT}{zF} \ln \frac{[\text{ion}]_{\text{out}}}{[\text{ion}]_{\text{in}}}$$

Na<sup>+</sup>      90 mV

K<sup>+</sup>        -90 mV

Cl<sup>-</sup>        -89 mV

Ca<sup>2+</sup>      136 mV

*R*: universal gas constant

*T*: temperature in degrees Kelvin

*F*: Faraday's constant

*z*: valence of the ion

## Neuron: Single Compartment

Kirchof's law states that the total current  $I$  is the sum of all ion-currents plus the membrane's capacitive current:

$$I = C\dot{V} + I_{Na} + I_{Ca} + I_K + I_{Cl}$$

If the system is in equilibrium ( $\frac{dV}{dt} = 0$ ) and the net current vanishes it follows that

$$V = \frac{g_{Na}E_{Na} + g_{Ca}E_{Ca} + g_K E_K + g_{Cl}E_{Cl}}{g_{Na} + g_{Ca} + g_K + g_{Cl}}$$



## Neuron: Hodgkin-Huxley equations

- Conservation of charge across the membrane of a cell:

$$C \frac{dV}{dt} = - \sum I_{ion} + I_{applied}$$

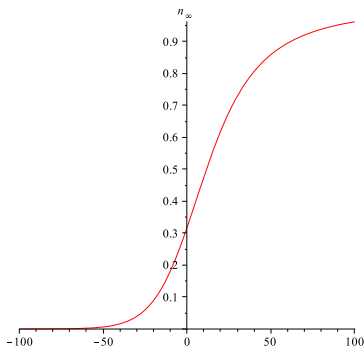
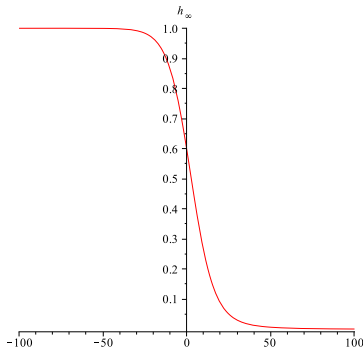
- $I_{ion} = \bar{g} m^j h^k (V - V_R)$
- Conductance  $\bar{g} m^j h^k$   
**activation** opens as the voltage increases  
**inactivation** closes as the voltage increases
- $m$  and  $h$  are functions of time. For each gate there is an auxiliary equation for the kinetics which describes how fast the (in)activation approaches its voltage dependent asymptotic value:

$$\frac{d\chi}{dt} = (\chi_{\infty}(V) - \chi) / \tau_{\chi}(V)$$

## Neuron: Voltage dependent conductance

$m$  and  $h$  are functions of time. For each gate there is an auxiliary equation for the kinetics which describes how fast the (in)activation approaches its voltage dependent asymptotic value:

$$\frac{d\chi}{dt} = (\chi_{\infty}(V) - \chi)/\tau_{\chi}(V)$$



## Neuron: Giant Squid

The full Hodgkin-Huxley equations are:

$$C\dot{V} = I - \bar{g}_K n^4 (V - E_K) - \bar{g}_{Na} m^3 h (V - E_{Na}) - \bar{g}_L (V - E_L)$$

