# Friction forces position the neural anlage during Zebrafish late gastrulation

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**in collaboration with Heisenberg's Lab:**

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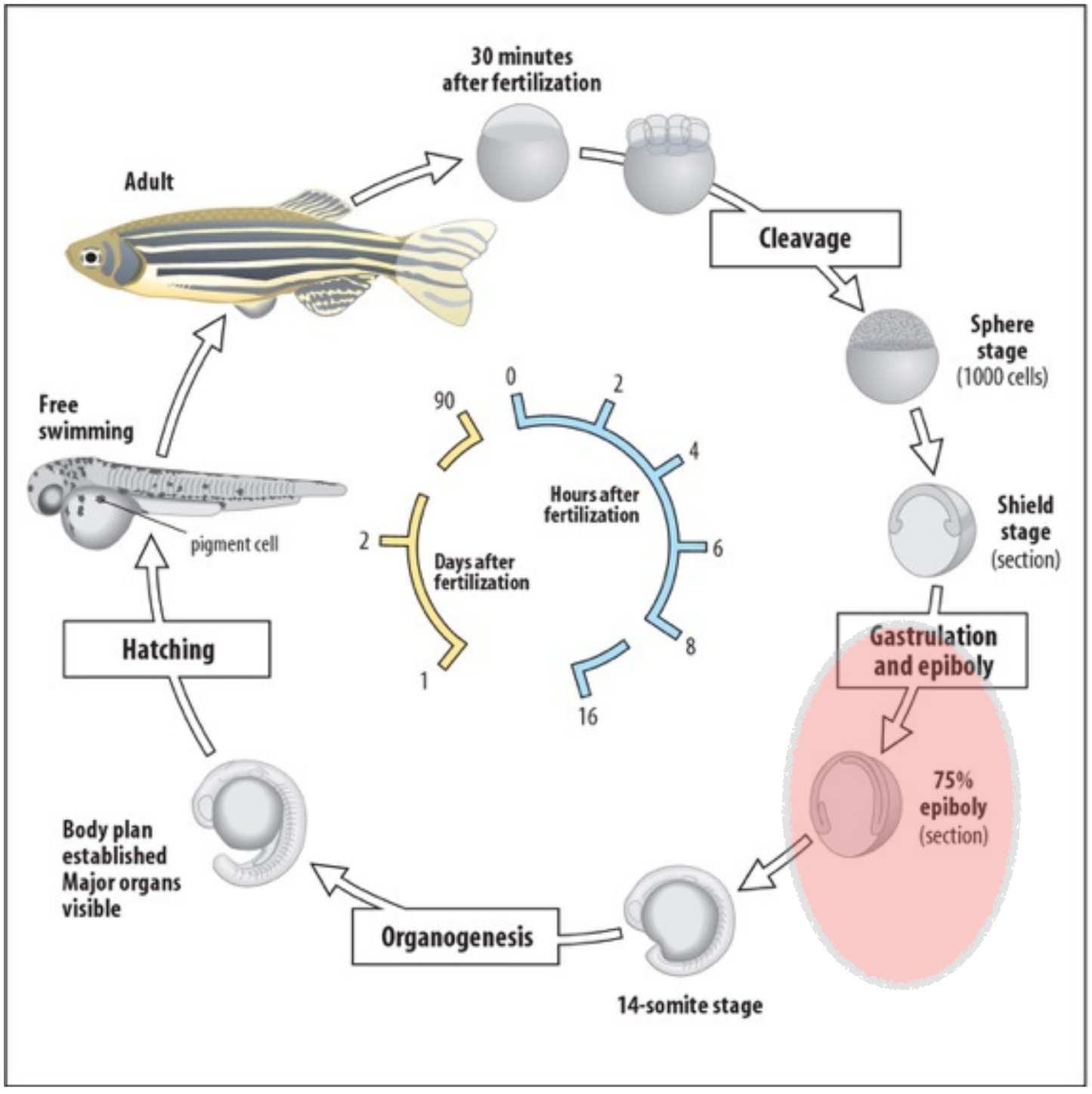
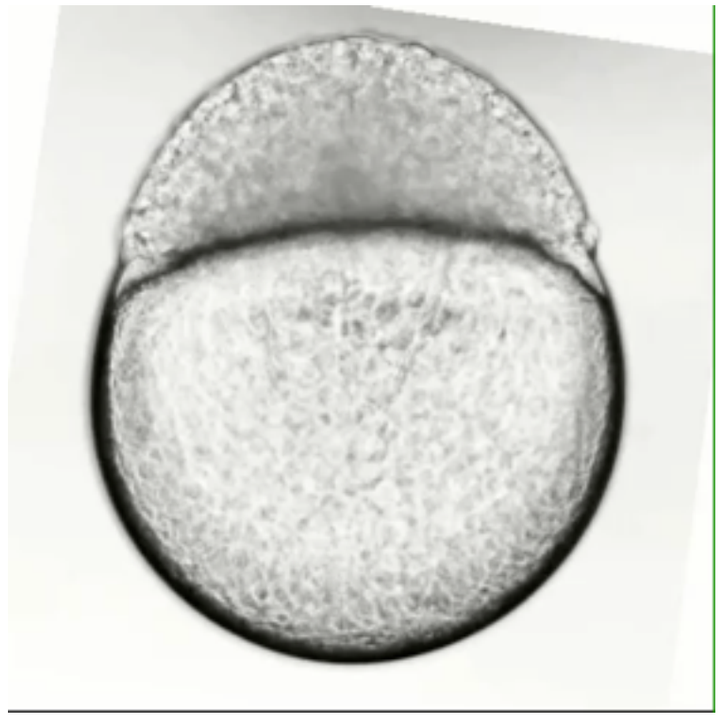
**Vicsek's Lab:**

**Zsusza Akos**

# Zebrafish gastrulation




L. Wolpert et al., *Principles of Development*



H. Morita et al., *Dev. Cell.*, 2017

# Neural system formation

At 70% of epiboly, the blastoderm already differentiated into

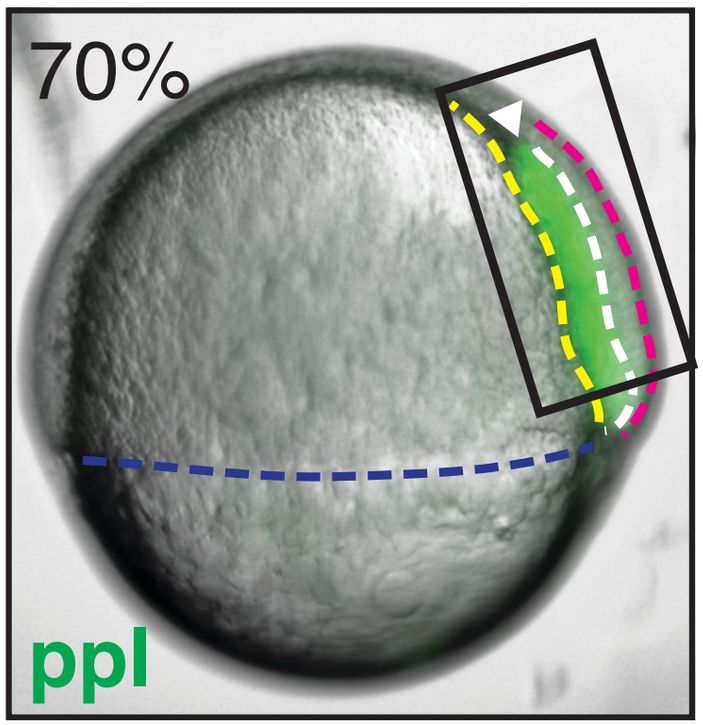
**mesoderm, endoderm and ectoderm.**

The **ectoderm** further differentiates into the **neurectoderm**

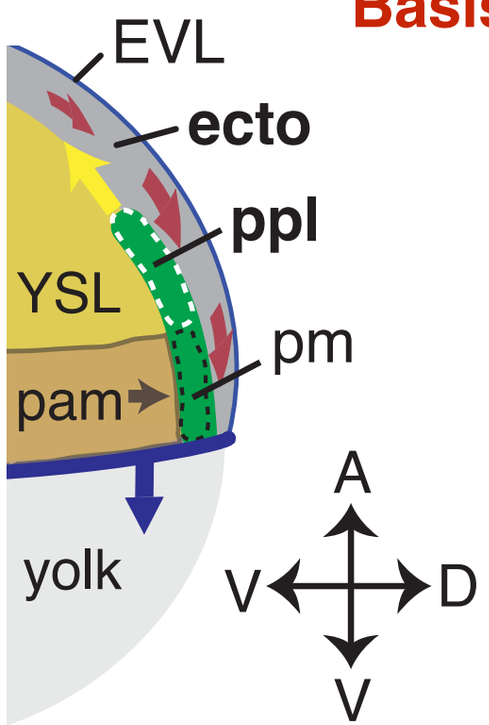
and part of the **mesoderm** into the **prechordal plate (PPL)**.

