





## The biophysics of malaria-infected red blood cells

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## Collaborative Research Center 1129: Quantitative Analysis of Pathogen Replication and Spread

<http://www.sfb1129.de>



SFB1129 - Aims of the SF.  
Prof. Dr. Hans-Georg Krausslich  
Dept. of Infectious Diseases - Virology

**SFB 1129** plans to obtain an integrative perspective on the mutual interplay of pathogen and host factors determining the outcome of an infection for individual events in systems of different complexity and at high spatial and temporal resolution.

Integration on several levels: scales, complexities, disciplines.

**SFB 1129 will...**

- ...comprehensively analyse replication and spread of human pathogens in a quantitative manner at high temporal and spatial resolution and at the level of stochastic events.
- ...delineate the influence of physical parameters and extracellular matrix on pathogen success and control.
- ...directly determine the course of individual pathogens and host countermeasures in culture systems of increasing complexity.

> 25.07.2019 | HIV Spreads Through Direct Cell-To-Cell Contact HIV-Ausbreitung über direkte Zell-Zell-Kontakte

> "Nacht der Forschung" in Heidelberg on Sept. 27th, 2019

> SFB scientists modeled the spread of HIV in tissue culture (Project B, Fackler group)

> New publication: Frischknecht group investigated the role of microtubules in malaria parasites

> 2nd Mechanobiology Meeting in Vietnam: When Physics meets Biology, July 2019





## Our experimental collaborators

Michael Lanzer  
parasitology



Motomu Tanaka  
physical chemistry





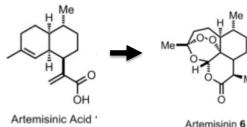

## Some basic facts on malaria

- The disease malaria is caused by a unicellular eukaryotic parasite from the genus *Plasmodium*.
- There are several *Plasmodium* species infecting humans and *P. falciparum* is the most dangerous one.
- According to the World Health Organization (WHO), there are more than 200 million new cases per year and each year there are around 500.000 deaths, with the main victims being children in Africa.
- There is still no effective vaccine for malaria. It can be treated well with drugs, but they are expensive. The standard choice is artemisinin, like quinine a herbal drug (Nobel Prize 2015), but resistance is increasing.
- No other disease has left a stronger imprint on our genome than malaria.
- Several genetic diseases related to blood disorders (e.g. sickle cell anemia resulting from hemoglobinopathies) provide some protection from malaria.

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**Artemisinin**

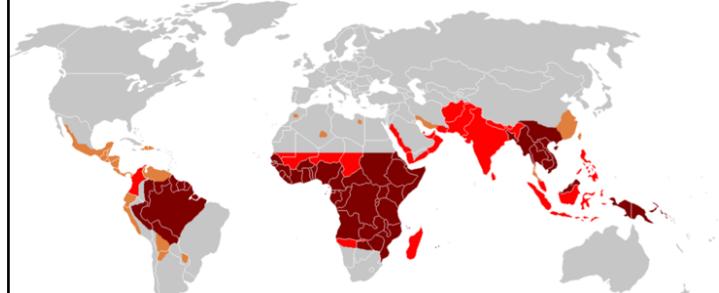
- Herbal drug isolated from the plant *Artemisia annua* („sweet wormwood“), used in combination therapy, is produced botanically or synthetically; a molecular precursor (artemisinic acid) can be produced by genetically-engineered yeast
- Discovered in 1972 by Tu Youyou, Nobel Prize for Medicine 2015
- Exact mechanism of action not known, leads to formation of free radicals when in contact with hemoglobin in the RBC



[Levesque and Seeberger, Continuous-Flow Synthesis of the Anti-Malaria Drug Artemisinin, Angew. Chem. Int. Ed. 51:1706-1709 (2012)]

