# On Fokker-Planck Equations with In- and Outflow of Mass

Jan-Frederik Pietschmann

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TECHNISCHE UNIVERSITÄT
CHEMNITZ

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# Neuron Growth

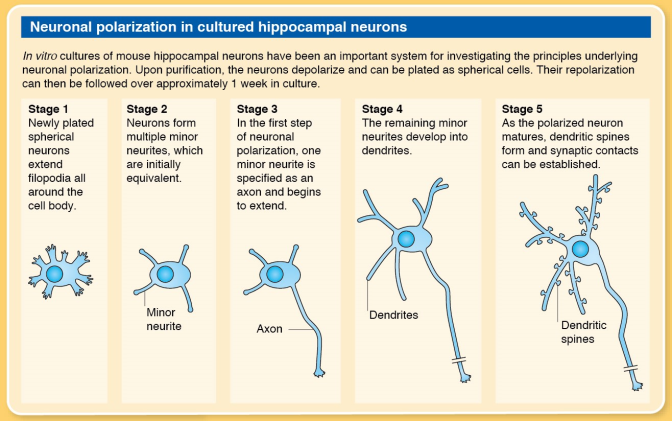


Figure: Neuronal Polarization in cultured hippocampal neurons, Source: http://dev.biologists.org/content/develop/142/12/2088/F1.poster.jpg

# Biological Vocabulary

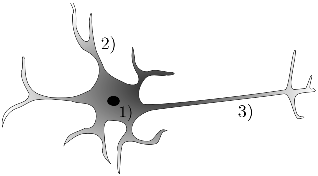


Figure: Sketch of a neuron (1) cell nucleus, 2) dendrite and 3) axon)

| | |
|---|---|
| Proximal axon | = Part of axon near to nucleus, distal axon (near the tip) |
| neurites | = refers to any projection from the cell body of a neuron |
| polarization | = "growing process" |

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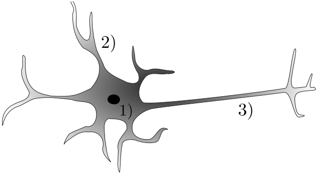


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# The Role of Vesicle Transport

Previously: Mostly modelling influence of protein regulation on growth process

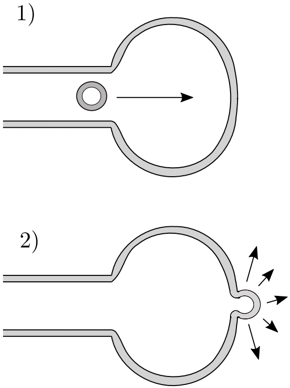


Figure: Vesicle merging with the cell membrane

Here: Role of vesicle transport

- vesicles = "*Building blocks* of the cell"
- **merge** with the cell membrane making the neurite grow
- parts of the membrane can be **separated** forming a vesicle and making it shrink

# Measurements (AG Püschel, WWU Münster)

p-DCX-eGFP-Vamp2

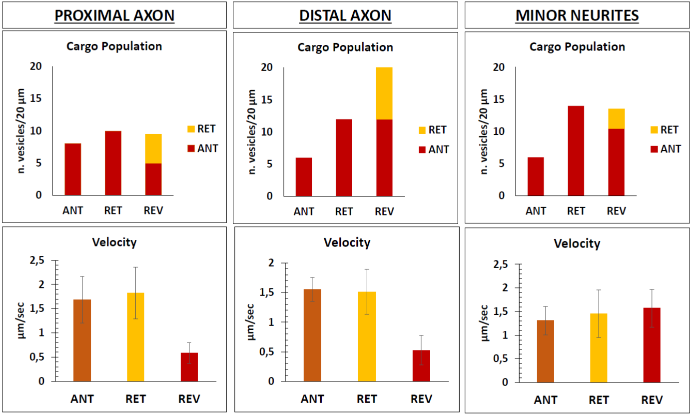


Figure: Measurements by Danila di Meo, AG Püschel, ANT = anterograde transport, i.e. movement towards the synapse, RET = retrograde, REV = reverse

# Neuron as Mathematical Object

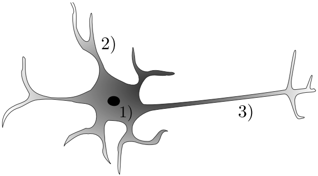


Figure: Sketch of a neuron

- View the axon as an one dimensional object
- Identify it with the unit interval $\Omega = [0, 1]$
- Model vesicle density with $\rho = \rho(x, t)$

In our setting: The point 0 describes the entrance of the vesicles and 1 the exit.

