

Band pattern of erythrocytes: A possible diagnostic tool ?

Competing aggregation and iso-density equilibrium lead to band pattern formation in density gradients

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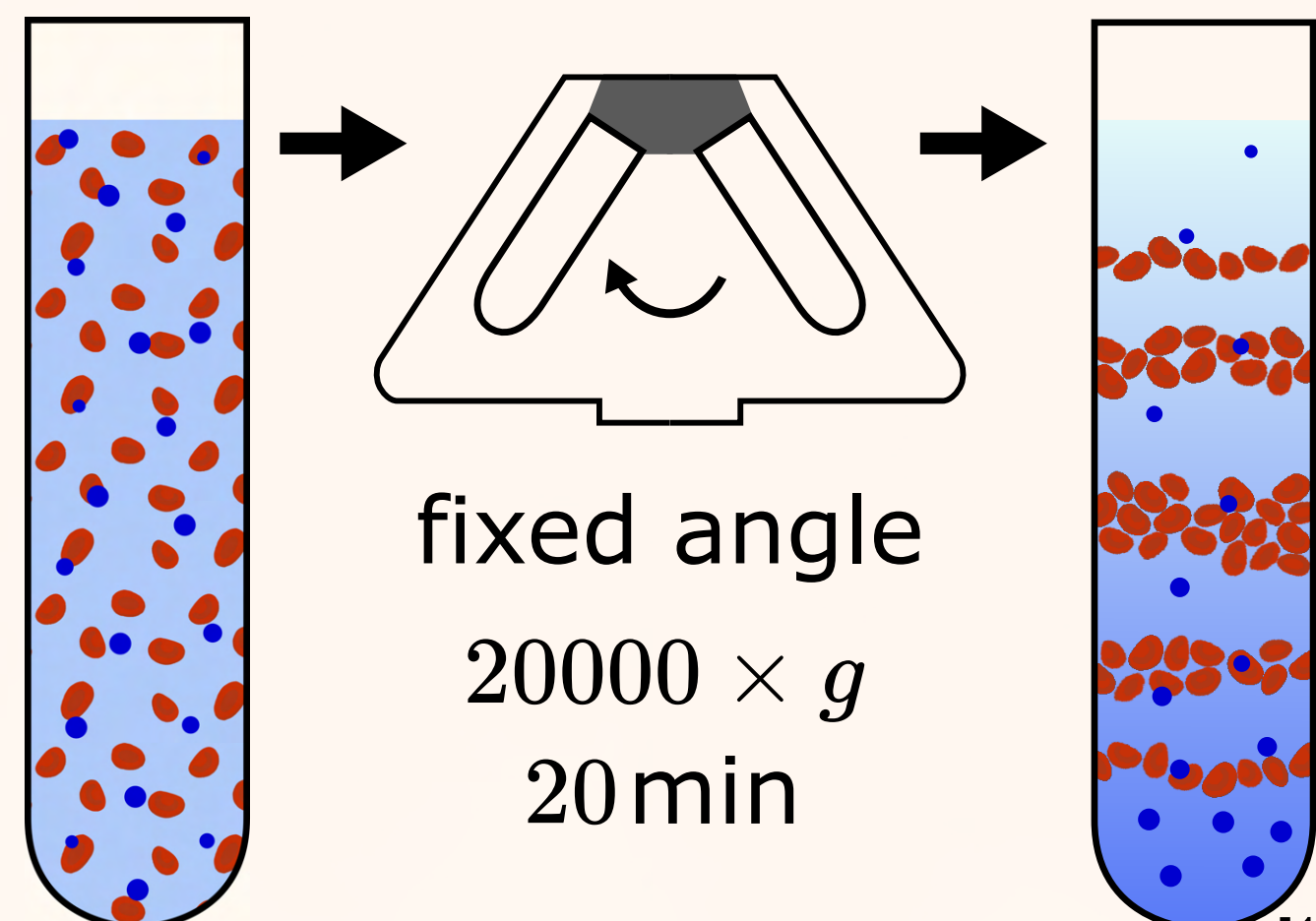
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Background

- during centrifugation in a density gradient red blood cells form patterns of distinct bands [2,3]
- the mechanisms leading to this phenomenon were unknown
- we can explain pattern formation describing red blood cells as a fluid of interacting particles