$$\dot{n} = (n_\infty(V) - n) / \tau_n(V)$$

$$\dot{m} = (m_\infty(V) - m) / \tau_m(V)$$

$$\dot{h} = (h_\infty(V) - h) / \tau_h(V)$$

# Synaps taken from Kandel

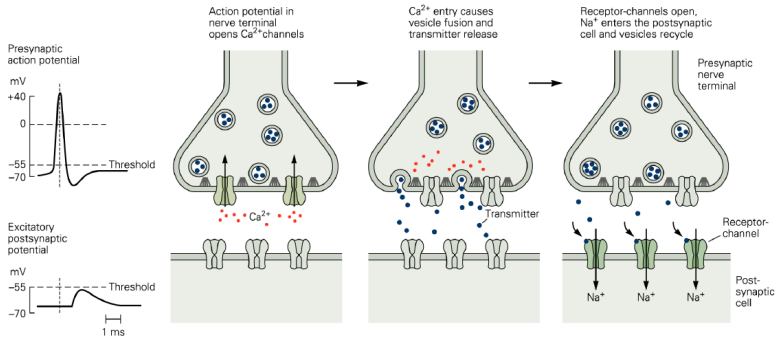
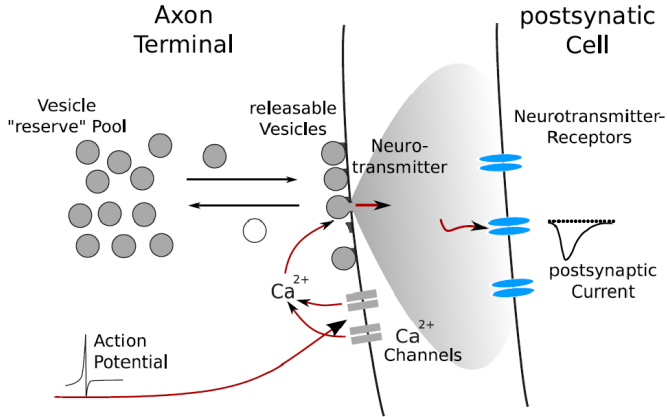


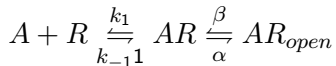
FIGURE 1. Basic stages of synaptic processing shown for an excitatory synapse. See text for details. [Adapted from Kandel *et al* [36]]

# Synaptic Process



From: M.H. Hennig, ANC, Informatics, University of Edinburgh

## Classic Binding Scheme (Magleby and Stevens (1972))



- A is the neurotransmitter or Agonist
- R is receptors
- $k_1$  and  $k_{-1}$  are the binding and unbinding rates of transmitter to the receptor in units of  $M^{-1}s^{-1}$  and  $s^{-1}$
- AR is the transmitter-receptor complex
- $\beta$  and  $\alpha$  are the channel opening and closing rates (1/s)

## Binding Scheme Simplified

- Neurotransmitter crosses the cleft and binds instantly to a certain number of receptors
- unbound neurotransmitter disappears (so no rebinding)



- Differential equations for transmitter-receptor complex

$$\frac{dAR}{dt} = -k_{-1}AR - \beta AR + \alpha AR_{open}$$
$$\frac{dAR_{open}}{dt} = \beta AR - \alpha AR_{open}$$

## Synaps dynamics

$$AR_{open}(t) = \frac{AR(0)\beta}{r_1 - r_2} (\exp(r_1 t) - \exp(r_2 t))$$

with

$$r_1 = -a + \sqrt{a^2 - b} \quad r_2 = -a - \sqrt{a^2 - b}$$
$$a = \frac{k_{-1} + \alpha + \beta}{2} \quad b = k_1 \alpha$$



## Synaptic Current

The resulting synaptic current is of the form

$$I_{syn}(t) = \frac{g_{max}}{\tau_1 - \tau_2} (\exp^{-t/\tau_1} - \exp^{-t/\tau_2})(V_m - E_{syn})$$

## Original 4D HH-model

$$C\dot{V} = I - \underbrace{\overline{g_K}n^4(V - V_K)}_{I_K} - \underbrace{\overline{g_{Na}}m^3h(V - V_{Na})}_{I_{Na}} - \underbrace{g_L(V - V_L)}_{I_L}$$

$$\dot{n} = \frac{n_\infty(V) - n}{\tau_n(V)}$$

$$\dot{h} = \frac{h_\infty(V) - h}{\tau_h(V)}$$

$$\dot{m} = \frac{m_\infty(V) - m}{\tau_m(V)}$$

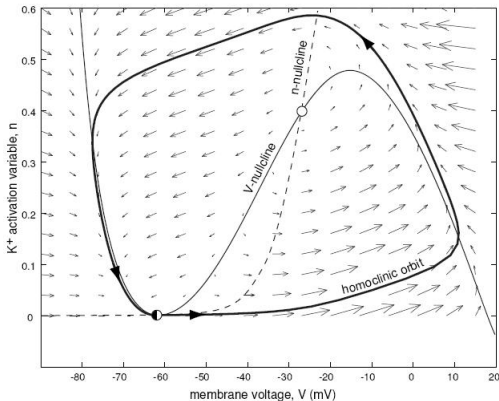
Multi time-scales due to the channel properties!