S. W. Wilson et al., *Dev. Cell.*, 2004

lateral view



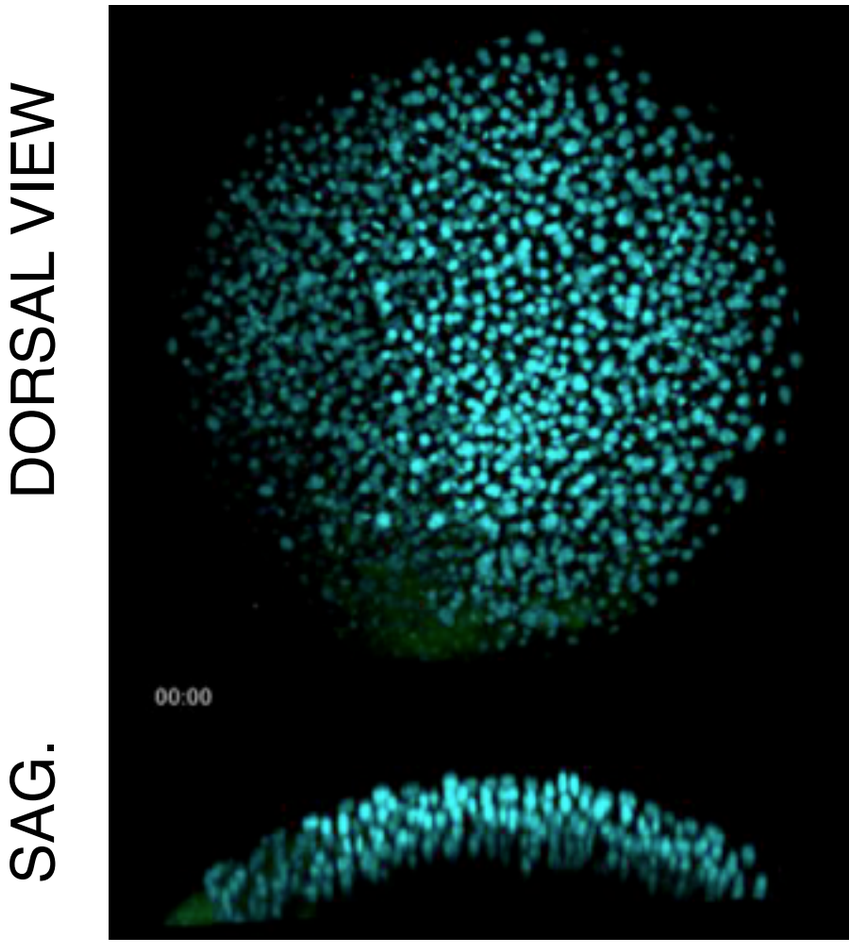

**Basis of neural system**

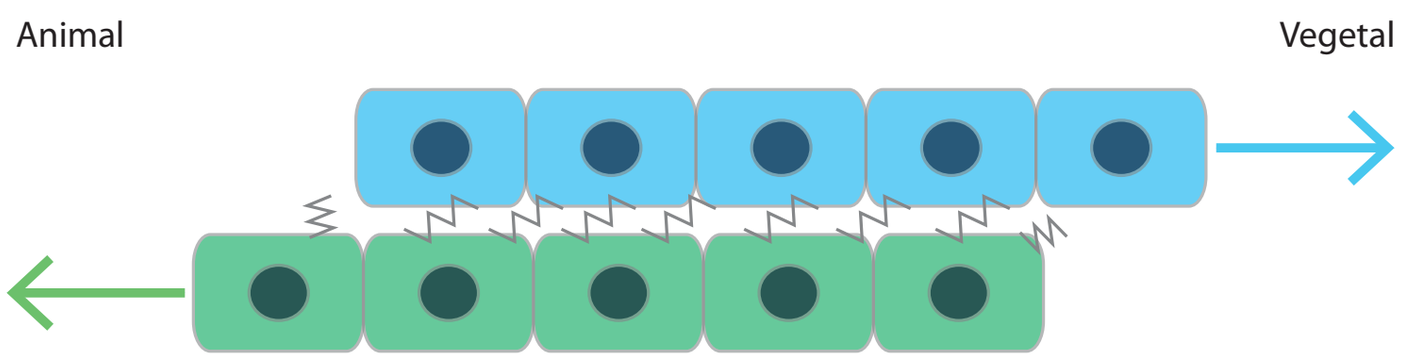


# PPL cells migration

Further differentiated mesoderm - **the Prechordal Plate (PPL)** -

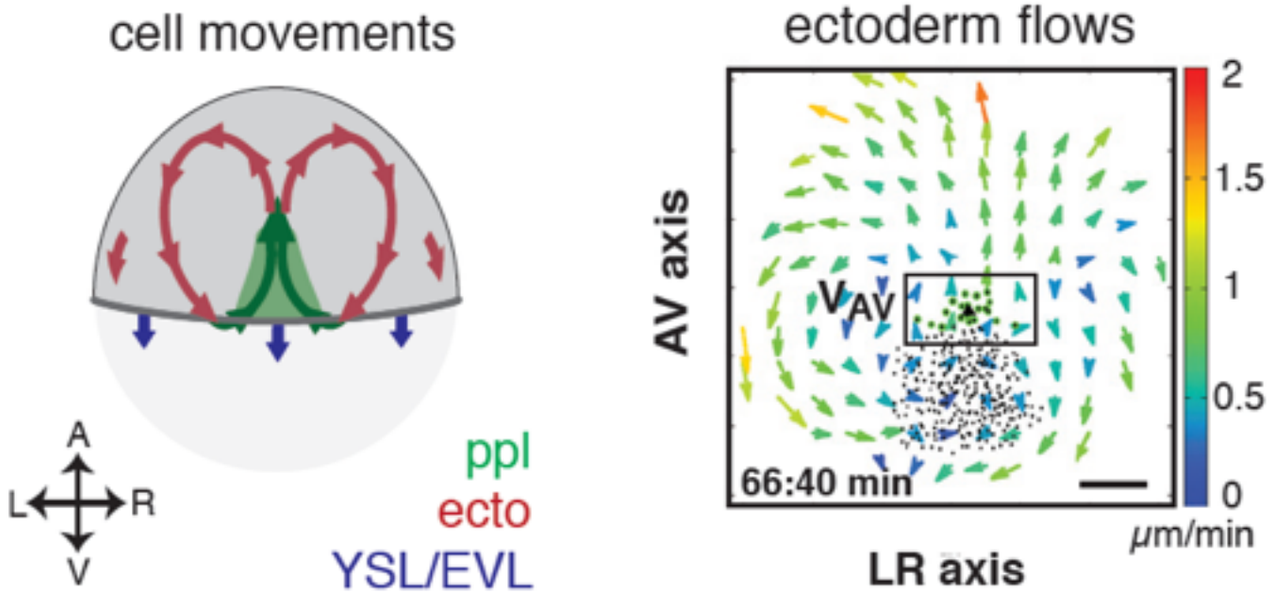
keeps on migrating towards the animal pole.