# Modelling

Use *Fokker-Planck* type equation to model vesicle density in neurites

$$\partial_t \rho + \nabla \cdot J = 0$$
$$\text{with } J = -\nabla \rho + f(\rho)\nabla V$$

for $t \geq 0$ and $x \in \Omega \subset \mathbb{R}^n$, and where $V = V(x)$.

- Linear or nonlinear transport

$$f(\rho) = \rho \text{ or } f(\rho) = \rho(1-\rho)$$

  (second choice enforces $\rho \leq 1$)
- Enter / Exit of vesicles

Flux boundary conditions

$$-J \cdot n = \alpha(1-\rho) \quad \text{at } x = 0,$$
$$J \cdot n = \beta\rho \quad \text{at } x = 1$$

No flux $J \cdot n = 0$ and reaction term

$$R(\rho) = \alpha(1-\rho) - \beta\rho.$$

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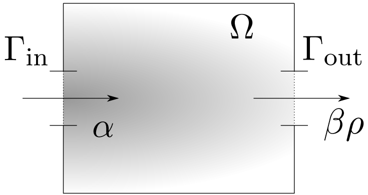


First Model:

Linear Transport
Boundary- In- and Outflow

# Boundary Conditions

$$\partial_t \rho = \nabla \cdot (\nabla \rho - \rho \nabla V) \text{ in } \Omega \times (0,T),$$
$$u(x,0) = u_0(x) \in L^2_+(\Omega) \quad \text{ in } \Omega$$

with boundary conditions

$$\begin{aligned} -J \cdot n &= \alpha && \text{on } \Gamma_{\text{in}} && \times (0,T), \\ J \cdot n &= \beta\rho && \text{on } \Gamma_{\text{out}} && \times (0,T), \\ J \cdot n &= 0 && \text{on } \partial\Omega \setminus \{\Gamma_{\text{in}} \cup \Gamma_{\text{out}}\} && \times (0,T), \end{aligned}$$

where $n$ is the normal outward.

In our context the factor $\alpha$ describes the vesicle influx and $\beta\rho$ corresponds to the vesicles merging with the neurite tip

# Assumptions / Existence

Assumptions

1. The connected and bounded domain $\Omega \subset \mathbb{R}^n$ has Lipschitz boundary $\partial\Omega$.
2. The potential satisfies $V(x) \in W^{1,\infty}(\Omega)$.
3. The initial concentration $\rho_0$ is non negative and fulfills $\rho_0 \in L^2(\Omega)$.
4. The sets $\Gamma_{\text{in}}, \Gamma_{\text{out}} \subset \partial\Omega$ are disjoint and open subsets of the boundary and $\Gamma_{\text{out}}$ is nonempty.
5. The functions $\alpha$ and $\beta$ fulfill $\alpha \in L^\infty(\Gamma_{\text{in}})$ with $\alpha \geq 0$ and $\beta \in L^\infty(\Gamma_{\text{out}})$ with $\beta \geq \beta_0 > 0$.

Existence weak / stationary solutions

- Existence of (unique) weak solution

$$\rho \in L^2((0,T); H^1(\Omega)) \cap H^1((0,T); (H^1)^*(\Omega))$$

  by standard arguments
- Existence of unique stationary solution

$$\rho_\infty \in H^1(\Omega)$$

  strictly positive and bounded

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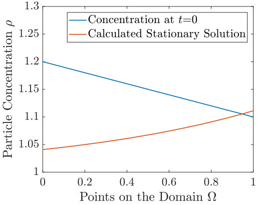
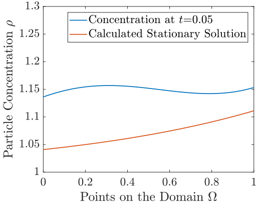
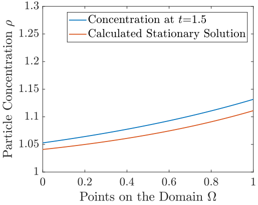
# Time evolution of $\rho$



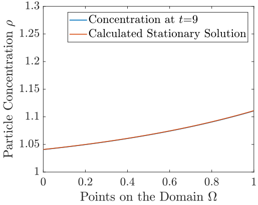

(a) $t = 0$




(b) $t = 0.05$




(c) $t = 1.5$




(d) $t = 9$

Figure: Evolution over Time of the Particle Concentration for $\alpha = 1, \beta = 0.9$, initial particle concentration $\rho(x) = -0.1x + 1.2$, potential $V(x) = x$ and $\Omega = [0, 1]$.