## The $I_{Na}$ - $I_K$ -model

- $m$  and  $h$  hebben dezelfde tijdschaal als  $V$ . Remove  $h$  and replace  $m$  by  $m_\infty(V)$
- High-threshold  $K^+$ : Saddle-node on invariant circle bifurcation
- Low-threshold  $K^+$ : Andronov Hopf bifurcation

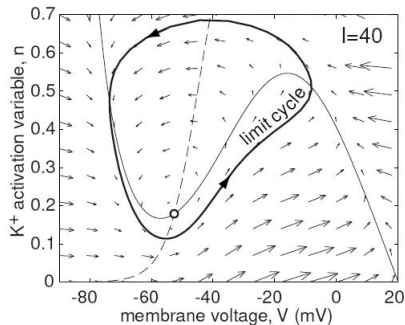
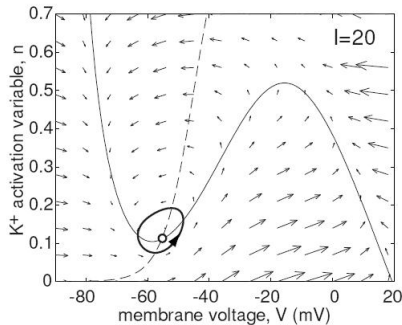
$$C\dot{V} = I - \overbrace{g_L(V - E_L)}^{I_L} - \overbrace{g_{Na}m_\infty^3(V)(V - E_{Na})}^{I_{Na}} - \overbrace{g_Kn(V - E_K)}^{I_K}$$
$$\dot{n} = \frac{n_\infty(V) - n}{\tau_n(V)}$$

## High threshold $K^+$ , Izhikevich



- $V$ -nullcline has shifted up
- Saddle and node coalesce
- transition from saddle-node to homoclinic to limit cycle

## Low threshold $K^+$ , Izhikevich



A small stable limit cycle after Hopf bifurcation

Size limit cycle increases with increasing  $I$

## Towards continuum models

- A continuum model for 1D neural mass will be derived with a lot of handwaving
- Traveling waves: numerics & analysis

## From spike to rate 1/2

Activity at the synapse:

$$Qg = \bar{g} \sum_m \delta(t - T_m)$$

$Q$ : second order (time) differential operator for the synapse.

Short-term spatial averaging, assuming that the synaptic response is slowly varying:  $\langle Qg \rangle_t$  is approximately constant, where

$$\langle x \rangle_t = \frac{1}{\Delta} \int_{t-\Delta}^t x(s) ds$$

then

$$Qg = f$$

Where  $f$  is the instantaneous firing rate.

## From spike to rate 2/2

- For a single neuron driven with a constant drive, the firing rate is a function of the drive alone.
- Assuming the neuron spends most of the time close to rest, where  $V = 0$ , the drive is proportional to  $V_s - V \approx V_s$
- Absorb the factor  $V_s$  in the conductance  $V$

For a single population with self-feedback:

$$Qg = w_0 f(g)$$

A common choice for the population firing rate function is the sigmoid:

$$f(g) = \frac{1}{1 + \exp(-\beta(g - h))}$$

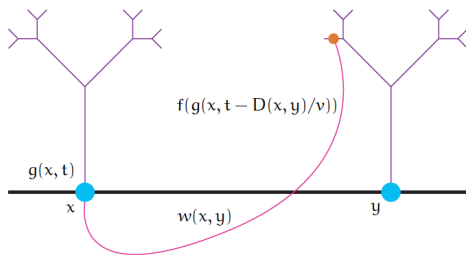


## 1-D tissue model

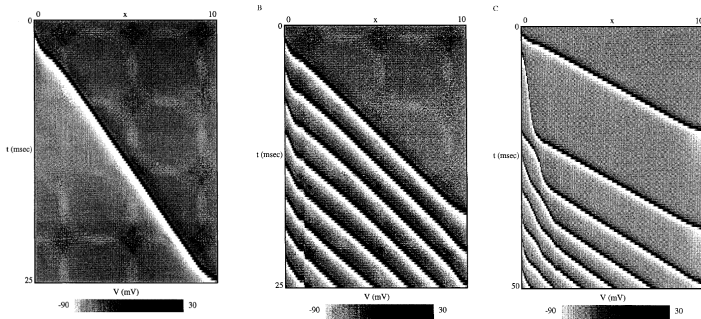
In one dimension we let  $g = g(t, x)$  and obtain the integro-differential equation:

$$Qg = \int_{-\infty}^{\infty} w(x, y) f(g(t - |x - y|/v, y)) dy$$

- $f$ : from synaptic activity to spike rate
- often:  $w(x, y) = w(|x - y|)$
- in which case the rhs is a convolution integral.