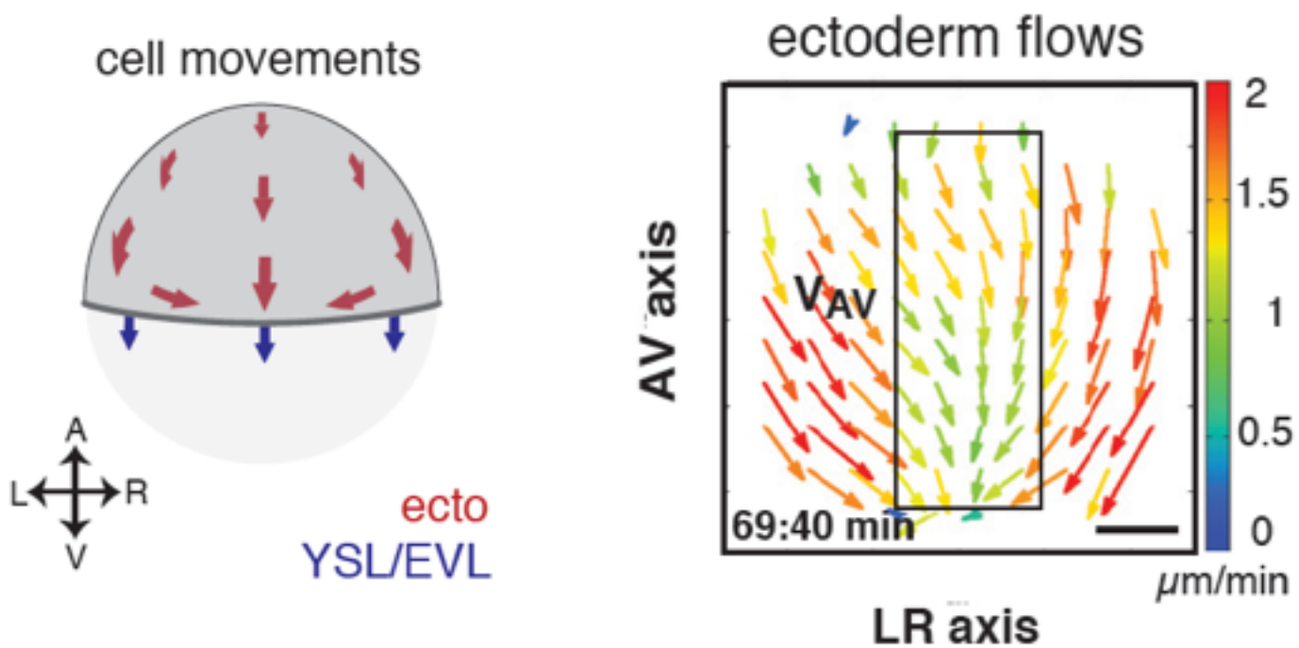



# Evidences of PPL cells influence

## WT



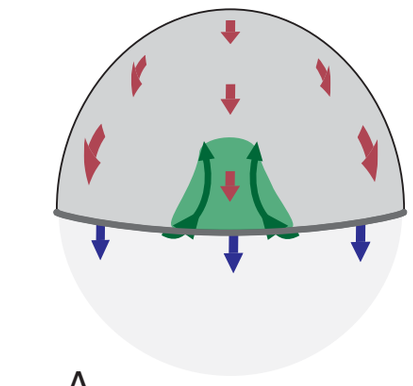

## MZoep (mutant with no PPL)



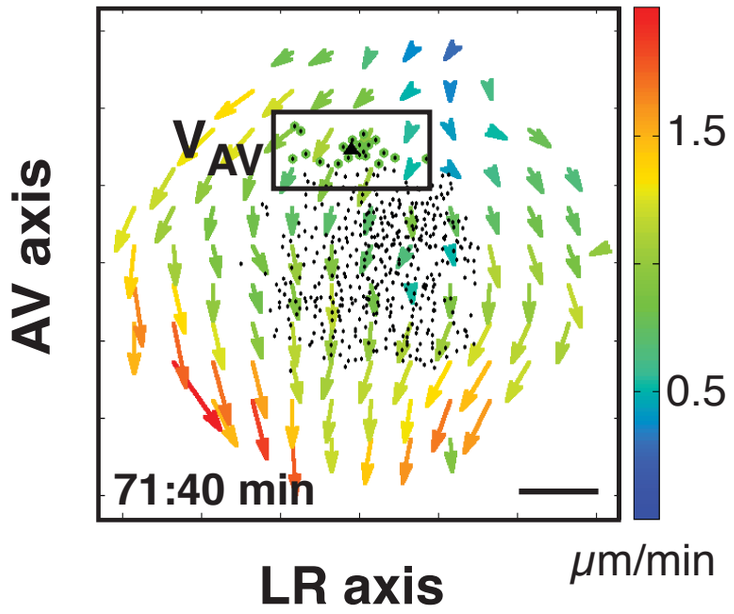
# Evidences of PPL cells influence

## *Slb* (mutant with PPL slowed down)

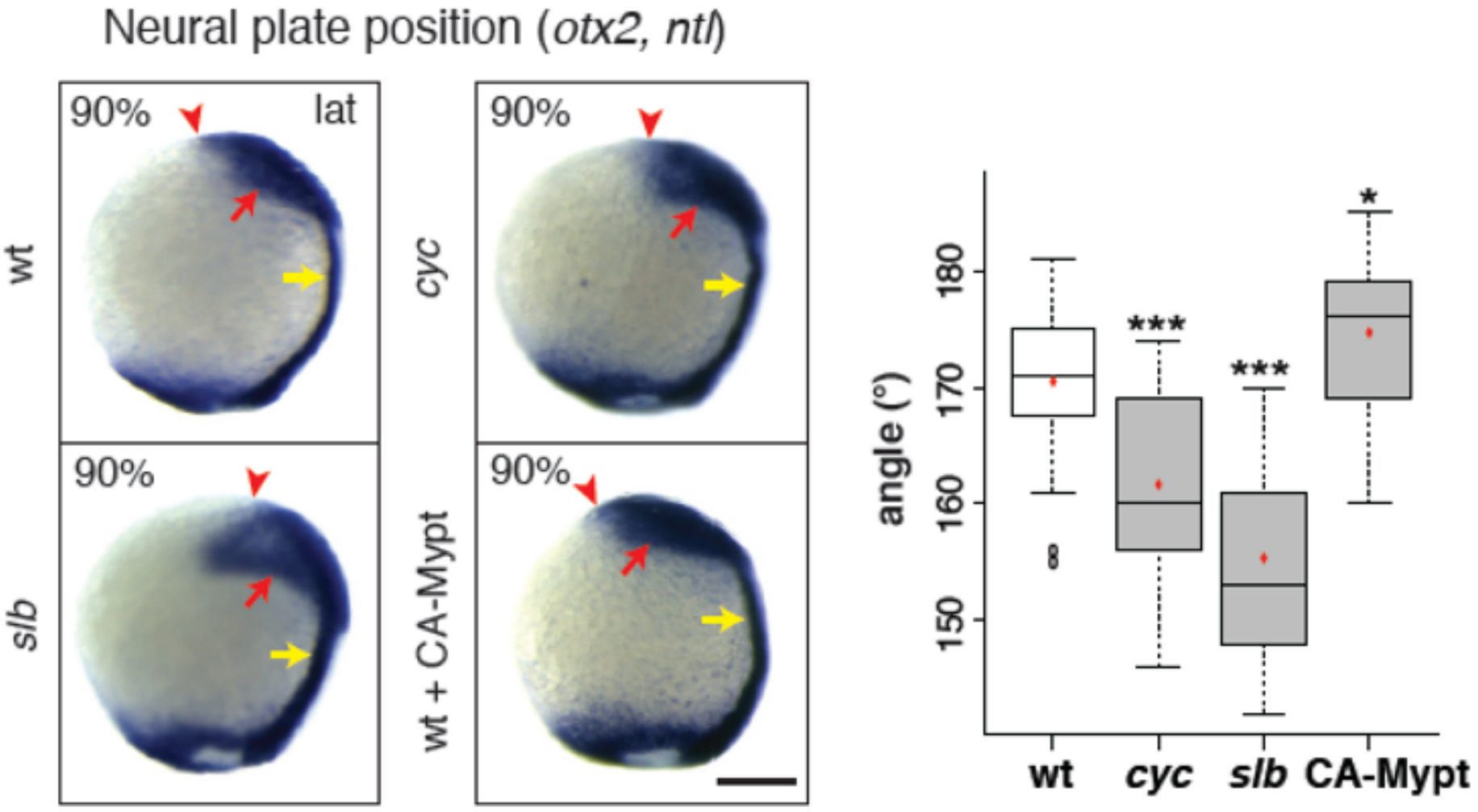
cell movements




ectoderm flows



# Neural plate position is determined by PPL movements



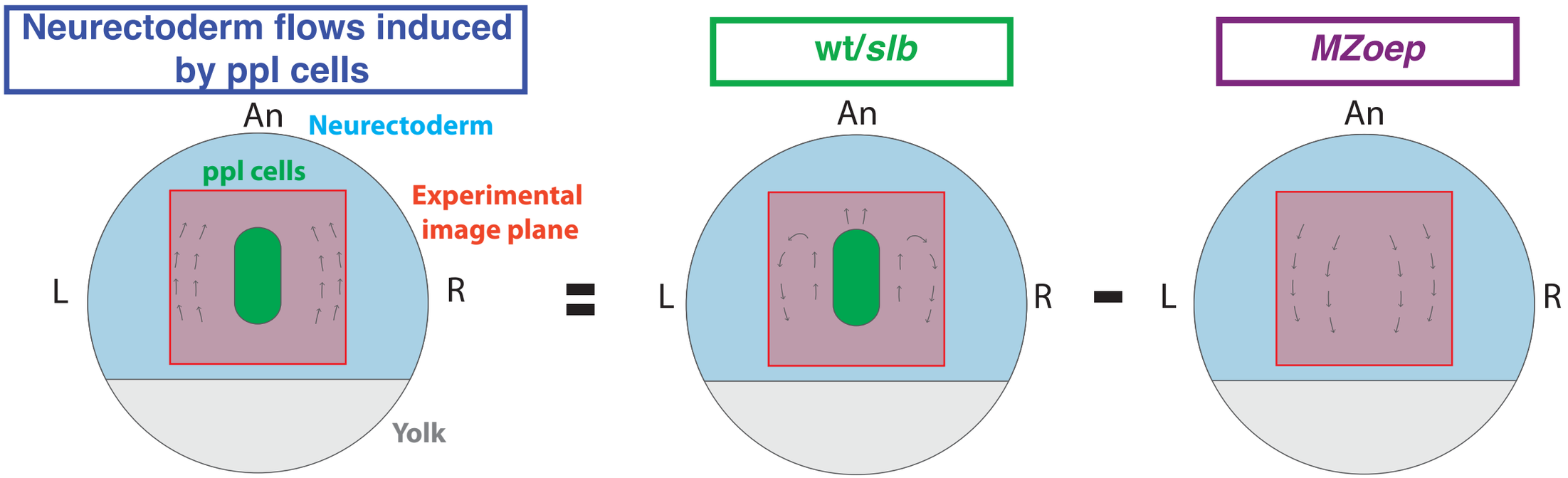
# Our questions

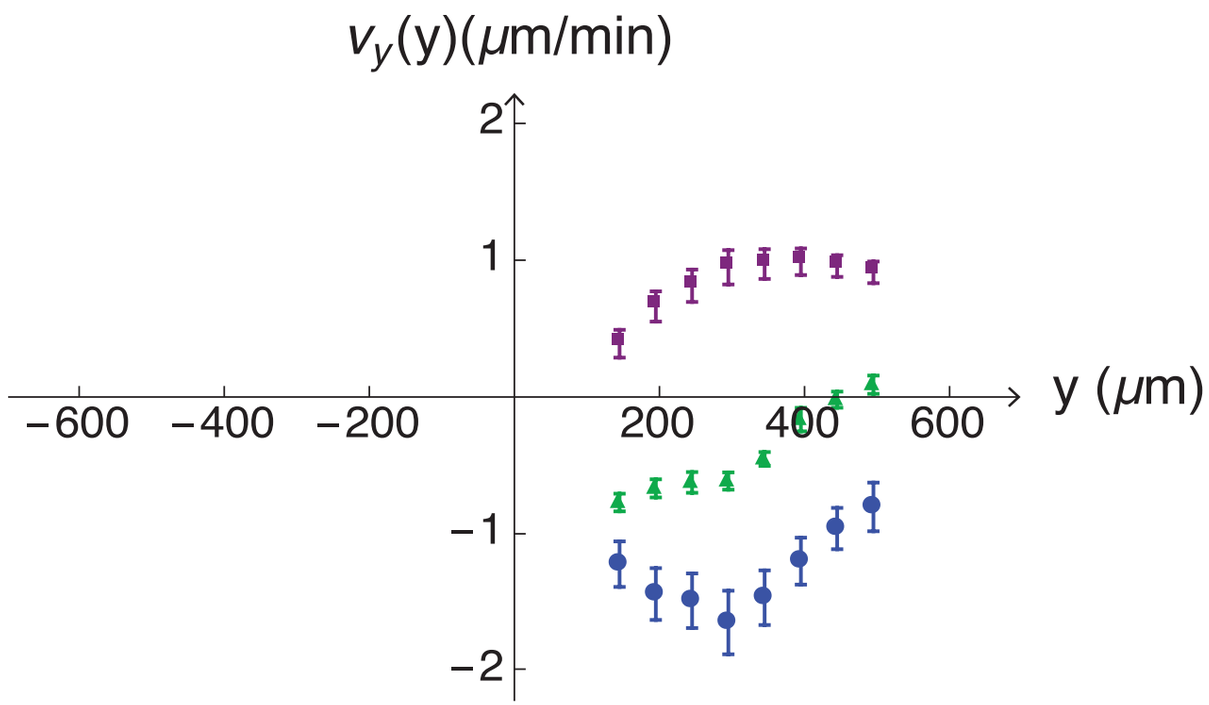
**Can we quantify exactly the interaction between neurectoderm and ppl?**

**What kind of forces mediate this interaction?**

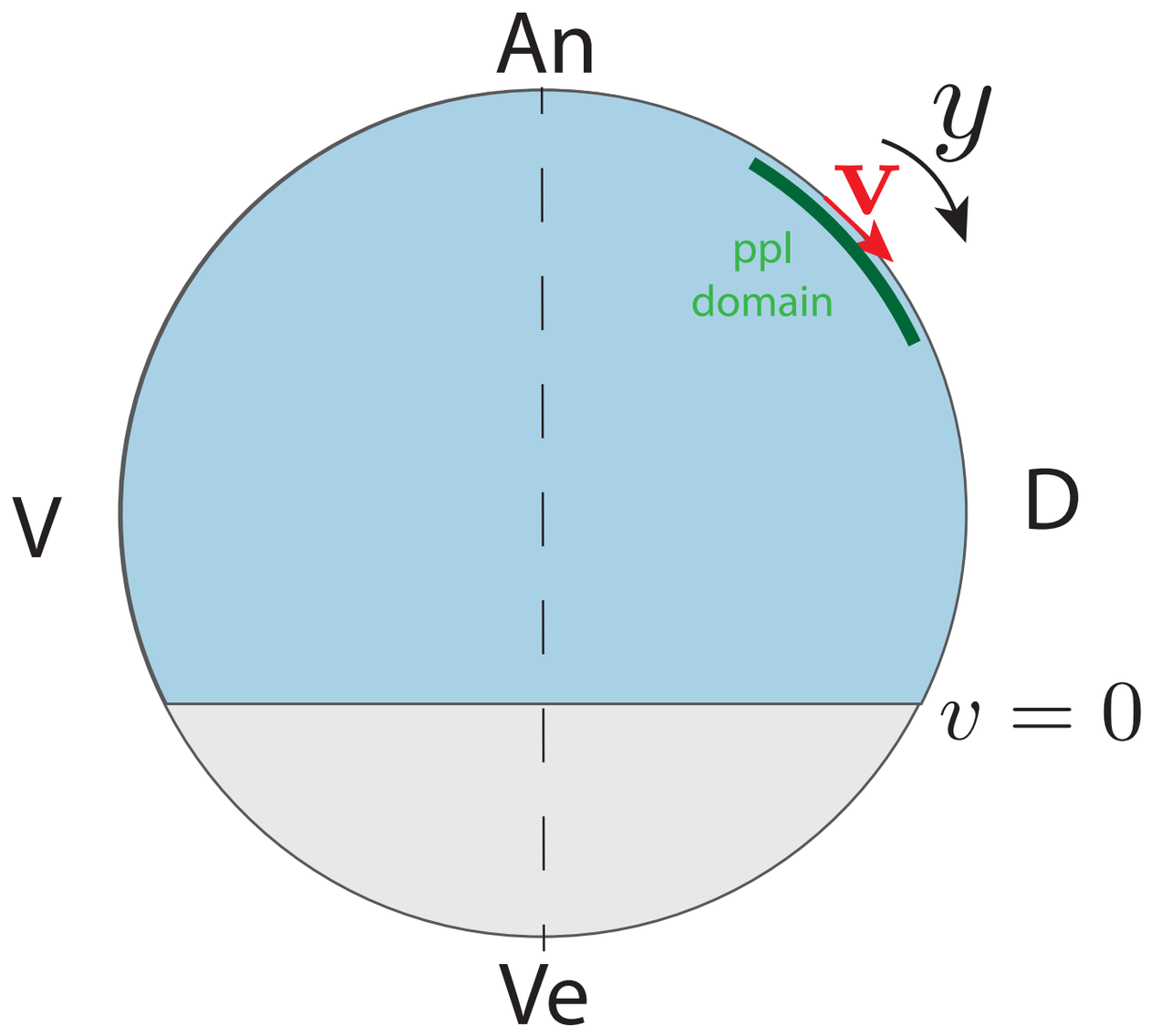
# Our approach

To highlight the effect of PPL cells:



# A simpler 1D model



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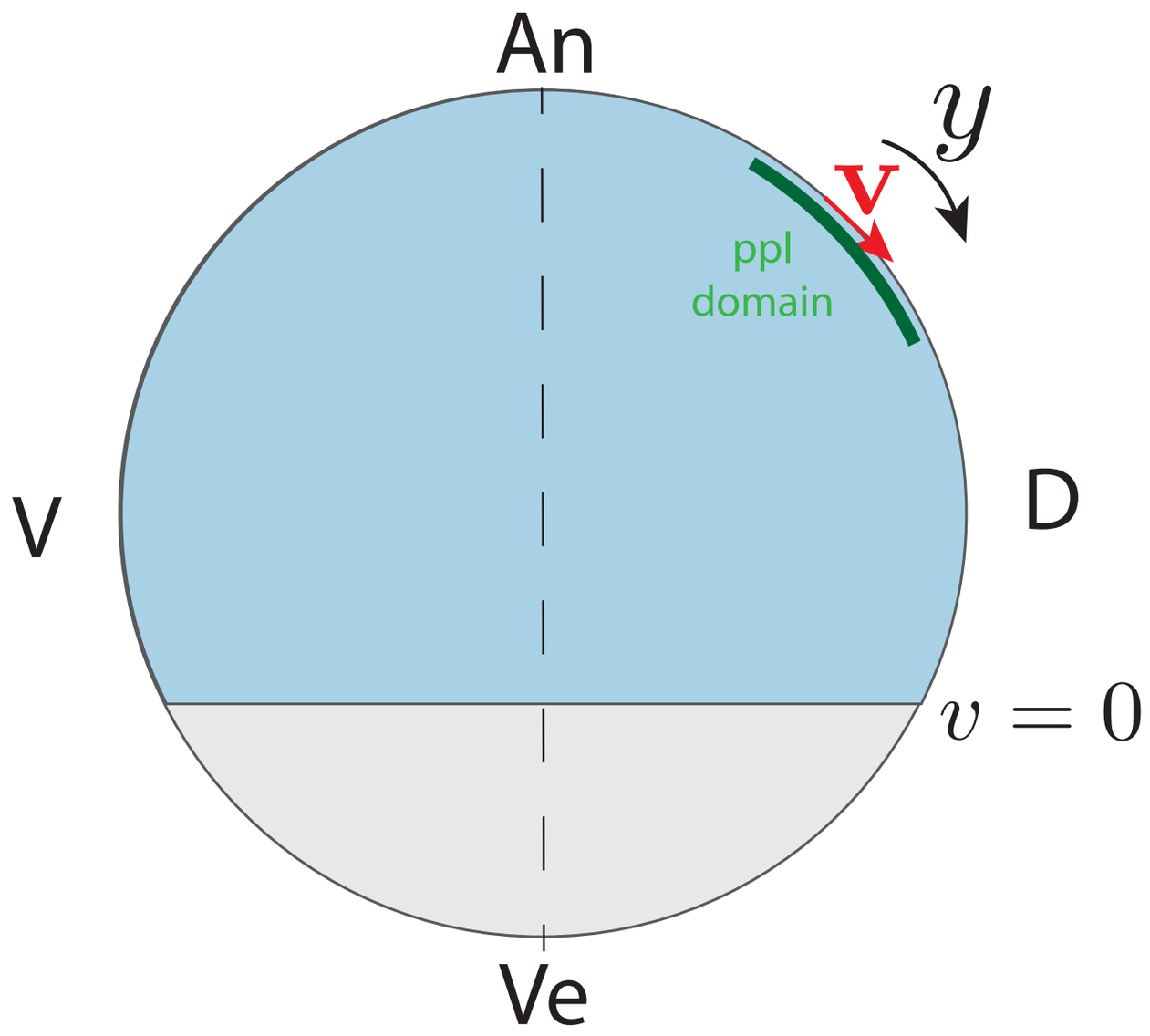



We model neurectoderm flows as a **passive viscous fluid**.

$$\sigma_{ij} = 2\eta\left[v_{ij} - \frac{1}{2}v_{kk}\delta_{ij}\right] + \eta_b v_{kk}\delta_{ij}$$

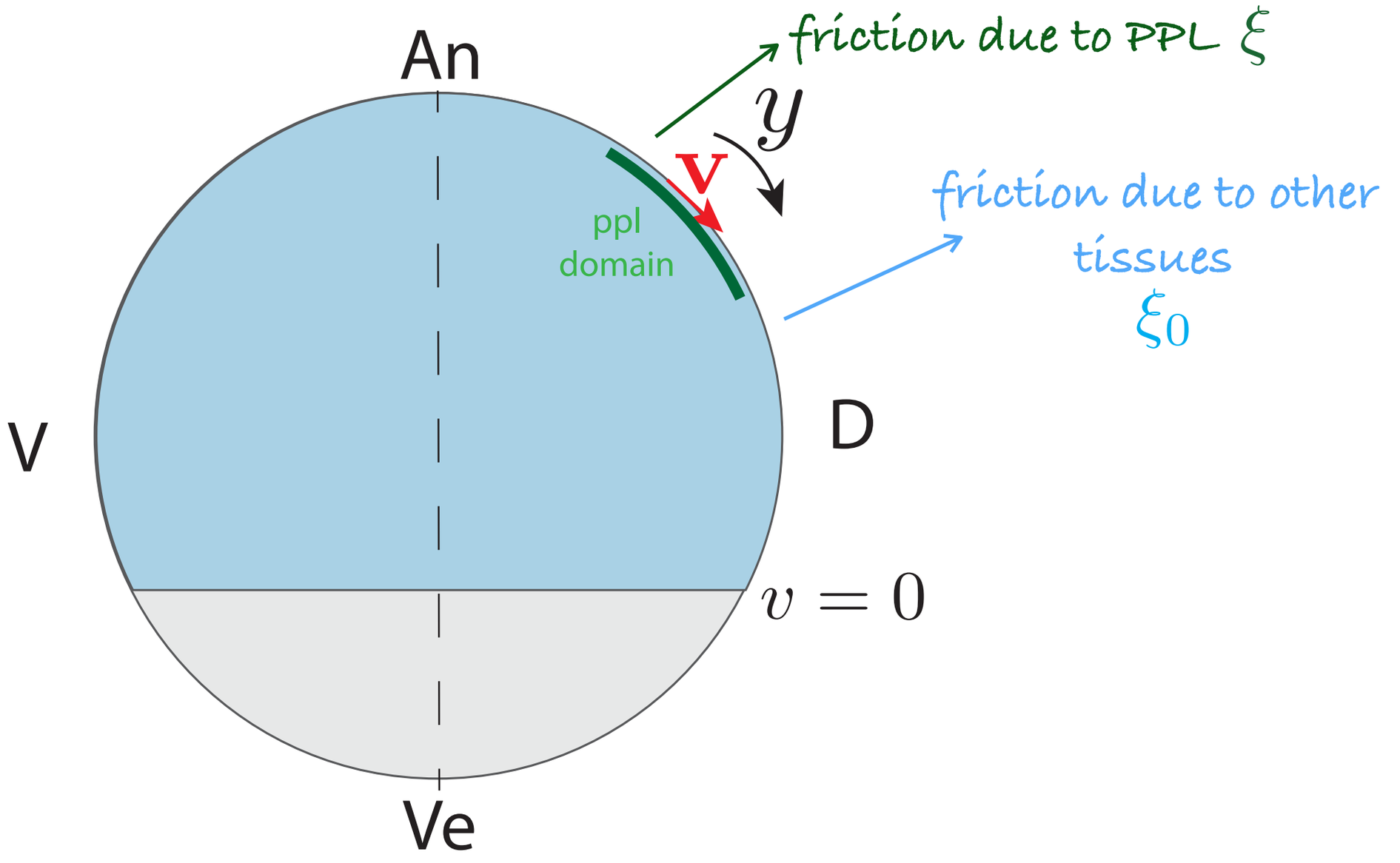
neurectoderm

shear viscosity

neurectoderm

bulk viscosity

# A simpler 1D model



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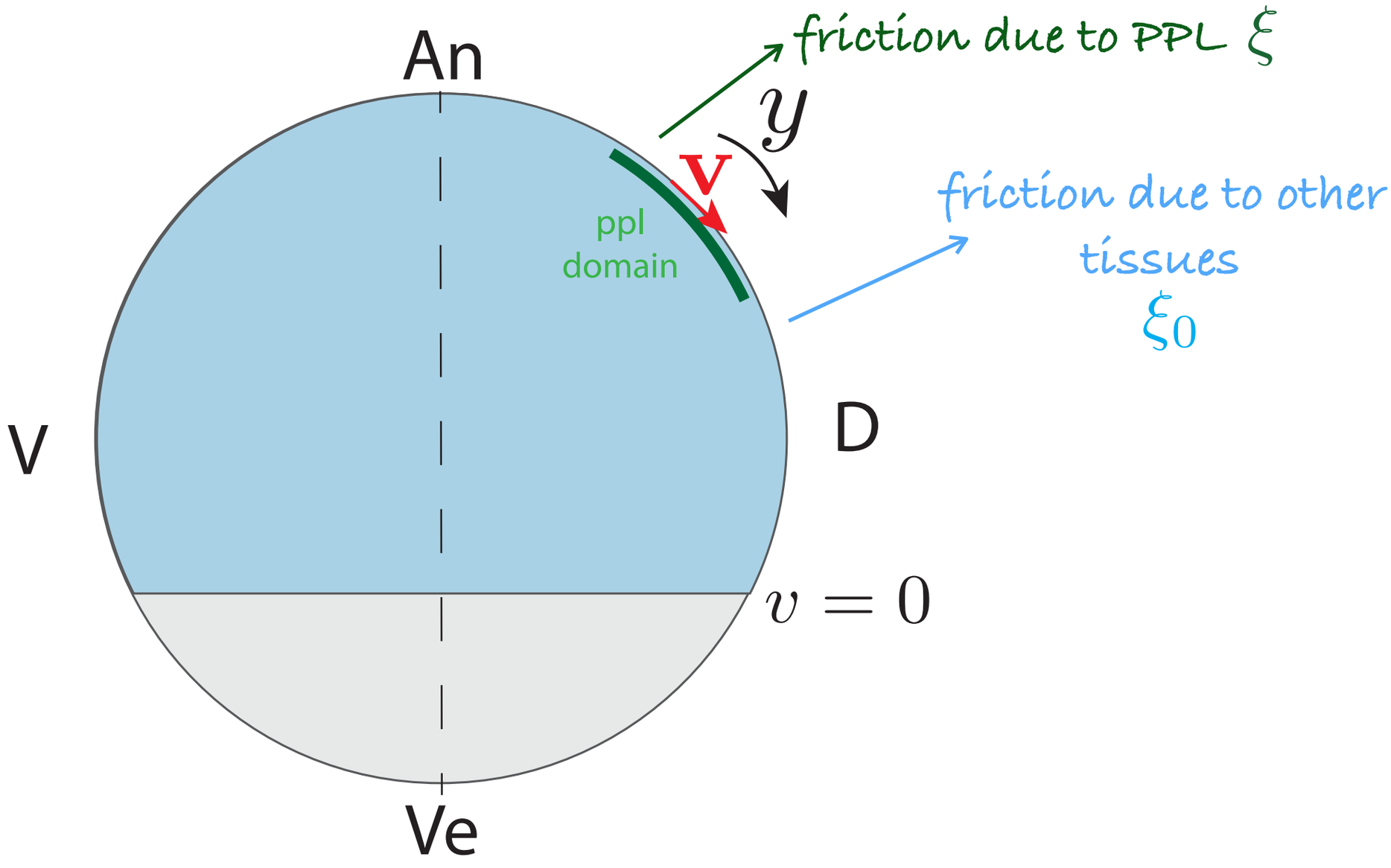


