Neural dynamics : a source of computational problems

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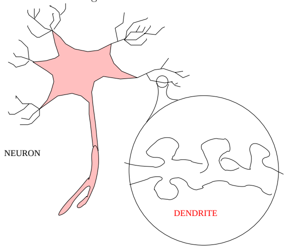
0. Abstract

We take as an example the Baer-Rinzel model of the dendrites in a single neuron. Computations show a rich dynamical structure with the co-existence of stable pulses and multipulses.

1. Dendrites on the Neuron

Looking at a model of dendrites of a *single* neuron

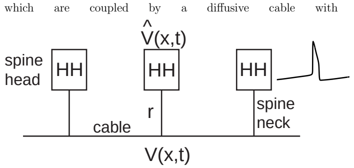


Dendritic spines are prominent in
- ◯ Cerebellar cortex, Basal ganglia, Cerebral cortex
- ◯ learning and memory, logical computations, pattern matching
- ◯ 80% spine heads are excitable
- ◯ travelling waves in distal dendritic trees

2. Baer & Rinzel Continuum Model [*J Neurophys*, 65, 1991]

Model of Dendrite :

Take Hodgkin-Huxley (HH) dynamics in the spine heads which are coupled by a diffusive cable with resistence r.



Voltage in cable: $V(t)$ Voltage in spine heads: $\hat V$

$$V_t = -g_L(V - V_L) + V_{xx} + \rho(x)\frac{\hat V - V}{r}$$

$$\hat V_t = -HH(\hat V, m, n, h) - \frac{\hat V - V}{r}$$

Conductance variables m, n, h take values between 0 and 1

$$\tau_X X_t = X_\infty - X, \qquad X \in \{m, n, h\}$$

Take $\rho(x)$ as constant ρ

3. Travelling wave solution: wavespeed c

Seek a travelling wave solution : $\xi = x - ct$.

$$\begin{aligned}
V' &= W \\
W' &= cW + g_L(V - V_L) - \rho(\hat V - V)/r \\
c\hat V' &= g_L(V_L - \hat V) - (\hat V + V)/r - g_K n^4(\hat V - V_k) - g_{Na} h m^3(\hat V - V_{Na}) \\
cX' &= (X_\infty - X)/\tau_X, \qquad X \in \{m, n, h\}
\end{aligned}$$

Get a 6D system of ODEs to solve. Key parameters in the system are

- Wave speed c
- Resistance r
- Density ρ

There is a unique fixed point : 5D stable manifold & 1D unstable manifold

4. Computation of Connections

Truncate & Rescale ODE system to interval [0, 1]

Apply Projection BC's [Beyn '90, Beyn '93] :

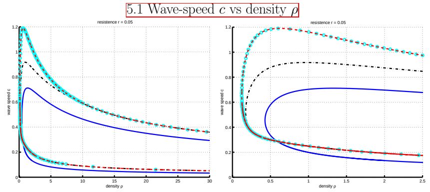
$x = 0$ Project out linear center-stable manifold
$x = 1$ Project out linear center-unstable manifold
$+$ Integral Phase Condition

Baer-Rinzel Model :

Initially seek homoclinic solutions to the unique fixed point:
→ Continue in any 2 of systems parameters
(Homoclinic in a codim 1 subset of parameter space)
Initial Guess for Newton:
(1) Large period approximation
(2) 'Cut and Paste' solutions together
Continuation of solution as BVP using auto97

5. Numerical results

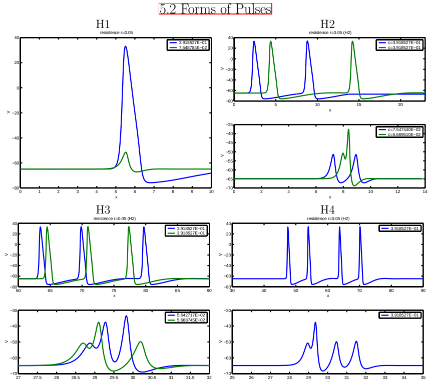
5.1 Wave-speed c vs density ρ



For small ρ Propagation failure

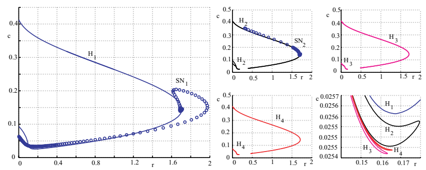
The speed of H_1, H_2, H_3 and H_4 for $r = 0.05$ as a function of the spine density ρ. For fixed (small) r multi-pulse solutions can exist at smaller values of ρ than H_1.

5.2 Forms of Pulses



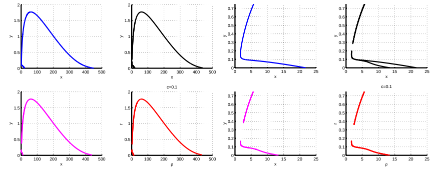
Different forms of pulse solutions to the Baer-Rinzel model. Note there are fast and slow forms of solutions. It is the fast $H1$ solution which is stable.