# Analysis of synaptically generated traveling waves



*Figure 1.* Space-time plots of voltage for the continuum model for synaptically generated waves using Traub's spiking model. Time increases downward, and space increases from left to right. A:  $\beta = 4$ , a very fast synapse, leads to a solitary pulse. B:  $\beta = 1$ , a slower synapse persists long enough for reexcitation leading to wave-trains. C:  $\beta = 2$  near the transition between a solitary pulse and repeated excitation; secondary waves arise with long delays due to the partial refractoriness.

## Ermentrout98 (2)

Discrete version:

$$C \frac{dV_j}{dt} = -I_{ion}(V_j, \text{gating\_variables}) - I_j^{syn}(t)$$

With the synapse current given by:

$$I_{syn}(t) = g_{syn} \sum_k w(|j - k|) s_k(t) (V - V_{syn})$$

and the synaptic gating variables either specified:

$$s_j(t) = \alpha((t - t_j)^+),$$

where  $t_j$  is the time of firing of cell  $j$  and  $\alpha$  a suitable  $\alpha$ -function, or with its own dynamics:

$$\frac{ds_j}{dt} = K(V_j(t))(1 - s_j) - \beta s_j.$$

## Ermentrout98 (3)

Continuous version:

$$\frac{\partial V(x, t)}{\partial t} = -I_{ion} - I_{syn}(x, t),$$

where

$$I_{syn}(x, t) = \int_{x_0}^{x_1} w(x - y)s(y, t) dy.$$

Examples for the connectivity function

$$w(x) = \frac{1}{2\sigma} e^{-|x|/\sigma}$$

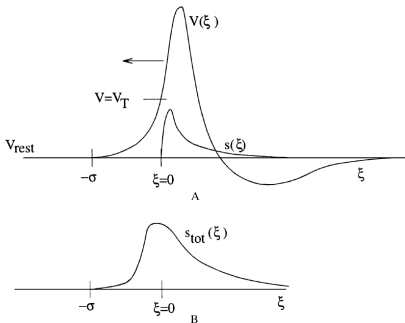
$$w(x) = \frac{1}{\sqrt{\pi}\sigma} e^{-(x/\sigma)^2}$$

$$w(x) = \begin{cases} \frac{1}{2\sigma} & \text{for } |x| < \sigma \\ 0 & \text{for } |x| \geq \sigma \end{cases}$$

## Ermentrout98 (4): traveling waves

Assume there is a **constant speed traveling wave**. The time of spiking of a cell is given by  $t^* = x/v$  and

$$s(x, t) = \alpha(t - x/v) = \alpha(\xi/v), \quad vt + x = \xi$$



$$s_{tot}(x, t) = s_{tot}(\xi) = \int_0^{\infty} w(\xi - \eta) \alpha(\eta/v) d\eta$$

## Ermentrout98 (5): Integrate and fire!

Integrate and fire model:

$$\frac{\partial V(x, t)}{\partial t} = -V(x, t) + I_{syn}(x, t),$$

where

$$I_{syn}(x, t) = g_{syn} \Delta \int_{-\infty}^{\infty} w(x - x') \alpha(t - t^*(x')) dx'.$$

Traveling wave Ansatz:  $V(x, t) = V(vt + x) = V(\xi)$ , where

$$v \frac{dV}{d\xi} = -V(\xi) + g_{syn} \Delta \int_0^{\infty} w(\xi - \eta) \alpha(\eta/v) d\eta$$

subject to the conditions:

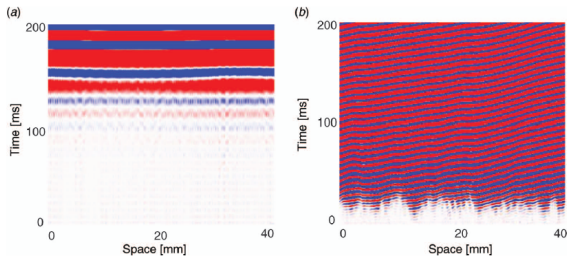
- (i)  $V(\xi) \rightarrow 0$  as  $\xi \rightarrow \infty$
- (ii)  $V(0) = V_T$
- (iii)  $V(\xi) \rightarrow 0$  as  $\xi \rightarrow -\infty$