# Long time behaviour

Use Entropy–Entropy-dissipation method

- Entropy functional $E(\rho|\rho_\infty) = \int_\Omega \dots \, dx$
- Its dissipation $D(\rho|\rho_\infty) = -\frac{d}{dt} E(\rho|\rho_\infty)$
- Show $D(\rho|\rho_\infty) \geq C E(\rho|\rho_\infty)$, so that

$$\frac{d}{dt} E(\rho|\rho_\infty) + E(\rho|\rho_\infty) \leq 0$$

Application of Gronwall's Lemma yields

$$E(\rho|\rho_\infty) \leq e^{-Ct} E(\rho_0|\rho_\infty).$$

By additional Cziszár-Kullback-Pinsker inequality

$$\|\rho - \rho_\infty\|_{L^1(\Omega)} \leq e^{-Ct} E(\rho_0|\rho_\infty).$$

# Failure of logarithmic Sobolev Inequality

Different to many other works, total mass of $\rho$ is not conserved

$$\frac{d}{dt}\int_\Omega \rho \; dx = \int_{\Gamma_{\text{in}}} \alpha \; d\sigma - \int_{\Gamma_{\text{out}}} \beta\rho \; d\sigma$$

If we define the logarithmic relative entropy as

$$E(\rho|\rho_\infty) = \int_\Omega \rho \log\big(\frac{\rho}{\rho_\infty}\big) - (\rho - \rho_\infty) \; dx.$$

Calculating the dissipation yields

$$\begin{aligned} D(\rho|\rho_\infty) &\geq \int_\Omega \rho \Big|\nabla \log\big(\frac{\rho}{\rho_\infty}\big)\Big|^2 dx \\ &= \int_\Omega \rho \; \frac{\rho_\infty}{\rho} \; \Bigg|\frac{\nabla \frac{\rho}{\rho_\infty}}{\sqrt{\frac{\rho}{\rho_\infty}}}\Bigg|^2 dx = 4\int_\Omega \rho_\infty |\nabla(\sqrt{\frac{\rho}{\rho_\infty}})|^2 dx. \end{aligned}$$

# Failure of Logarithmic Sobolev Inequality

Dissipation

$$D(\rho|\rho_\infty) \geq 4\int_\Omega \rho_\infty |\nabla(\sqrt{\frac{\rho}{\rho_\infty}})|^2 dx.$$

Define $\phi = \sqrt{\frac{\rho}{\rho_\infty}}$. In order to obtain

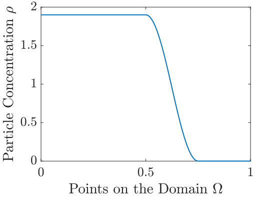
$$D(\rho|\rho_\infty) \geq E(\rho|\rho_\infty)$$

would need *Logarithmic Sobolev Inequality*

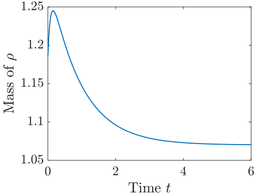
$$\int_\Omega |\nabla\phi|^2\,dx \geq C\Big(\int_\Omega \phi^2\log(\phi^2) - \phi^2 + 1\,dx - \int_{\Gamma_{\text{out}}} \phi^2\log(\phi^2) - \phi^2 + 1\,d\sigma\Big),$$

But: Cannot hold (as scaling $\phi \to K\phi$ for $K > 0$ shows)
$\Rightarrow$ Due to lack of mass conservation

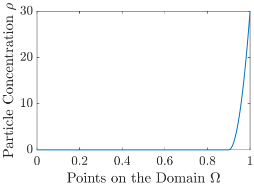
# Mass evolution



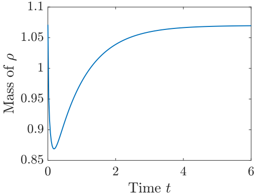

(a) $\rho_0$




(b) Mass evolution




(c) $\rho_0$




(d) Mass evolution

Figure: Two examples for non monotone mass evolution for $\alpha = 1$ and $\beta = 0.9$.