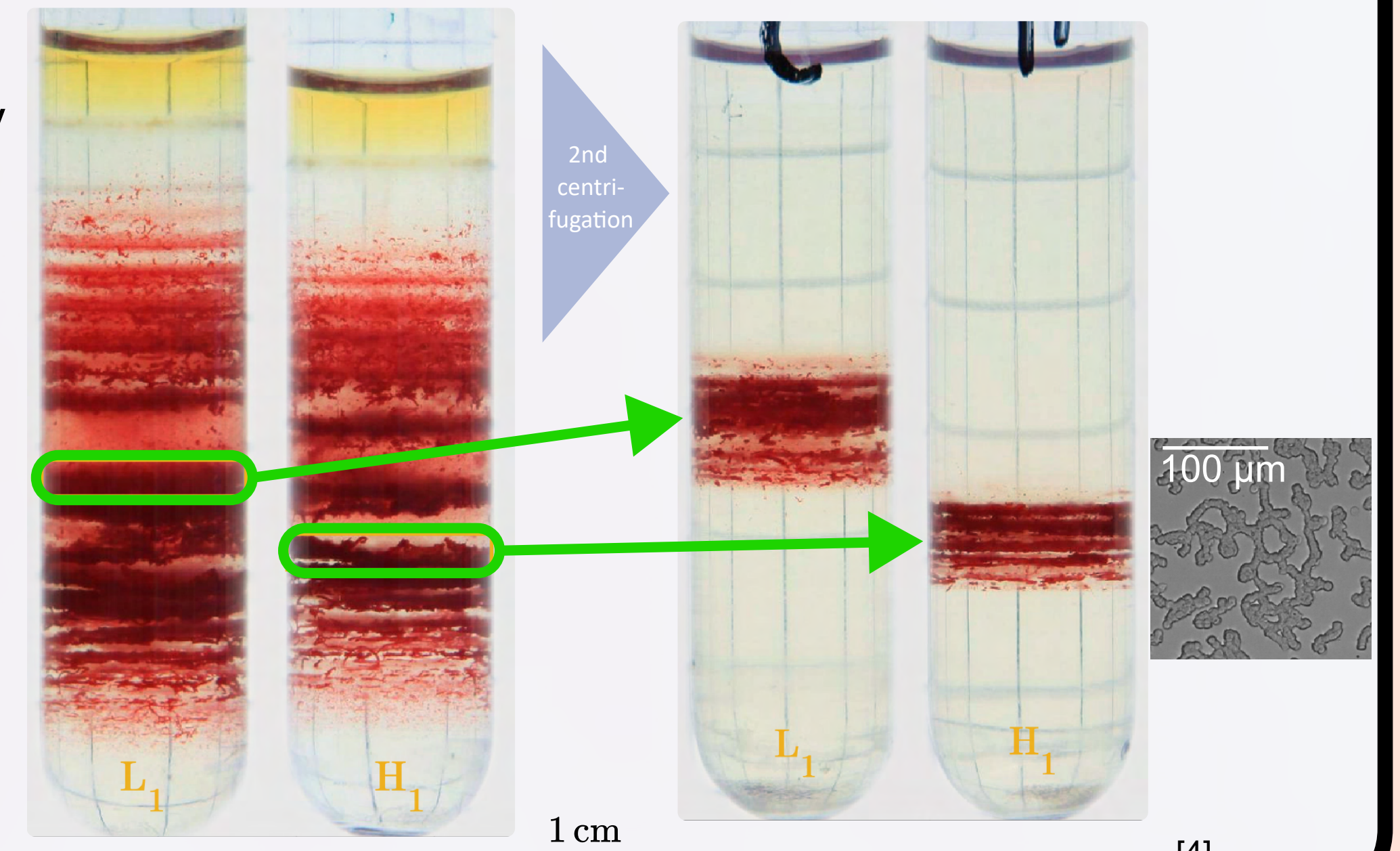


Percoll nanoparticles

[1]

Subband Experiment

- the full cell population was resolved in a density gradient
- single bands were extracted and centrifuged a second time
- subbands appear indicating a collective aggregation, also visible microscopically