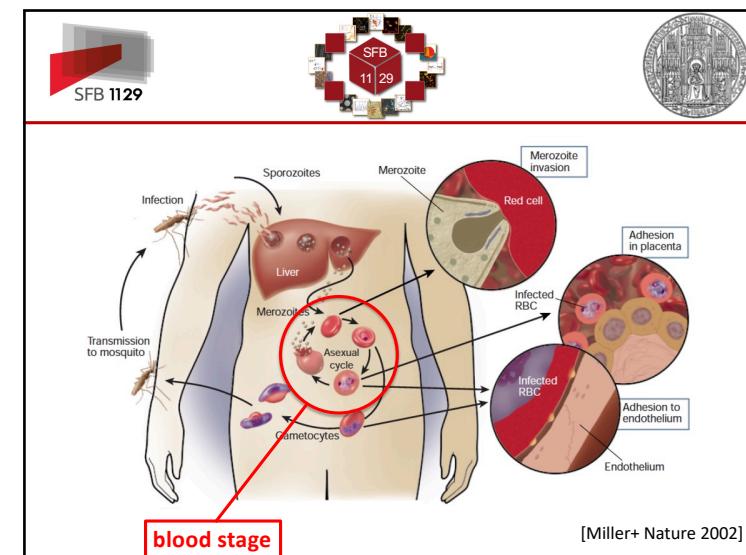
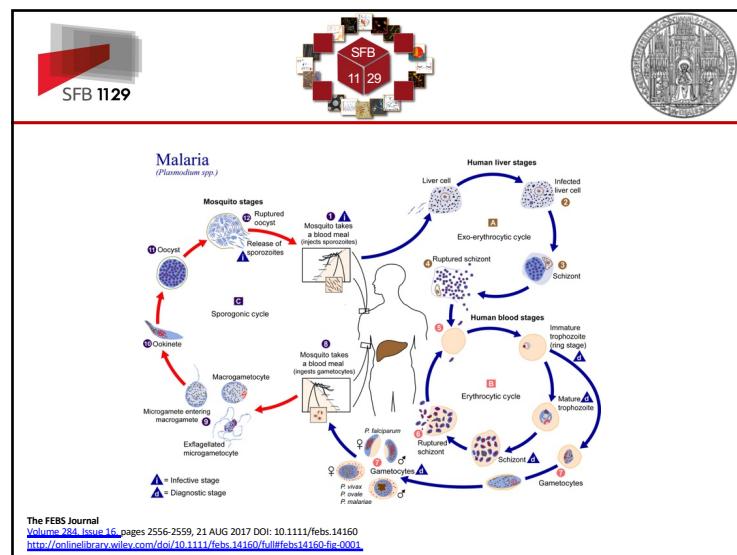
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## Geographical distribution of malaria



Mainly equatorial regions are affected (mosquitos need water puddles to lay their eggs). Example for the growing problem of drug resistance: chloroquine can now only be used in the orange regions.