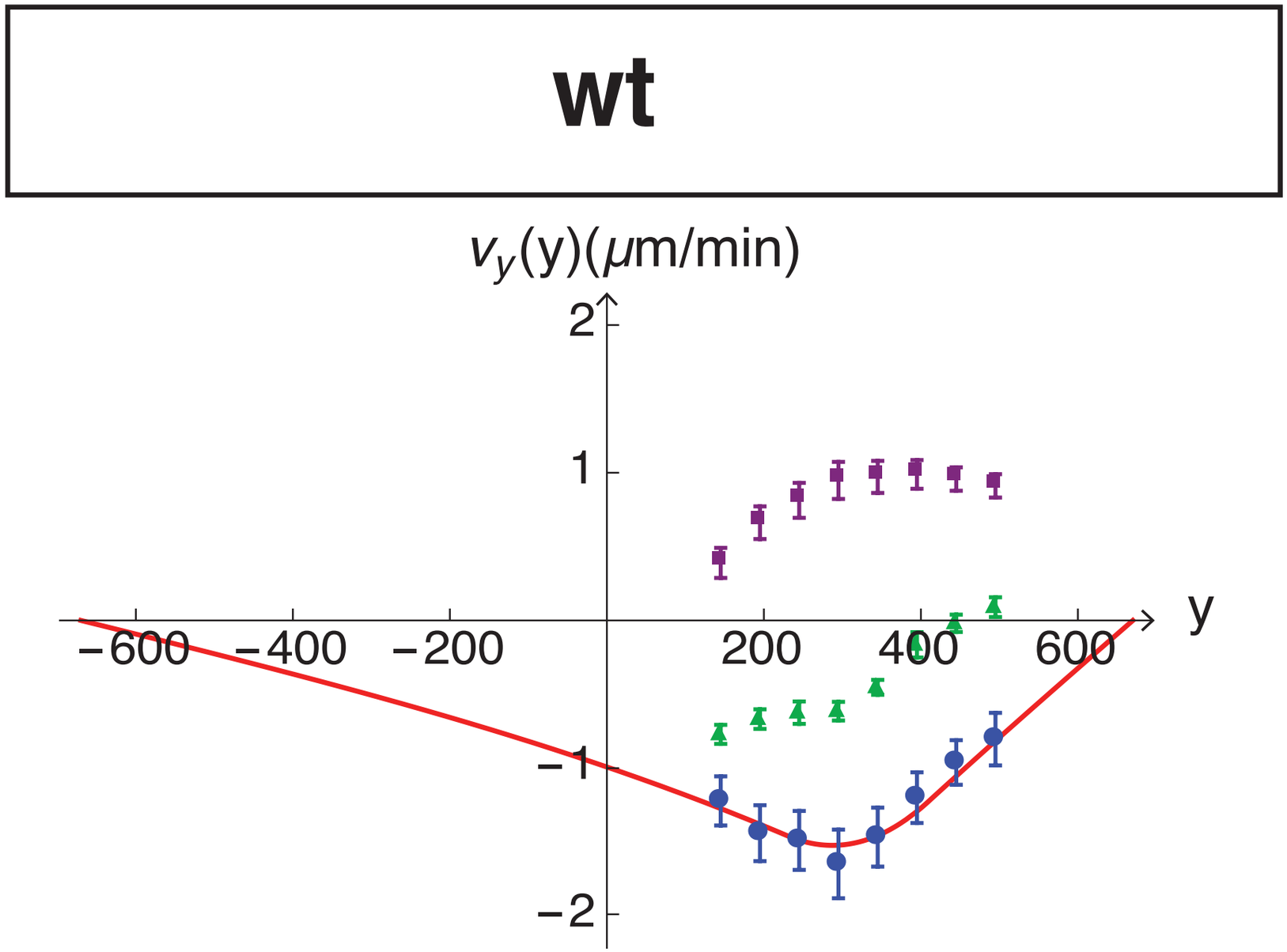

$$\partial_y \sigma_y = \xi_0 v_y \text{ outside PPL domain}$$

$$\partial_y \sigma_y = \xi_0 v_y - f \text{ inside PPL domain}$$

$$f = \xi(\langle v_y^{ppl} \rangle - \langle v_y^{\mathrm{tot}} \rangle)$$

**Friction density force**

# A simpler 1D model



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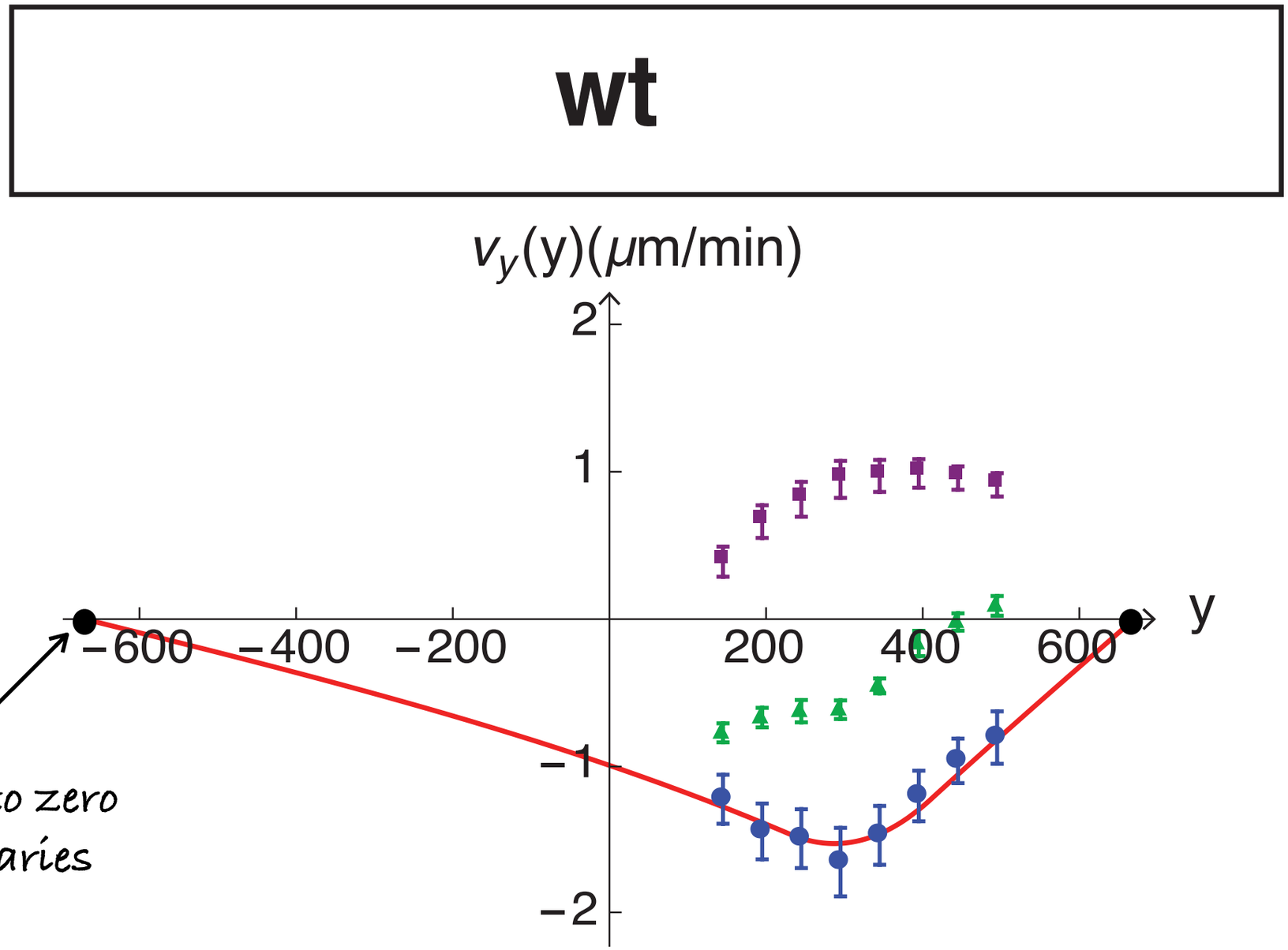
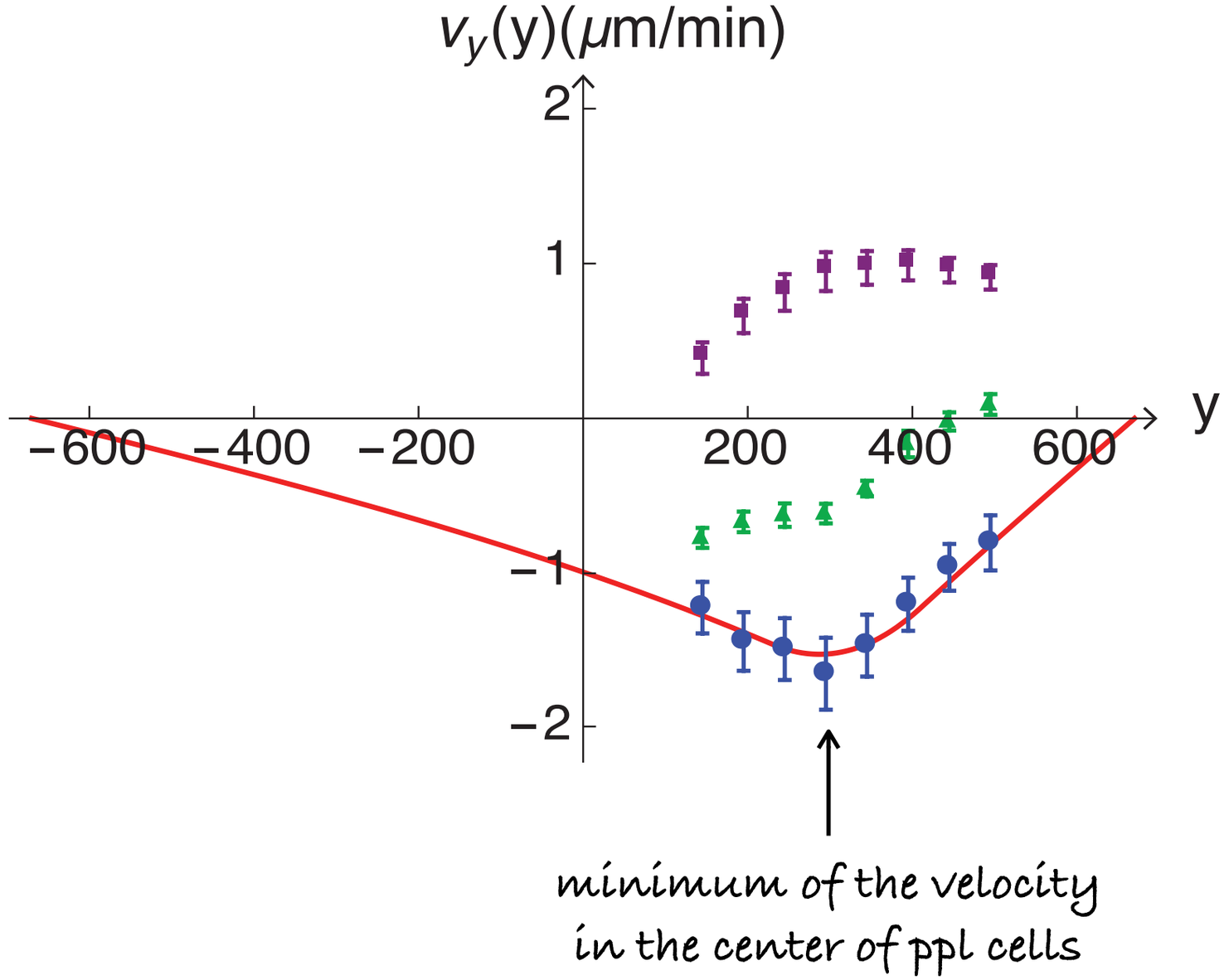