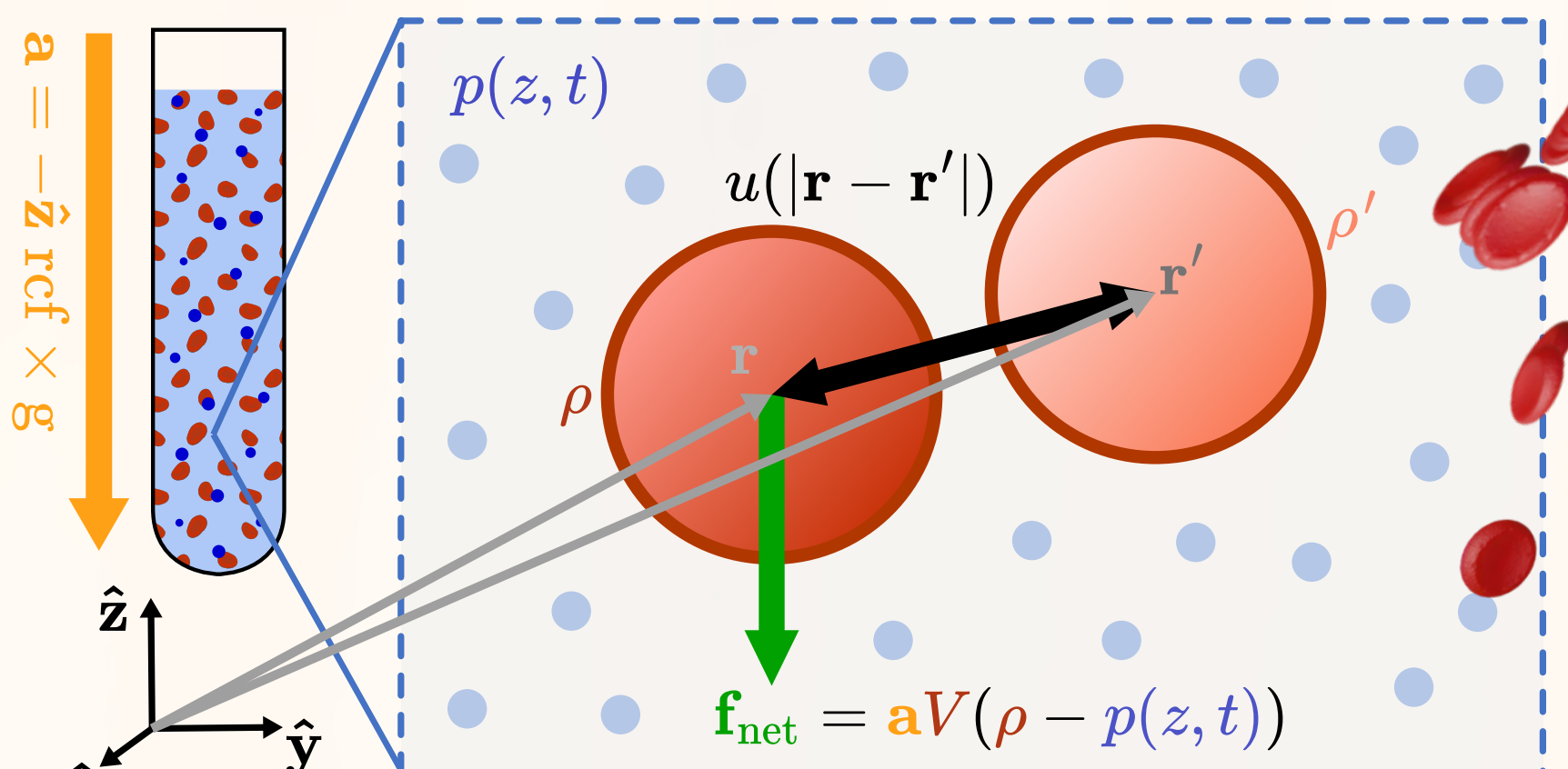


[4]

Modelling

microscopic scale

consider forces on single cells



- buoyancy force $\mathbf{f}_{bou} = -p(\mathbf{r}, t)V\mathbf{a}$
- external acceleration $\mathbf{f}_{acc} = \rho V\mathbf{a}$
- Stokes friction $\mathbf{f}_{stokes} = -6\pi R\eta\mathbf{v}$
- cell interaction force $\mathbf{f}_{int} = -\partial_r u(r) \frac{\mathbf{r}}{r}$

$$\mathbf{f}_{net} = \mathbf{a}V(\rho - p(\mathbf{r}, t))$$

macroscopic scale

- red blood cell volumetric density fulfils continuity equation
- interaction is described by an effective potential