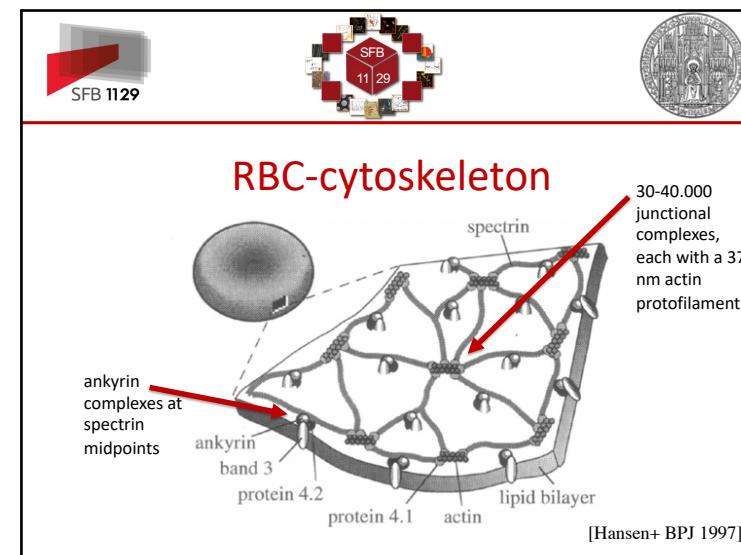
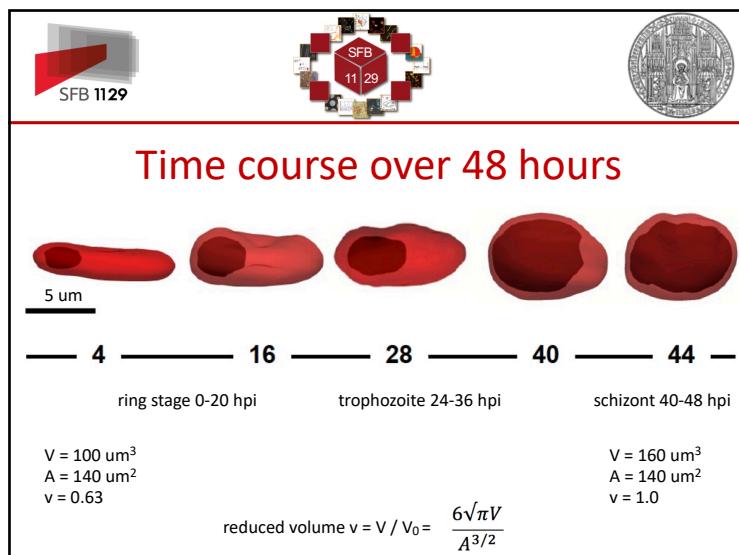
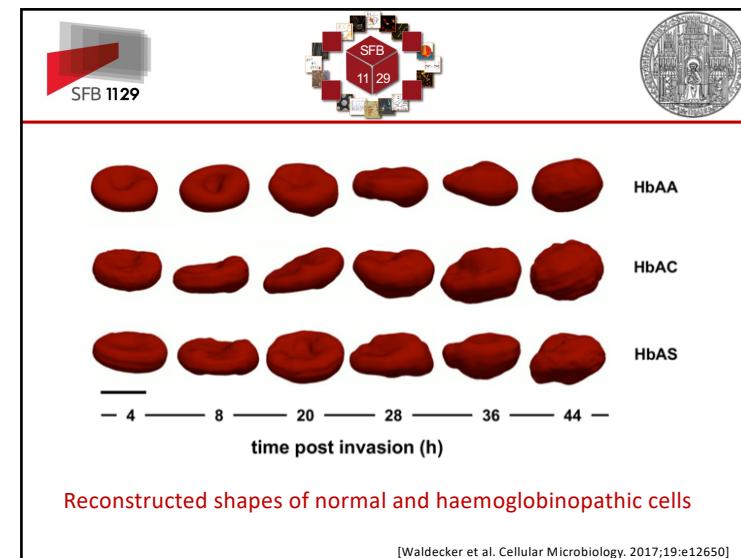
[Wikipedia]