# Quadratic entropy

Way out: Linear structure of the PDE allows for different entropy functional

Define the quadratic relative entropy as

$$E(\rho|\rho_\infty) = \frac{1}{2}\int_\Omega \frac{(\rho-\rho_\infty)^2}{\rho_\infty}\,dx.$$

Log-Sobolev inequality can be replaced by variant of Friedrich's inequality

$$\int_\Omega u^2\,dx \le C_F\Big(\int_\Omega |\nabla u|^2\,dx + \int_\Gamma u^2\,d\sigma\Big)$$

## Theorem

*We have following exponential decay towards equilibrium*

$$||\rho-\rho_\infty||^2_{L^1(\Omega)} \le 2\max\{\rho_\infty\}E(\rho_0|\rho_\infty)e^{-C_F K_1 t}\quad \forall t\ge 0,$$

*where* $K_1 = \min\{\frac{\beta_0}{2},1\}$, $C_F$ *being the constant of Friedrich's inequality,* $\rho_\infty$ *being the stationary solution, and* $E(\rho_0|\rho_\infty)$ *being the relative entropy at* $t=0$.

# Proof (Sketch)

$$D(\rho|\rho_\infty) = -\int_\Omega (-\nabla\rho + \rho\nabla V) \cdot \nabla\Big(\frac{\rho - \rho_\infty}{\rho_\infty}\Big)\ dx - \int_{\Gamma_{\text{in}}} \alpha\ \frac{\rho - \rho_\infty}{\rho_\infty}\ d\sigma + \int_{\Gamma_{\text{out}}} \beta\rho\ \frac{\rho - \rho_\infty}{\rho_\infty}\ d\sigma$$

We test the equation $-\nabla \cdot J_\infty = 0$ with $\phi = \frac{\rho - \rho_\infty}{\rho_\infty}$ and add it onto our equation:

$$\begin{aligned} D(\rho|\rho_\infty) &= \int_\Omega \Big(\nabla(\rho - \rho_\infty) + (\rho_\infty - \rho)\nabla V\Big) \cdot \nabla\Big(\frac{\rho - \rho_\infty}{\rho_\infty}\Big)\ dx + \int_{\Gamma_{\text{out}}} \beta \frac{(\rho - \rho_\infty)^2}{\rho_\infty}\ d\sigma \\ &= \int_\Omega \rho_\infty |\nabla\phi|^2\ dx + \frac{1}{2}\int_\Omega \phi^2\ \nabla \cdot J_\infty\ dx + \int_{\Gamma_{\text{in}}} \frac{\alpha}{2}\phi^2\ d\sigma + \int_{\Gamma_{\text{out}}} \frac{\beta}{2}\rho_\infty\phi^2\ d\sigma \\ &\geq \int_\Omega \rho_\infty |\nabla\phi|^2\ dx + \frac{\beta_0}{2}\int_{\Gamma_{\text{out}}} \rho_\infty\phi^2\ d\sigma, \end{aligned}$$

where the last inequality holds as $\nabla \cdot J_\infty = 0,\ \beta \geq \beta_0$ and the influx term is positive. With $K_1 = \min\{\frac{\beta_0}{2}, 1\}$ and $C_F$ being a special version Friedrich's constant, and as $\rho_\infty$ is strictly positive we gain

$$D(\rho|\rho_\infty) \geq \frac{1}{2}C_F K_1 \int_\Omega \rho_\infty|\phi|^2\ dx = C_F K_1 E(\rho|\rho_\infty).$$

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# Rate of convergence

When calculating dissipation: All manipulations are equalities !