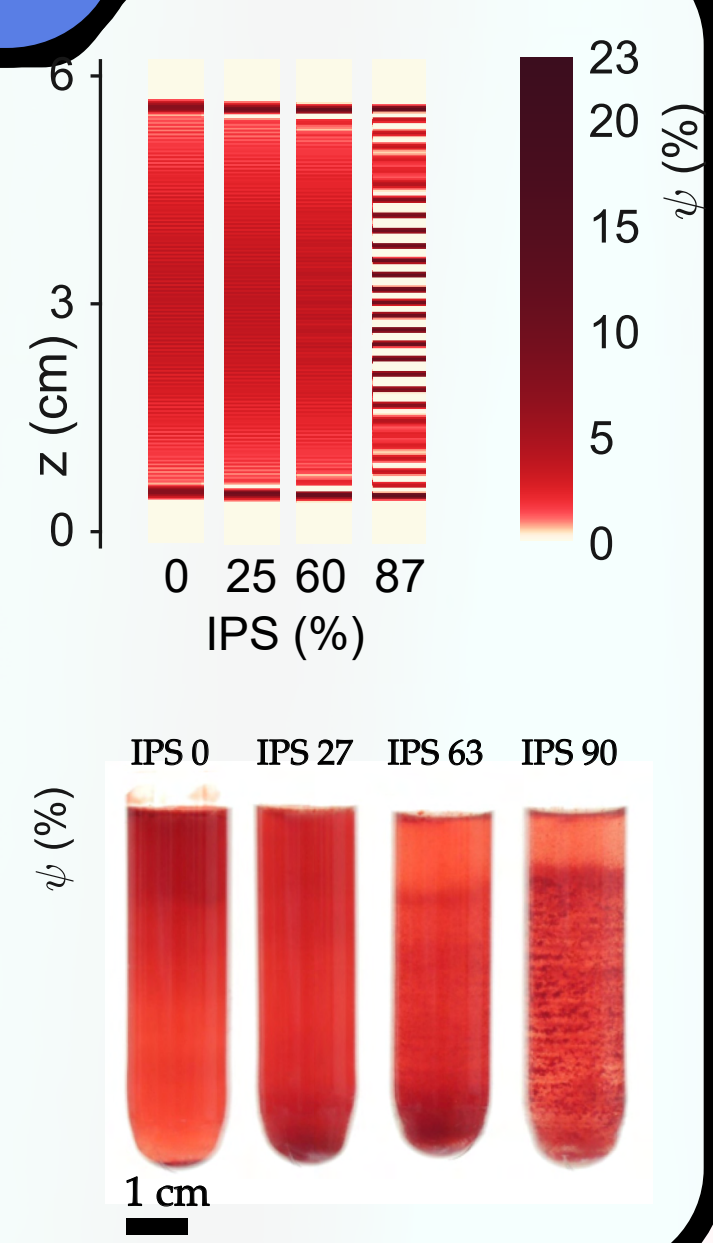
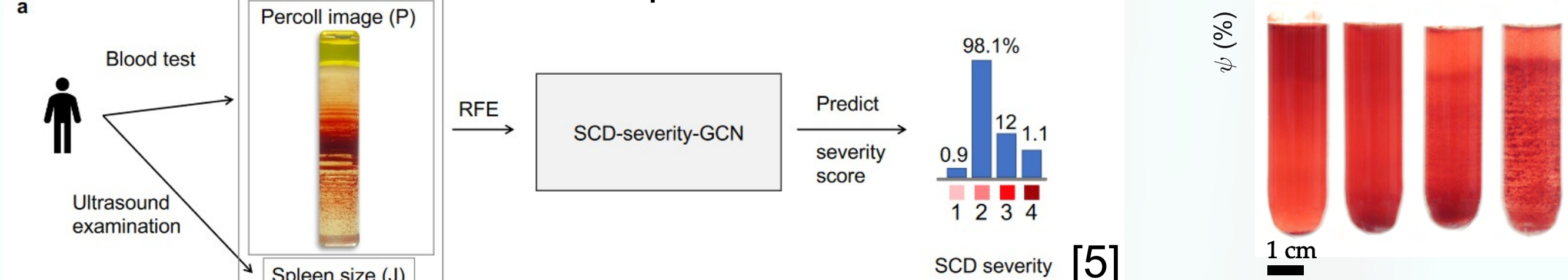
$$\zeta \partial_t \varphi = \frac{2\pi}{V} \partial_z \left(\varphi \int (z' - z) \tilde{u}(|z' - z|) \psi' dz' \right) + aV \partial_z (\varphi (\rho - p(z, t)))$$