## Ermentrout98 (6) wavespeed

The implicit relation between the wave velocity  $v$  and the threshold is given by the relation:

$$V_T = \frac{g_{syn}\Delta}{v} \int_{-\infty}^0 d\xi e^{\xi/v} \int_0^{\infty} d\eta w(\xi - \eta)\alpha(\eta/v).$$

# Waves in Neural media, Hutt & Rougier 2010



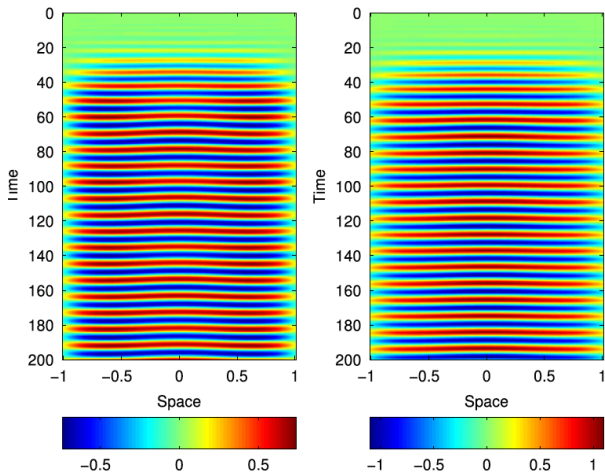
Numerical integration of

$$LV(x, t) = \int_{\Omega} K(x - y) S \left( V(y, t - \frac{|x - y|}{c}) \right) dy + I(x, t)$$

revealing oscillations and traveling waves



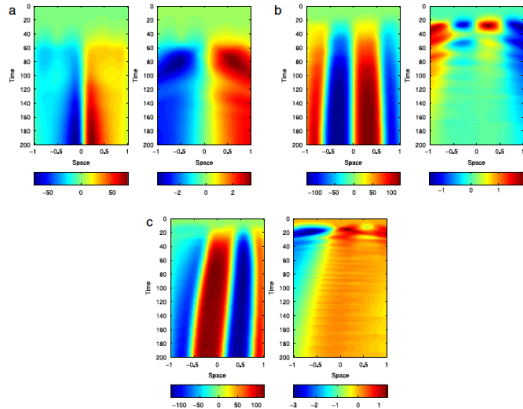
# Hopf in two-layers neural field



Faye & Faugeras, Physica D 2010.

# Two neural layers continued

G. Faye, O. Faugeras / *Physica D* 239 (2010) 561–578



Faye & Faugeras, *Physica D* 2010.

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## Suggestions for contributions

- a The study of the original and very influential papers of Wilson & Cowan ('72/'73) and Amari ('77).
- b Coombes lecture notes lecture 1: section 1.4 is about the Turing instability in a 1D neural wave equation. The application to visual hallucination is especially interesting. Numerical simulation is encouraged.
- c Coombes lecture notes lecture 2: In this lecture the amplitude equations are derived in one and two dimensions. It is especially challenging (and meaningful!) to extend the derivation to two 1D-layers.
- d Coombes lecture notes lecture 3: This lecture is on stability analysis via an Evans function approach in the case of a Heaviside nonlinearity.
- e Coombes lecture notes lecture 4: This lecture is on interface dynamics in random neural media.
- f Binocular rivalry is a mechanism very well studied, both experimentally, psychophysically and theoretically. In Kilpatrick & Bressloff (2010) this is studied in a network with synaptic depression. Extended project: perform the numerical experiments mentioned in the paper and investigate the outcome with periodic stimuli in its dependence on on-off times. This has been done by Suren Jayasuriya & Zachary P. Kilpatrick in "Effects of Time-Dependent Stimuli in a Competitive Neural Network Model of Perceptual Rivalry", *Bulletin of Mathematical Biology* (2012). The results for long off-times are not in agreement with the experiments. What model gives better agreement?
- g Hallucinations is another subject where math modeling is crucial. Present the original ideas of Ermentrout and Cowan and the follow up by Bressloff, Golubitsky and Cowan. This involves dynamics with the symmetry of the