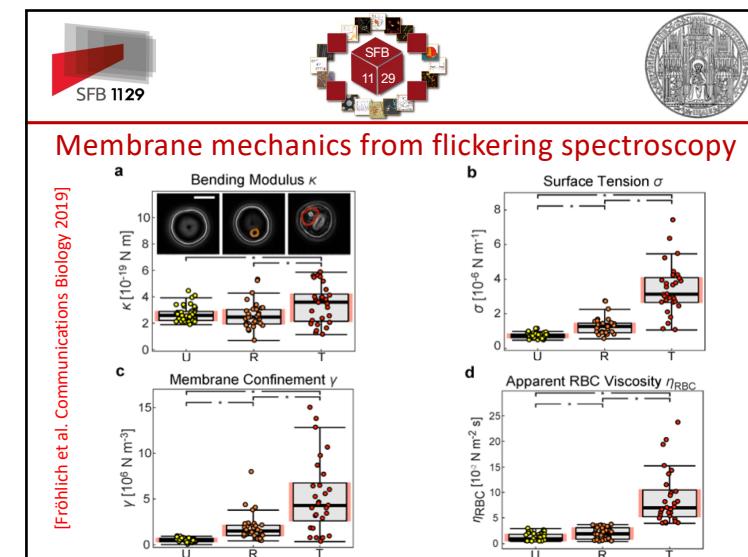
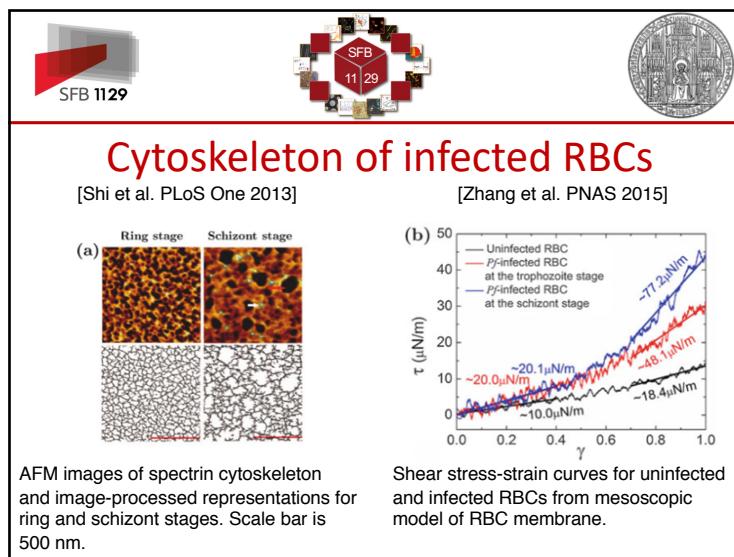
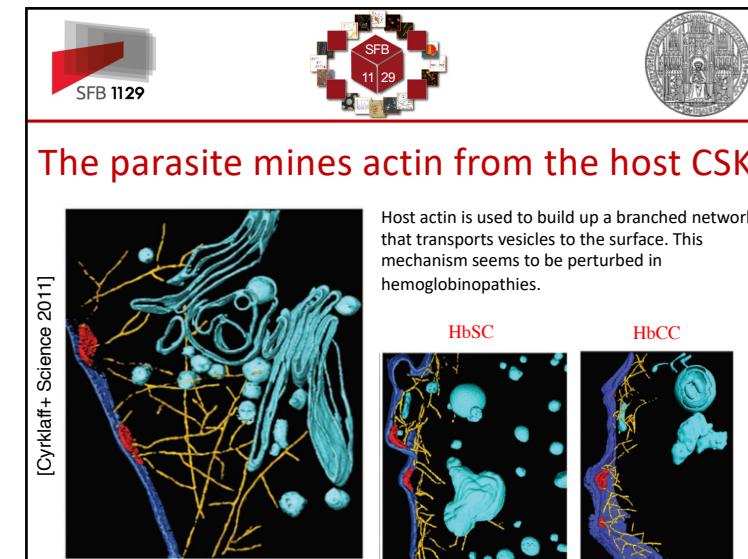
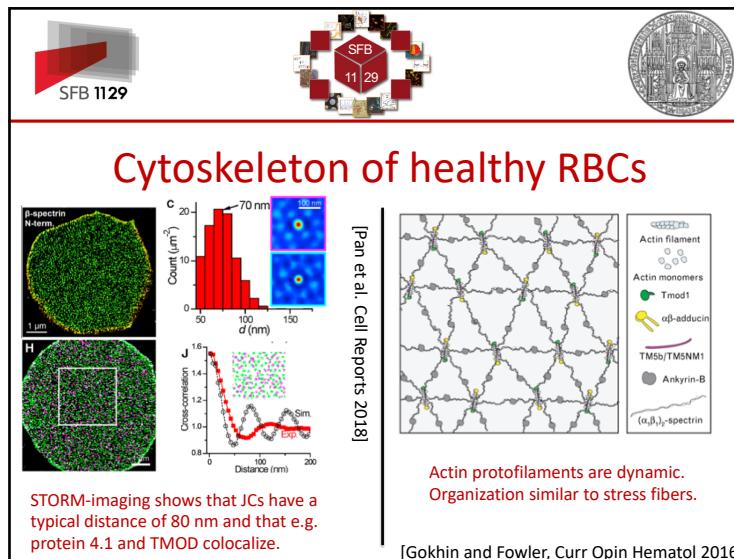