- equilibrium: balance between **interaction** and **net buoyancy force**

Potential as diagnostic tool

- the band pattern depends on the aggregation energy between red blood cells
- the aggregation energy varies if physical properties of the cells (shape, rigidity,...) are altered.
- Samples from Sickle Cell patients have shown potential to link score and band patterns. [5]

=> towards rationalisation and optimisation!

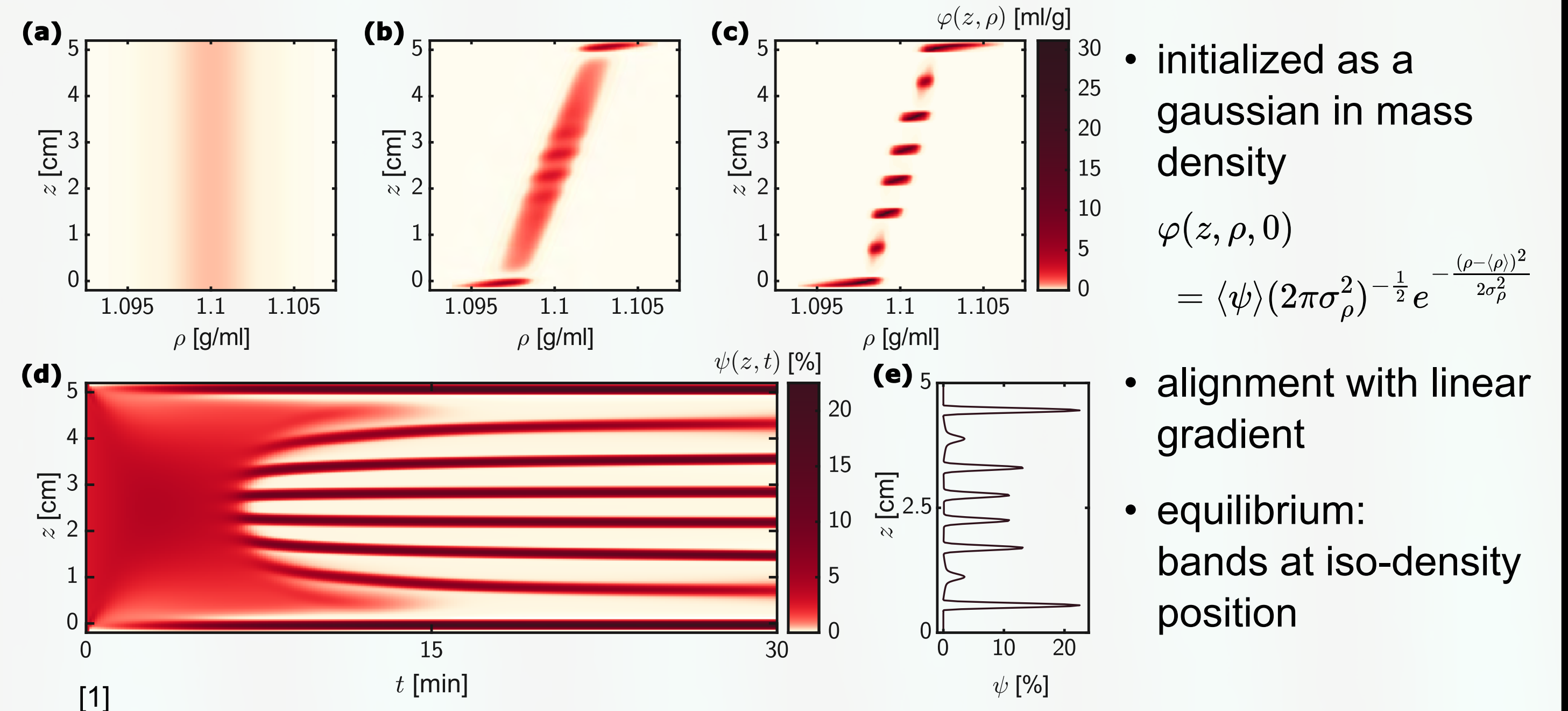


Conclusion

- we show that a short range potential can lead to macroscopic pattern formation
- Percoll has been identified as a strong depletant
- alterations to patterns have been reported in pathological conditions
- sensitive structure forming systems have potential diagnostic applications
- Next fundamental step: accurately link aggregation potential and cell properties