5.3 Wave-speed c vs resistence r

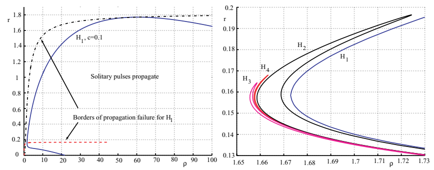


We show the speed of the pulse H_1 as a function of the spine-stem resistance r for $\rho = 25$. The open circles denote the limit point of periodics. Note the gaps where for $H2, H3, H4$ cease to exist. This small r phenomena is shown in the blow up.

5.4 Density ρ vs resistance r

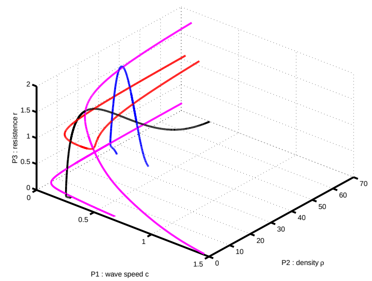


Fixed Wave speed $c = 0.1$ and small density blow up showing gap in solutions.



Continuation of limit points of homoclinics shows the propagation failure of $H1$. Also plotted $H1$–$H4$ on the same diagram showing propagation failure in the small gap.

5.5 $H1$ in 3D Parameter space



Existence of the $H1$ in 3D parameter space with continuation of the limit points giving boundary of existence.

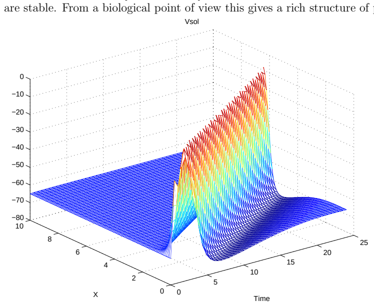
6. Propagation Failure & Stability

Propagation Failure of pulses for :
- ◯ too large a spine stem resistance
- ◯ too small a density ρ

Co-existence of multi-pulse solutions :
A small change in parameters result in many different types of pulse solutions.

Stability

Numerics indicate that the pulse $H1$ is stable (see below). Once stability of this branch is established the by [Sandstede '98] infinitely many of the multi-pulse solutions are stable. From a biological point of view this gives a rich structure of pulses.

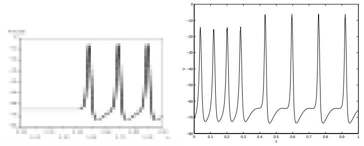


7. Challenges:

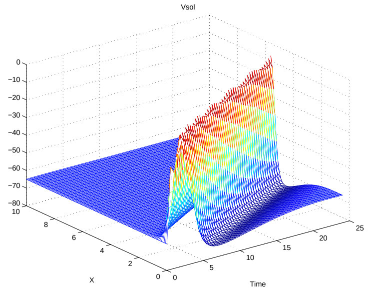
A key tool in dynamical systems analysis is the numerical continuation of solutions as parameters vary. This allows both stable & *unstable* solutions.

For the Baer-Rinzel model discussed here it would be interesting to have a more complete picture of the dynamics in the system.

As part of these dynamics Heteroclinic connections are also observed. Some of these can be computed using the techniques outlined in Box 4.



1. Non-uniform density:
From the biology (Box 1.) the density of the spines is non-uniform along the dendrite.



In this figure a sigmoidal density function was taken along the dendrite. There are interesting questions of computing travelling wave type solutions in non-heterogeneous media [Xin,2000].

If the spine heads are taken at discrete sites then the computation of dynamics over *lattices* is important. There are many direct computations on lattices & some results continuing connections on lattices (eg [Elmer & van Vleck '99]). Other models lead to Integro-Differential type models.

2. Structure in dendrites & Neuron
These calculations all assume a single cable and ignore the branching structure found in the dendrites. Extensions include : more 'realistic' geometries with branching (and thickening) of the dendrite and integration into a 'full' model of a neuron. However, these lead to complex and large systems.

3. Stability and existence of pulse solutions under stochastic forcing [Kuske & Baer '01, Xin '00].
Since no neuron is fully isolated, stochastic forcing may be used to model the background field. Travelling waves can be generalized to the stochastic case and can be calculated by direct numerical simulation. Under stochastic forcing with multiplicative noise there exists a single fixed point - with stable and unstable manifolds. A natural question is if there exists a homoclinic connection - and how this might be continued or computed.

4. *Need to validate with Biology and Experiments !*

References

Elmer & van Vleck '99 Analysis and Computation of Travelling Wave Solutions of bistable differential-differnce equations, Nonlinearity, 12, 771-798.
Kuske & Baer, '01 Asymptotic Analysis of Noise Sensitivity in a Neuronal Burster, preprint.
Sanstede, 98 Stability of Multiple-Pulse Solutions, Trans. A.M.S., 1998.
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