# A simpler 1D model

**wt**



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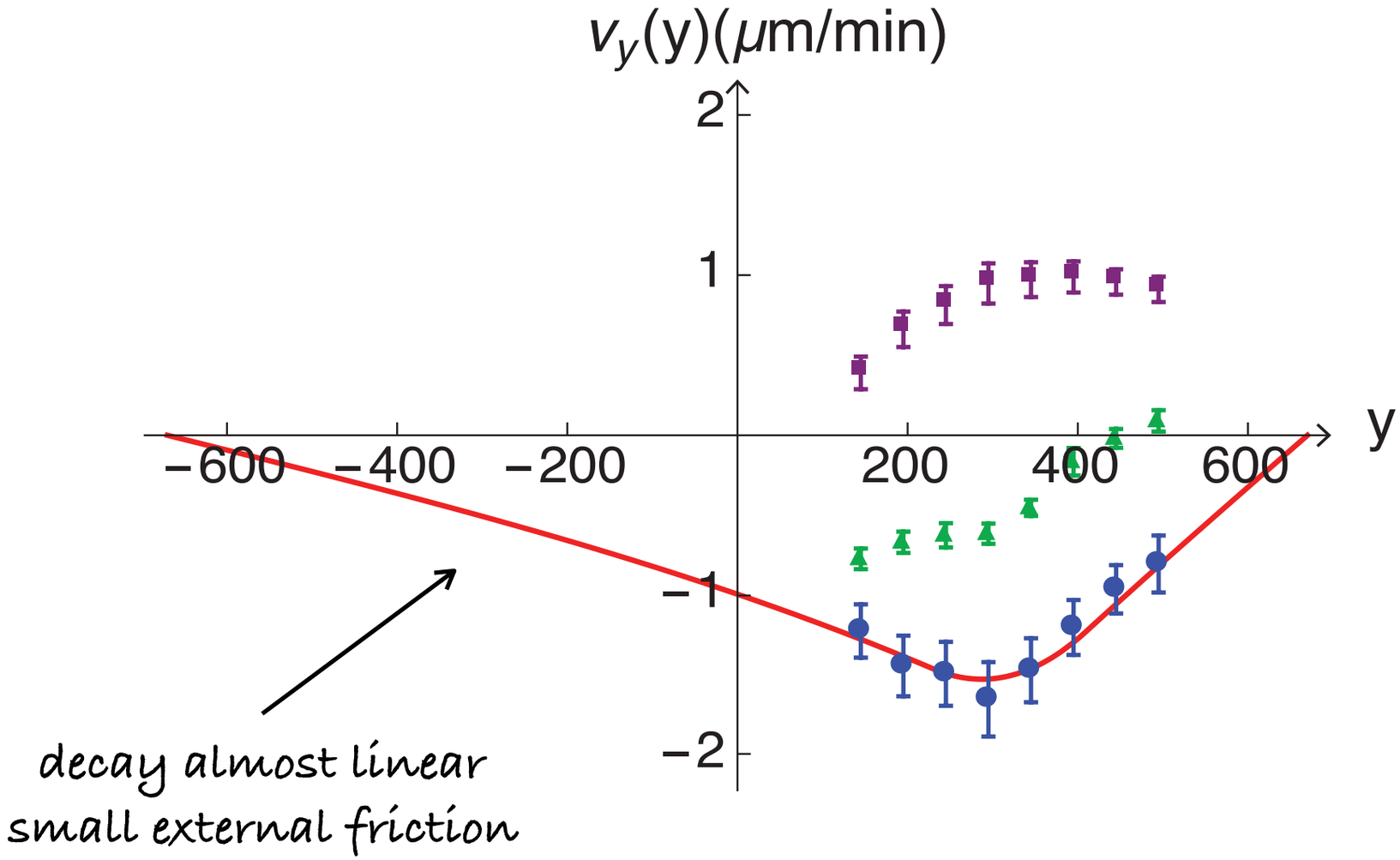
**wt**



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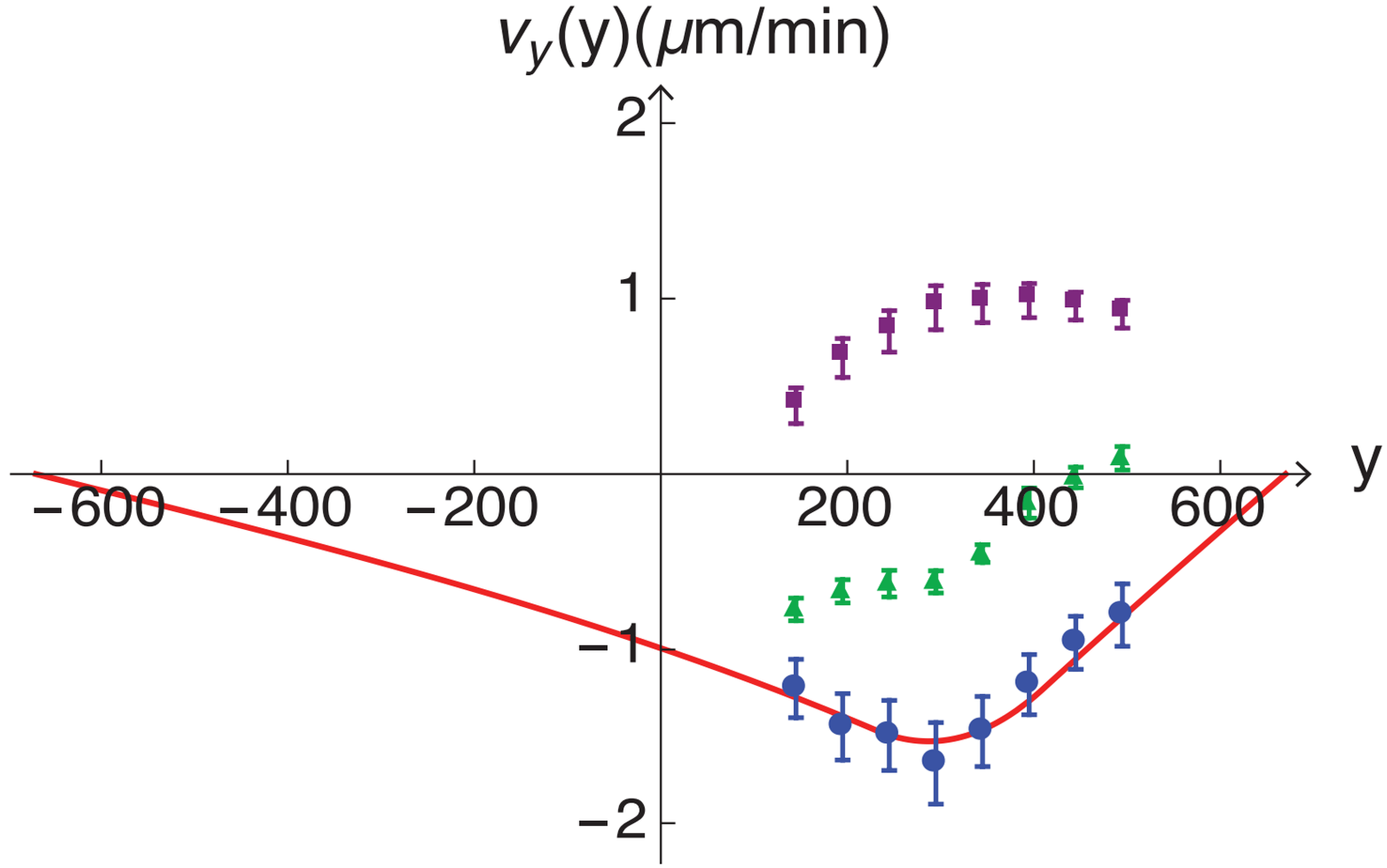
**wt**