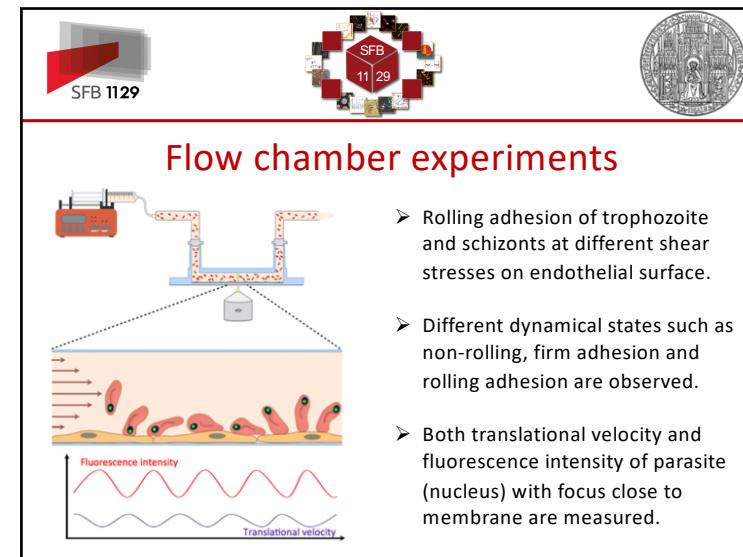
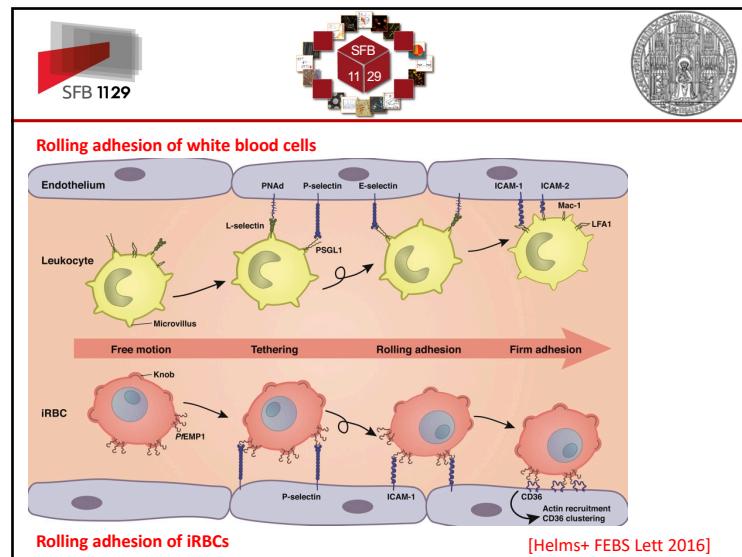
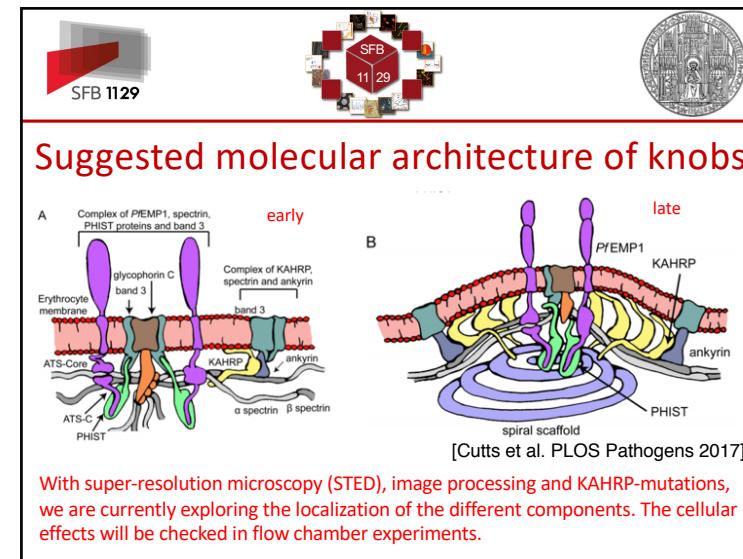
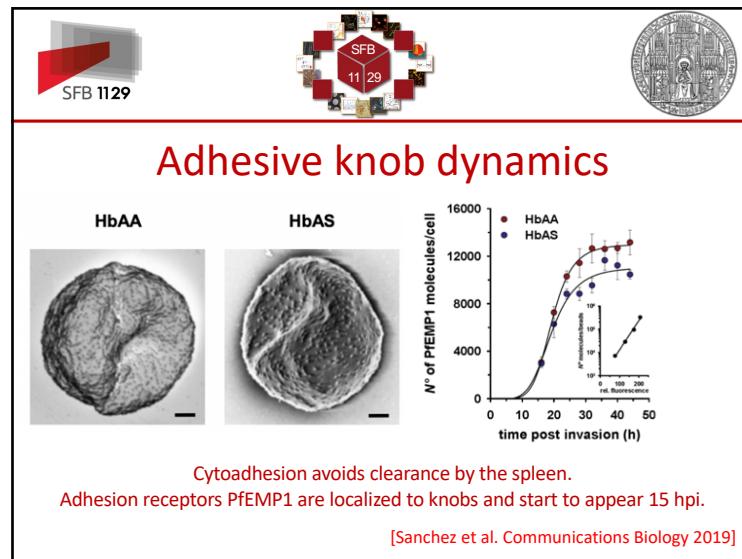
**Malaria blood stage**