$\to$ Rate of convergence determined by constant in Friedrich's inequality

Chose $\alpha = \beta = 1$ (yields $\rho_\infty = 1$). Rate of convergence $m_a$ determined by

$$\frac{1}{2} m_a = \inf_\phi \frac{\int_0^1 (\phi')^2 \, dx + \frac{1}{2}\phi(0)^2 + \frac{1}{2}\phi(1)^2}{\int_0^1 \phi^2 \, dx} =: \lambda.$$

Can be calculated and yields $m_a = 2\lambda = \inf 2k^2 \approx 1.8439.$

Remark: Also corresponds to smallest Eigenvalue of $-\Delta$ with our boundary conditions

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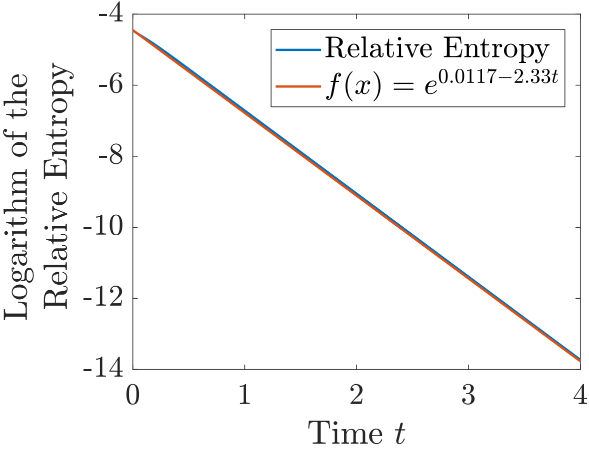
# Numerical results




But numerics show faster convergence with rate $m_n \approx 2.33$. Why?

# Skew-symmetric part

Can be explained by the fact that the operator

$$A[\rho, \psi] = \int_0^1 \rho' \psi' + (\rho\ V')' \psi\ dx + \beta \rho(1) \psi(1)$$

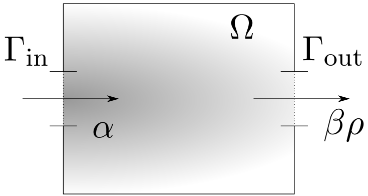
is symmetric except for drift which is skew-symmetric.

Any symmetric operator $A$ the spectral gap $\lambda$ determines the slowest possible convergence rate as

$$u' = -Au + f \quad \Leftrightarrow \quad u(t) \leq \Big( u_0 + \int_0^1 f\ dx \Big) e^{-\lambda t},$$

by Gronwall's lemma.

However, skew-symmetric part can however mix the eigenvalues which can result in a faster rate of convercence.




## To summarize:

- Failure of logarithmic Sobolev inequality
  (no conservation of mass)
- Exponential convergence via quadratic entropy
- "Fast convergence" due to Skew-symmetric part

# Remaining Modells

Linear model with reaction terms

$$\partial_t \rho + \nabla \cdot (-\nabla \rho + \rho \nabla V) = \alpha - \beta \rho e^{-V} \text{ on } \Omega \times (0,T),$$
$$J \cdot n = 0, \text{ on } \partial\Omega \times (0,T)$$
$$u(x,0) = u_0(x) \in L^2_+(\Omega) \quad \text{ in } \Omega$$

- Existence of unique weak solution

$$\rho \in L^2((0,T); H^1(\Omega)) \cap H^1((0,T); (H^1)^*(\Omega))$$

  as before
- Explicit stationary solutions

$$\rho_\infty = \frac{\alpha}{\beta} e^V$$

# Exponential convergence

Logarithmic entropy

$$E(\rho|\rho_\infty) = \int_\Omega \rho \log\left(\frac{\rho}{\rho_\infty}\right) - (\rho - \rho_\infty)\, dx.$$

Yields

$$||\rho - \rho_\infty||^2_{L^1(\Omega)} \leq \frac{1}{K_4} E(\rho_0|\rho_\infty) e^{-\frac{4\beta K_2}{K_1} t},$$

where $K_1 = K_1(\max\{||\rho_\infty||_\infty, ||\rho_0||_\infty\})$, $K_2 = \inf\{e^{-V}\}$ and $K_4$ from Cziszár-Kullback-Pinsker inequality

> Dissipation generated by reactions terms yields exponential convergence, bulk dissipation ignored.