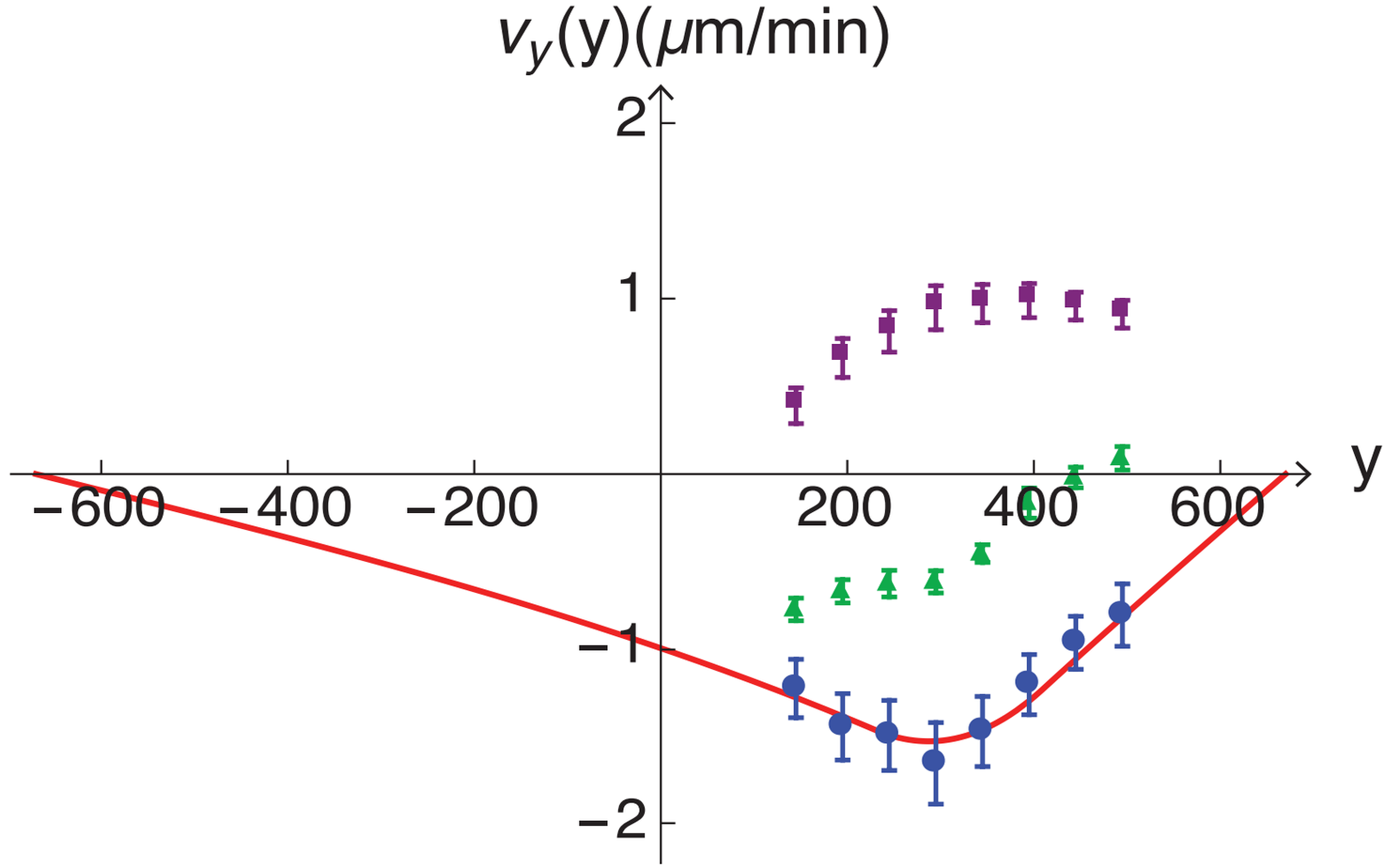



**1\ Pure friction forces could describe the observed velocity profiles;**

**2\ External (outside of PPL) friction is negligible.**

# A simpler 1D model

**wt**

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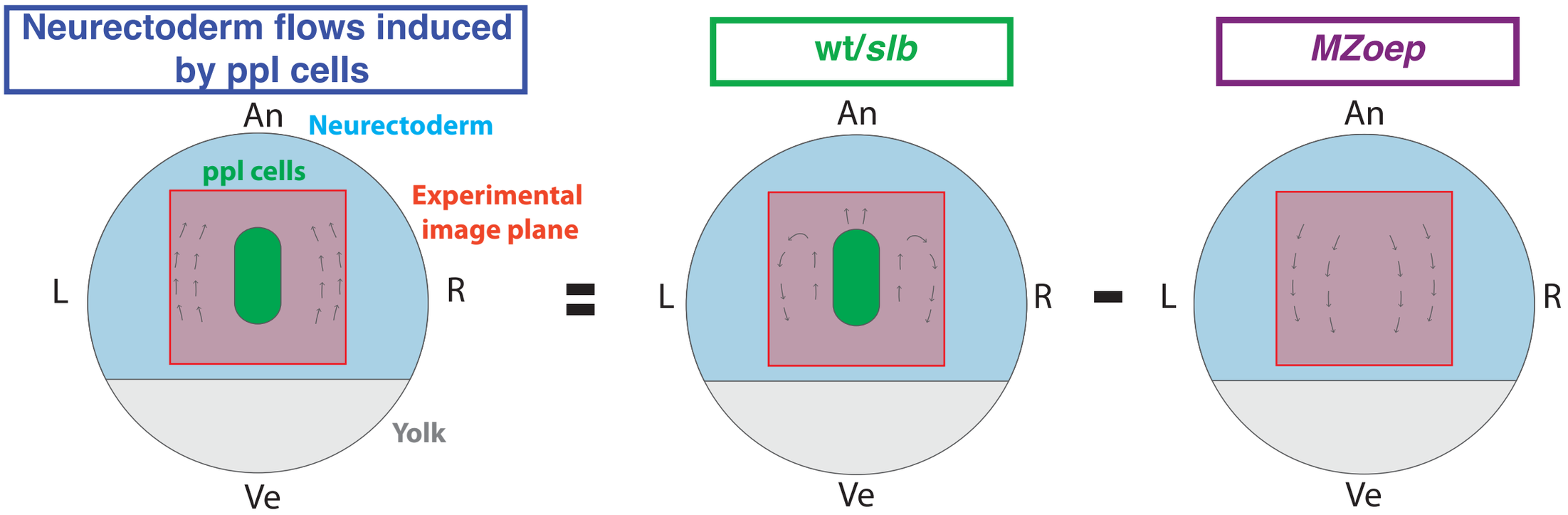
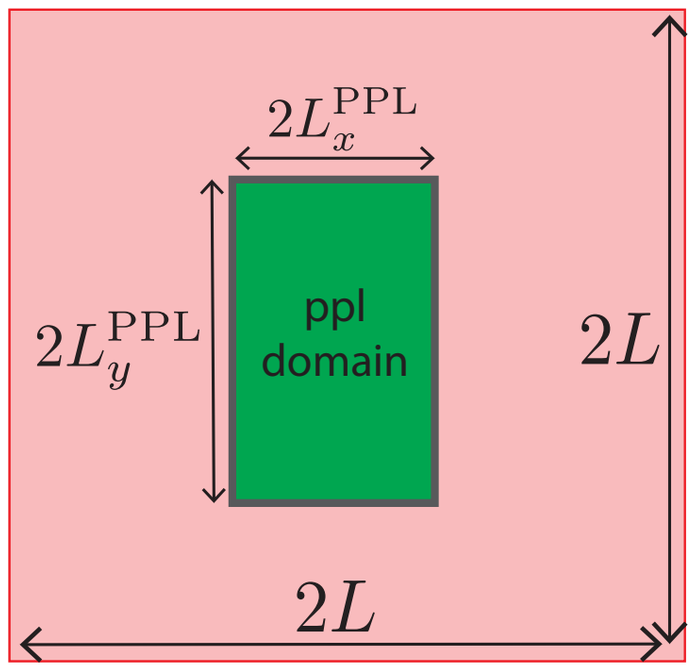
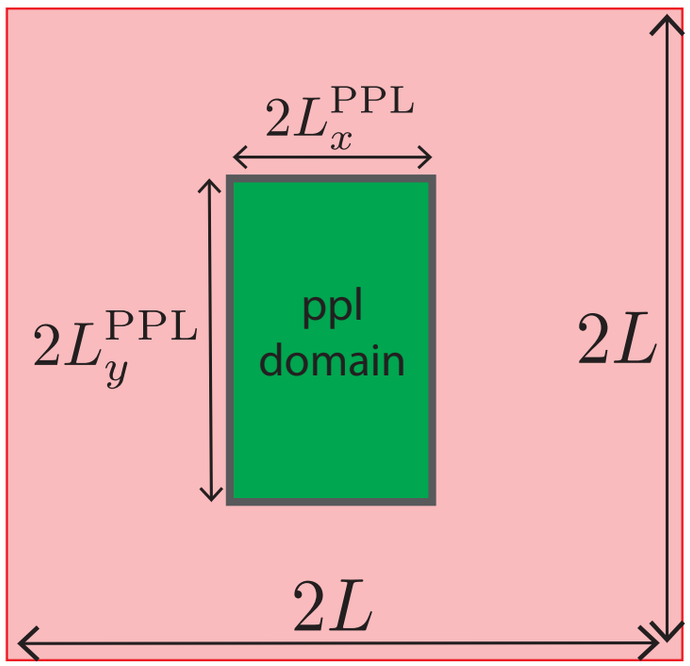
# 2D model




**Experimental imaging plane**

# Solving the 2D model




**Experimental imaging plane**

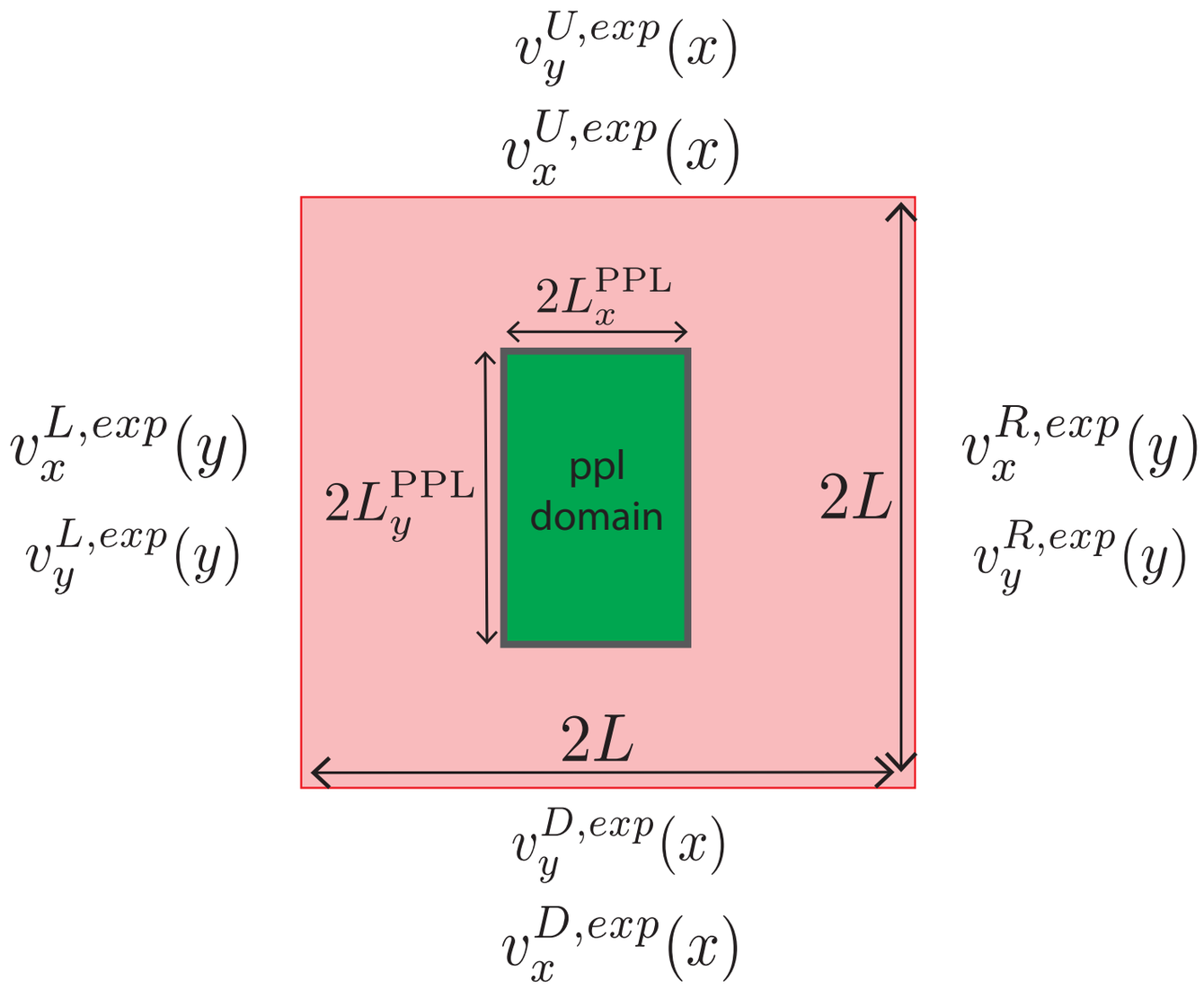
$$\mathbf{v} = \mathbf{v}^{\mathrm{tot}} - \mathbf{v}^{\mathrm{MZ}}$$

$$\sigma_{ij} = 2\eta\left[v_{ij} - \frac{1}{2}v_{kk}\delta_{ij}\right] + \eta_b v_{kk}\delta_{ij}$$

$$\partial_i \sigma_{ij} = -f_j^{\mathrm{ppl}}$$

$$f_j^{\mathrm{ppl}} = f\left(\mathcal{H}[x + L_x^{\mathrm{ppl}}] - \mathcal{H}[x - L_x^{\mathrm{ppl}}]\right) \times \left(\mathcal{H}[y - y^{\mathrm{ppl}} + L_y^{\mathrm{ppl}}] - \mathcal{H}[y - y^{\mathrm{ppl}} - L_y^{\mathrm{ppl}}]\right)\delta_{jy}$$

# Solving the 2D model




Boundary conditions are imposed to be

the **same as the experimental boundary profiles**.

# Solving the 2D model

The problem is **linear**.
Therefore we can use this linearity to divide the problem
into simpler solvable subproblems.

The full solution can be given by:

$$v_x(x,y) = v_x^{\mathrm{per}}(x,y) + \bar{v}_x(x,y)$$
$$v_y(x,y) = v_y^{\mathrm{per}}(x,y) + \bar{v}_y(x,y)$$

$$\partial_i \sigma_{ij} = -f_j^{\mathrm{ppl}}$$

$$\begin{cases} \eta \partial_y^2 \tilde{v}_x + \eta_b i k_x \partial_y \tilde{v}_y - (\eta + \eta_b) k_x^2 \tilde{v}_x = 0 \\ (\eta + \eta_b) \partial_y^2 \tilde{v}_y + \eta_b i k_x \partial_y \tilde{v}_x - \eta k_x^2 \tilde{v}_y = C(k_x) \mathcal{H}_y \end{cases}$$

$$\begin{cases} \eta \Delta \bar{v}_x + \eta_b (\partial_x^2 \bar{v}_x + \partial_y \partial_x \bar{v}_y) = 0, \\ \eta \Delta \bar{v}_y + \eta_b (\partial_y^2 \bar{v}_y + \partial_y \partial_x \bar{v}_x) = 0 \end{cases}$$

matching the remaining
experimental boundary conditions

# Comparing with the data

$\eta$ $\eta_b$ $f_y$

$\eta > \eta_b$ no vortices

$\eta < \eta_b$ vortices

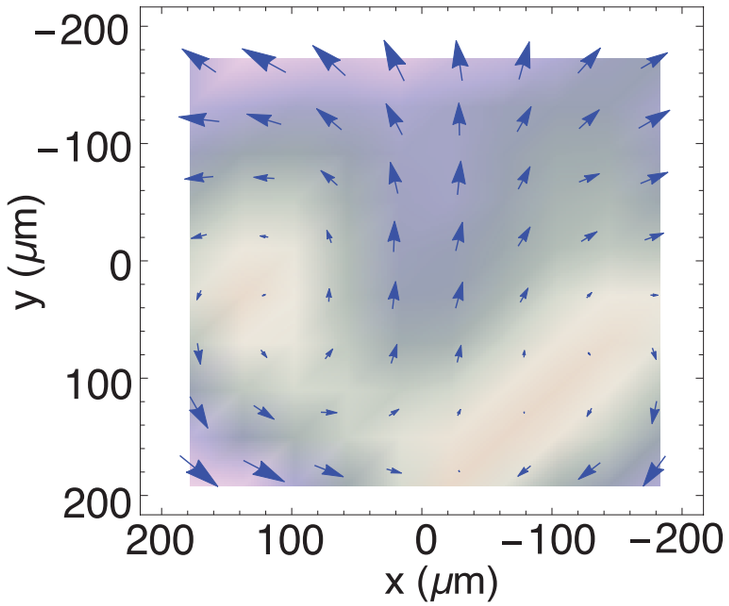
$\eta = \eta_b$

We find the best value of the **rescaled density force reproducing WT data**.