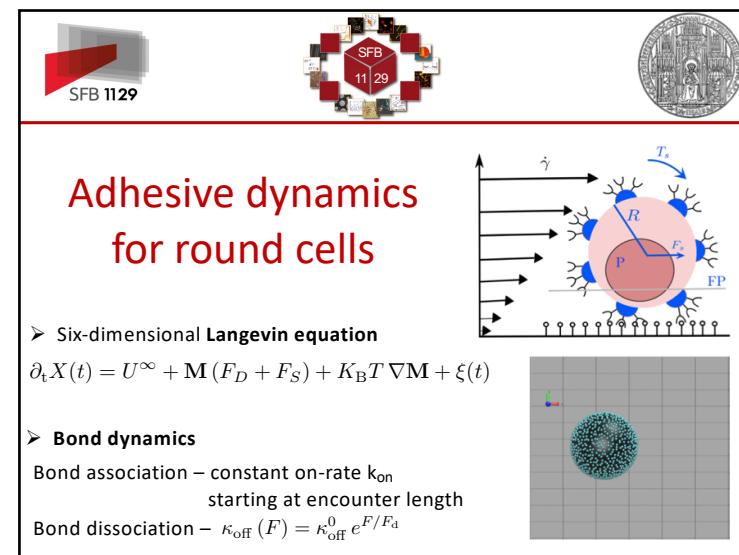
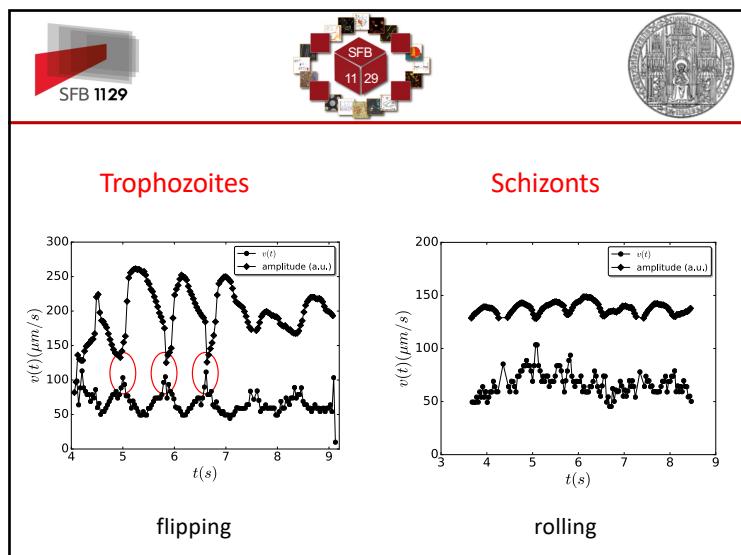
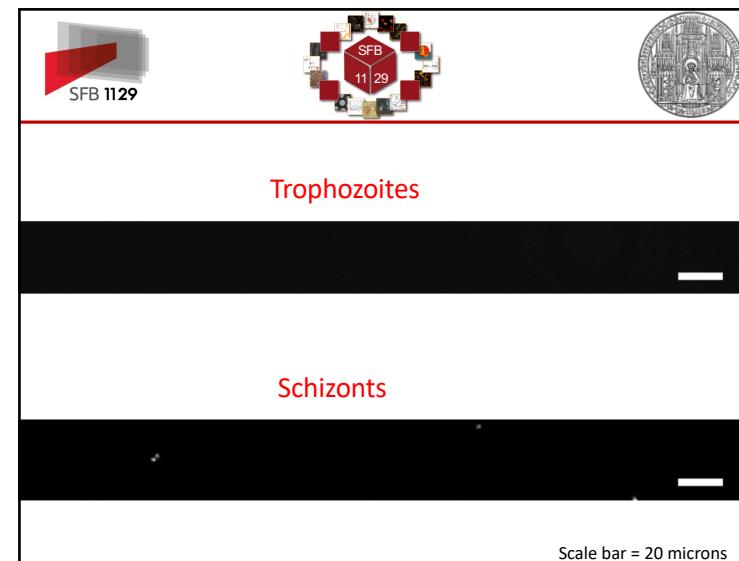
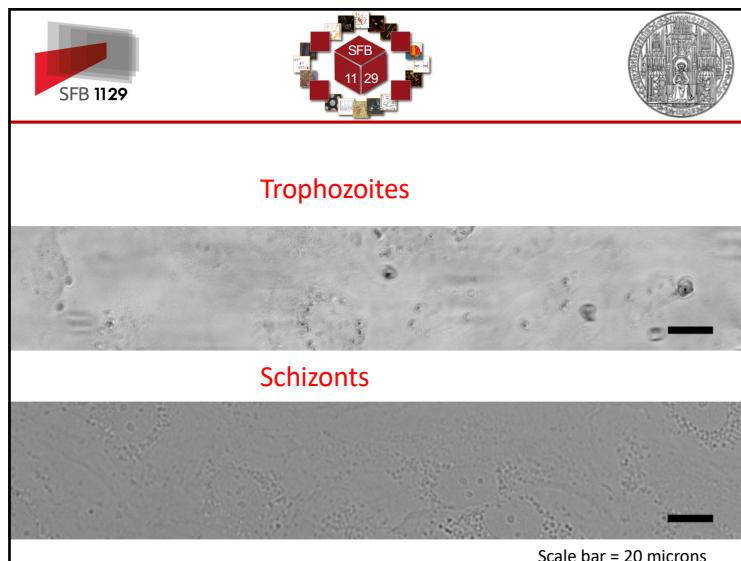
- The blood stage of the infection can be divided into three stages:
  - Ring stage (0-24 hpi)
  - Trophozoite stage (24-36 hpi)
  - Schizont stage (40-48 hpi)
- At 15 hpi, iRBC starts developing adhesive knobs on its surface.
- Cytoadherence of iRBC avoids clearance by spleen and leads to capillary obstruction.