# Remaining Modells

With reaction terms and nonlinear transport

$$\partial_t \rho + \nabla \cdot (-\nabla \rho + \rho(1-\rho)\nabla V) = \alpha - \beta \rho e^{-V},$$
$$J \cdot n = 0$$

Logarithmic entropy

$$E(\rho) = \int_\Omega h(\rho)\, dx \quad \text{with} \quad h(\rho) = \rho \log(\rho) + (1-\rho)\log(1-\rho) + \rho V.$$

with corresponding relative entropy

$$E(\rho|\rho_\infty) = \int_\Omega \rho \log\left(\frac{\rho}{\rho_\infty}\right) + (1-\rho)\log\left(\frac{1-\rho}{1-\rho_\infty}\right)\, dx$$

# Existence of weak solutions

Proof based one implicit Euler discretization + gradient flow structure

Define entropy (dual) variable

$$u := h'(\rho) = \log(\rho) - \log(1-\rho) + V$$

Exploiting formal gradient flow structure

$$\partial_t \rho + \nabla \cdot (\rho(1-\rho)\nabla u) - \alpha(1-\rho) + \beta \rho e^{-V} = 0.$$

Now fix $N \in \mathbb{N}$ and consider discretization of $(0,T]$ into subintervals $(0,T] = \cup_{k=1}^N [(k-1)\tau, k\tau]$ with time steps $\tau = \frac{T}{N}$

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In particular, using the transformation $\rho_{k+1} \leftrightarrow u_{k+1}$ enforces the bounds $0 \leq \rho_{k+1} \leq 1$ (sometimes called boundedness by entropy)

# Existence of weak solutions

Proof based one implicit Euler discretization + gradient flow structure

Define entropy (dual) variable

$$u := h'(\rho) = \log(\rho) - \log(1-\rho) + V$$

Exploiting formal gradient flow structure

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Define entropy (dual) variable

$$u := h'(\rho) = \log(\rho) - \log(1-\rho) + V \quad \Leftrightarrow \quad \rho = \frac{e^{u-V}}{1+e^{u-V}} \in [0,1]$$

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# Existence of weak solutions

- Testing with $\phi = u_k \in H^1(\Omega)$ obtain discrete entropy dissipation

$$\int_\Omega h(\rho_k)\ dx + \tau \int_\Omega \rho_k(1-\rho_k)|\nabla u_k|^2\ dx - \tau \int_\Omega \alpha(1-\rho_k)u_k\ dx \\ + \tau \int_\Omega \beta \rho_k e^{-V} u_k\ dx \le \int_\Omega h(\rho_{k-1})\ dx.$$

- Solving the recursion then yields

$$\int_\Omega h(\rho_k)\ dx + \tau \sum_{j=1}^{k} \Big( \int_\Omega \rho_k(1-\rho_k)|\nabla u_k|^2\ dx - \int_\Omega \alpha(1-\rho_k)u_k\ dx \\ + \int_\Omega \beta \rho_k e^{-V} u_k\ dx \Big) \le \int_\Omega h(\rho_0)\ dx.$$

- Limit $\tau \to 0$: Denote $\rho_\tau(x,t) = \rho_k(x)$ for $x \in \Omega$ and $t \in ((k-1)\tau, k\tau]$.

  A priori $H^1$-bounds $\to$ Strong convergence in $L^2$, weak convergence in $H^1$

# Exponential convergence

As in the previous cases, we obtain

$$||\rho - \rho_\infty||^2_{L^1(\Omega)} \leq \frac{1}{K_4} E(\rho_0|\rho_\infty) e^{-\frac{4\beta K_2}{K_1} t},$$

where $K_1 = K_1(\max\{||\rho_\infty||_\infty, ||\rho_0||_\infty\})$, $K_2 = \inf\{e^{-V}\}$ and $K_4$ from Cziszár-Kullback-Pinsker inequality

Again: Dissipation generated by reactions terms yields exponential convergence, bulk dissipation ignored.

# Neuron Growth

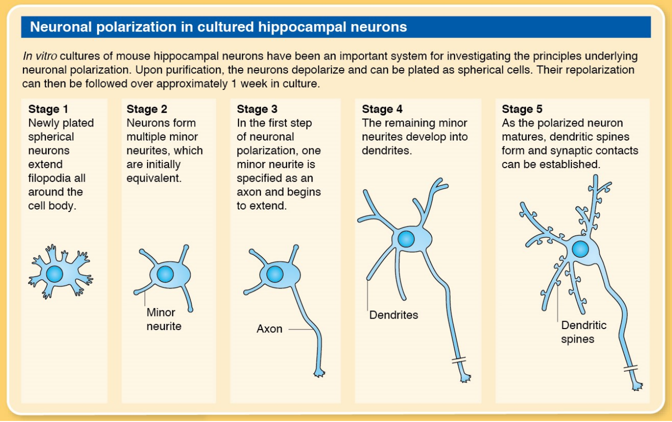


Figure: Neuronal Polarization in cultured hippocampal neurons, Source: http://dev.biologists.org/content/develop/142/12/2088/F1.poster.jpg