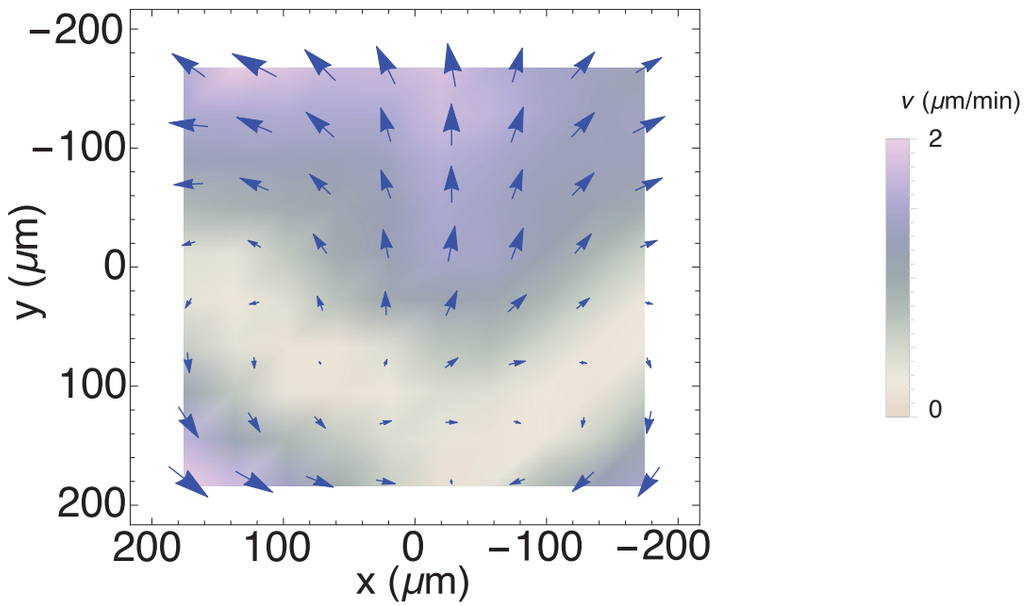
# Our result: velocity fields

## WT

**Model vector field**



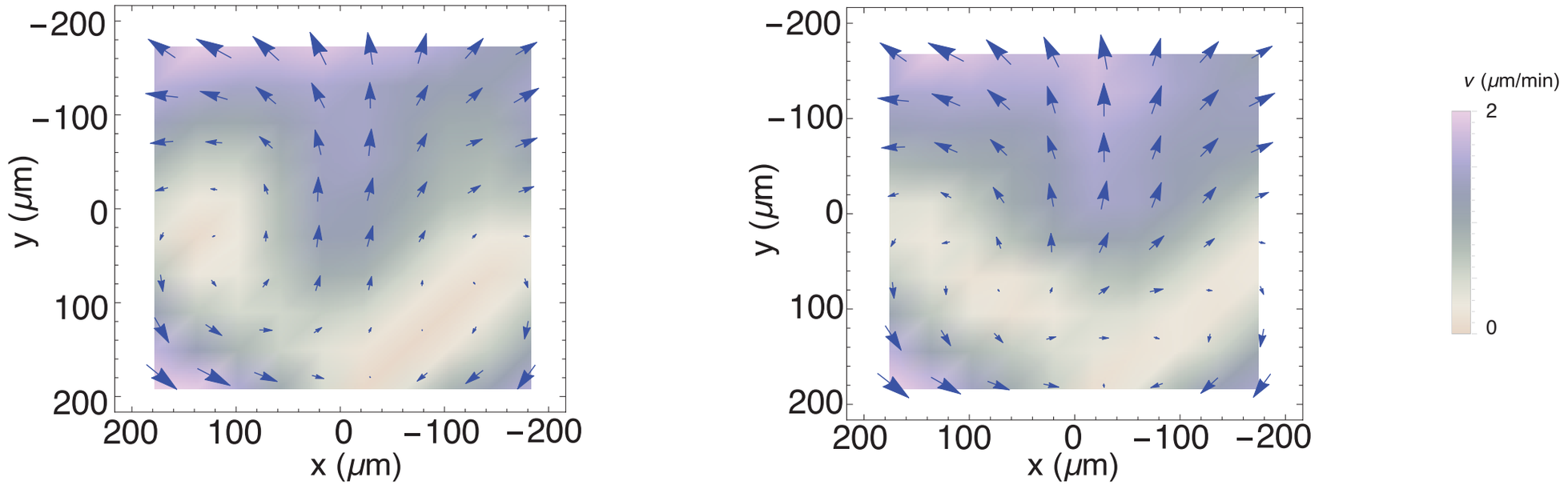

**Experimental vector field**



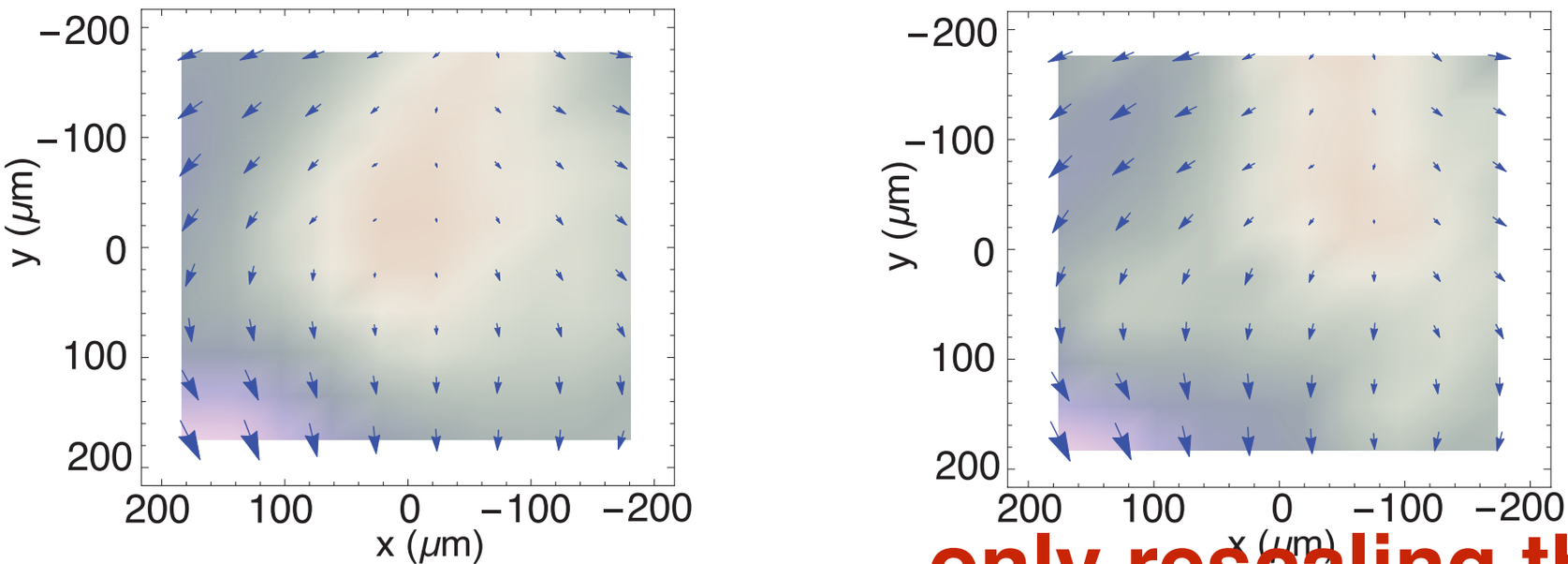
# Our result: velocity fields

## WT

**Model vector field** | **Experimental vector field**




## *Slb*




**only rescaling the WT fit**

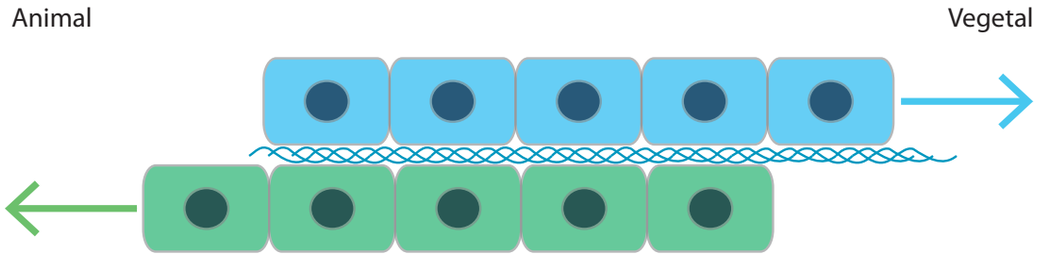
# Our result: parameters' estimate

Using the estimate of the bulk viscosity given by our work on epiboly movements

(H. Morita et al., *Dev. Cell.*, 2017),

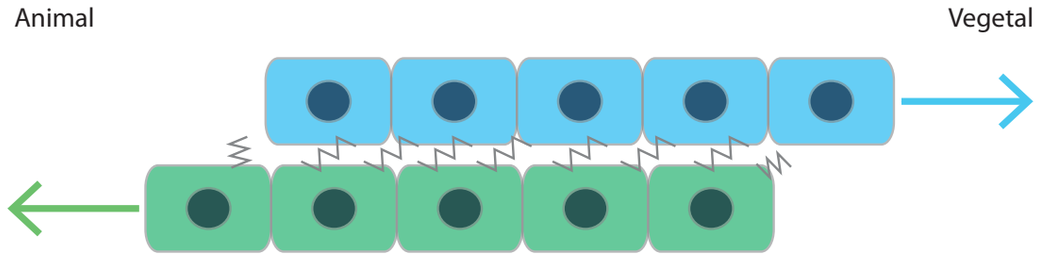
we can compute a friction coefficient value:

$$\xi \simeq 1 \ \mathrm{Pa.s.}\mu\mathrm{m}^{-1}$$




**Layer of water** of thickness h = 100 nm

the friction coefficient is **100 times smaller.**




**Bonds of E-cadherin**

the friction coefficient is **1 million times higher.**

**Friction might be instead generated by transient bonds.**

# Conclusions

The position of the neural anlage is determined
**by the interaction between PPL cells and the neurectoderm**.

Our **solely friction-based model** well reproduced the data
allowing us to validate our hypothesis that

**friction forces position the neural anlage**.

M. Smutny, Z. Ákos, S. Grigolon, S. Shamipour, …, G. Salbreux, C.-P. Heisenberg,
*Nature Cell Biology, 2017*

# Acknowledgments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Michael Smutny
Shayan Shamipour

**Vicsek's Lab**

Tamas Vicsek
Zsusza Akos

# Thank you

# for your attention