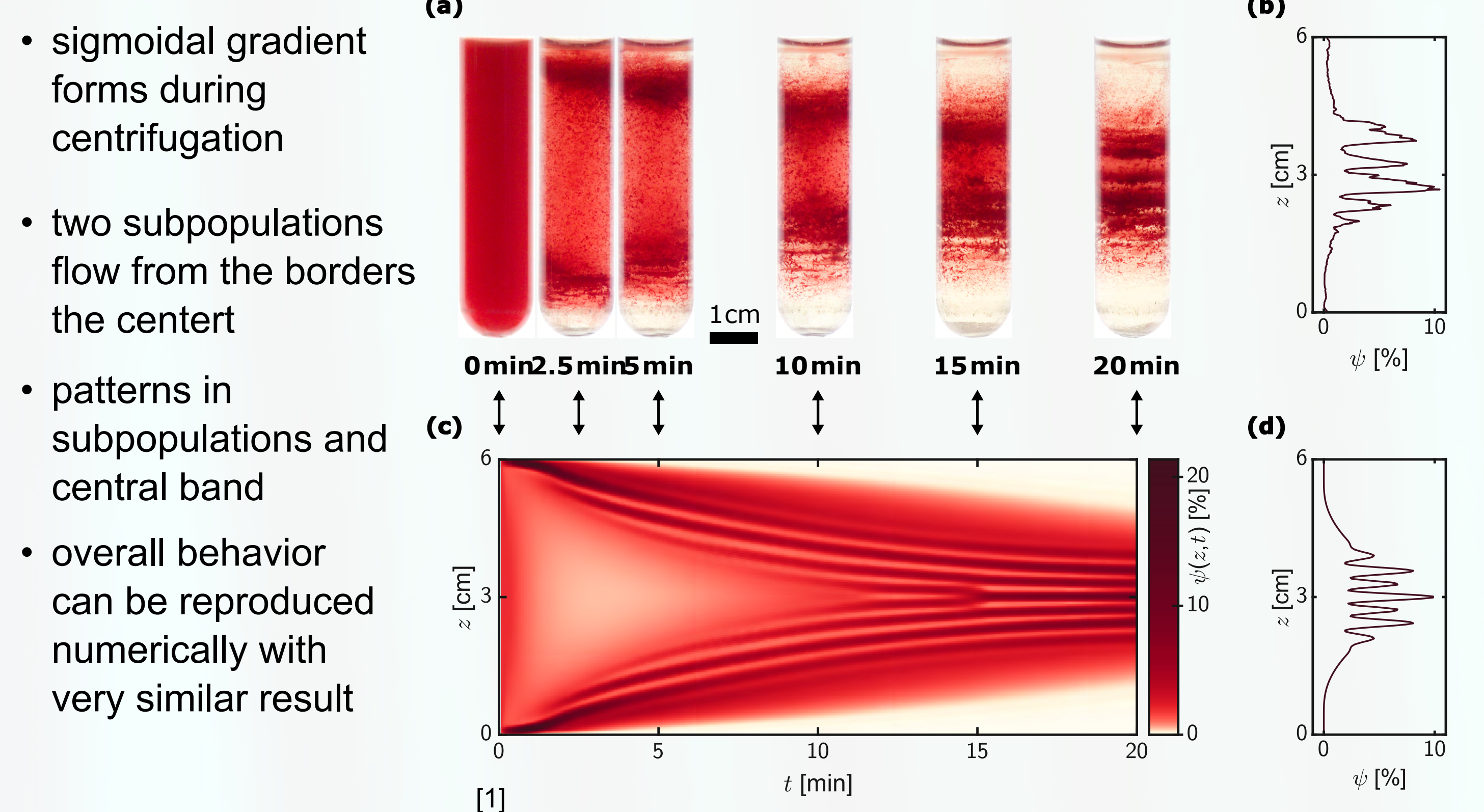
Solutions

time progression of RBC density function



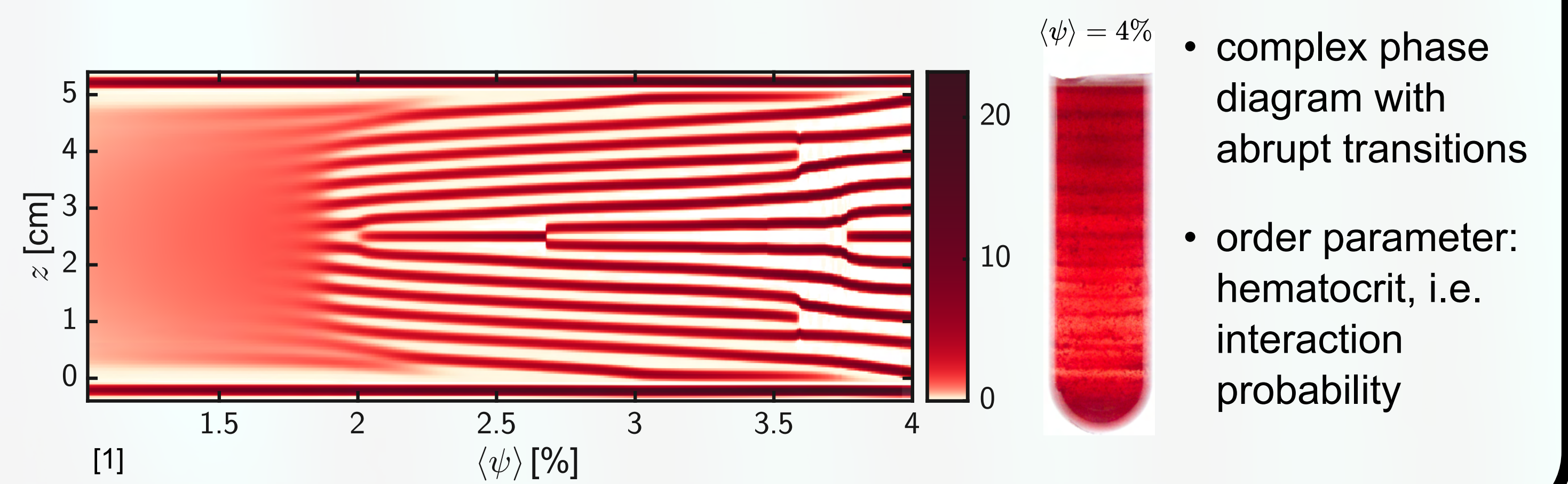
- initialized as a gaussian in mass density $\varphi(z, \rho, 0) = \langle \psi \rangle (2\pi\sigma_\rho^2)^{-\frac{1}{2}} e^{-\frac{(\rho-\langle \rho \rangle)^2}{2\sigma_\rho^2}}$
- alignment with linear gradient
- equilibrium: bands at iso-density position

simulation of standard protocol experiment



- sigmoidal gradient forms during centrifugation
- two subpopulations flow from the borders the center
- patterns in subpopulations and central band
- overall behavior can be reproduced numerically with very similar result

phase diagram as a function of hematocrit



- complex phase diagram with abrupt transitions
- order parameter: hematocrit, i.e. interaction probability

[1] Maurer, F., Romero, C., Lerch, N., John, T., Kaestner, L., Wagner, C., & Darras, A. (2025). Band pattern formation of erythrocytes in density gradients is due to competing aggregation and net buoyancy. PNAS, 122(51), e2515704122.
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 [5] Sadafi, A., Makro, A., Livshits, L., Navab, N., Bogdanova, A., Albarqouni, S., & Marr, C. (2021, September). Sickle cell disease severity prediction from percoll gradient images using graph convolutional networks. In MICCAI Workshop on Domain Adaptation and Representation Transfer (pp. 216-225). Cham: Springer International Publishing.

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