# There is room for improvement!

- Work with an axon and a dendrite
- Work with two types of vesicles (ANT and RET) and deal with cross diffusion
- Work with pools of vesicles

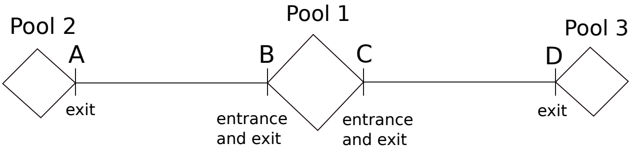


Figure: Scheme for the improvement

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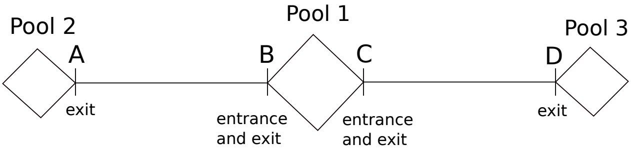


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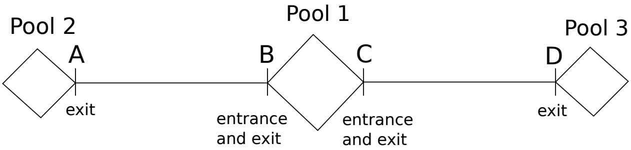


Figure: Scheme for the improvement

p-DCX-eGFP-Vamp2

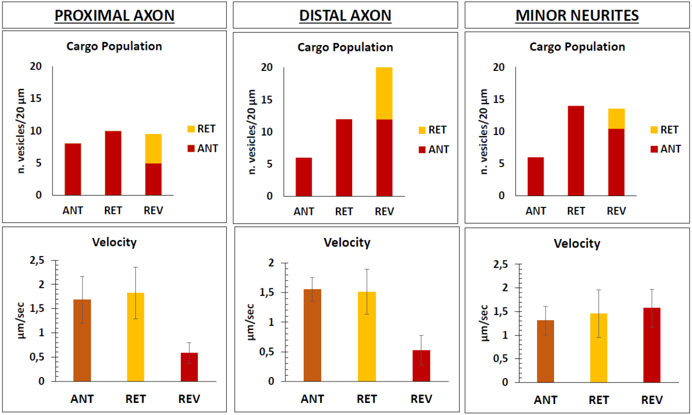


Figure: Measurements by Danila di Meo, AG Püschel, ANT = anterograde transport, i.e. movement towards the synapse, RET = retrograde, REV = reverse

# Improved modelling

Model anterograde and retrograde transport seperately

$$\partial_t a + \nabla \cdot [-\epsilon(1-\rho)\nabla a - \epsilon a \nabla \rho + a(1-\rho)\nabla V_a] = \partial_t a + \nabla \cdot J_a = 0,$$
$$\partial_t r + \nabla \cdot [-\epsilon(1-\rho)\nabla r - \epsilon r \nabla \rho + r(1-\rho)\nabla V_r] = \partial_t r + \nabla \cdot J_r = 0$$

with $\rho(x,t) = a(x,t) + r(x,t)$ (where $V_a(x), V_r(x)$ are two given potentials).

Boundary conditions

$$\begin{aligned}
-J_a \cdot n &= \alpha_a(1-\rho) && \text{on } \Gamma_0 \times (0,T),\\
J_a \cdot n &= \beta_a a && \text{on } \Gamma_1 \times (0,T),\\
J_r \cdot n &= \beta_r r && \text{on } \Gamma_0 \times (0,T),\\
-J_r \cdot n &= \alpha_r(1-\rho) && \text{on } \Gamma_1 \times (0,T),\\
J_a \cdot n &= J_r \cdot n = 0 && \text{on } \partial\Omega \setminus \{\Gamma_0 \cup \Gamma_1\} \times (0,T),
\end{aligned}$$

Eventually

- Model growth/shrinkage $\rightarrow$ free boundary problem
- Model external influences (random effects)

Thank you for your attention!

Questions?

Reference:

M. Burger, I. Humpert, J.-F. Pietschmann
*On Fokker-Planck Equations with In- and Outflow of Mass*.
Preprint, arXiv:1812.07064, 2018