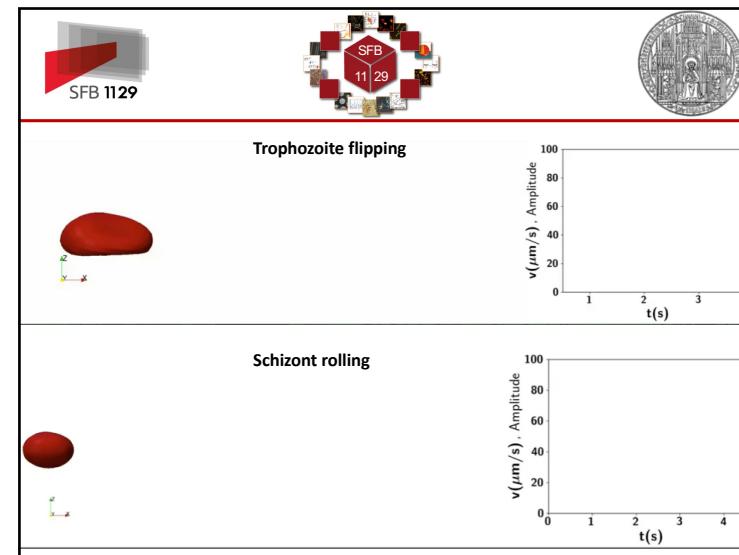
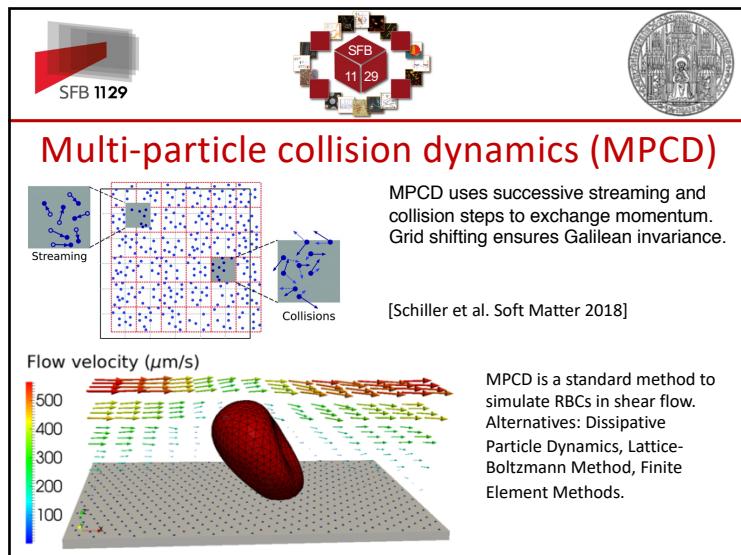
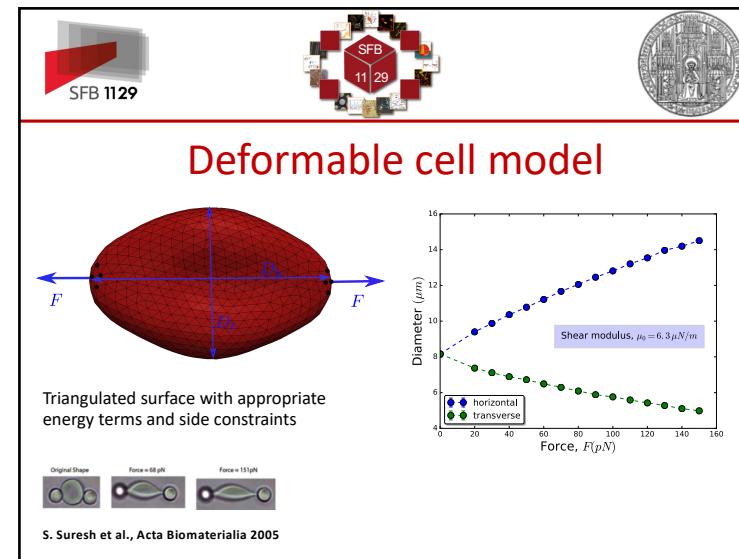
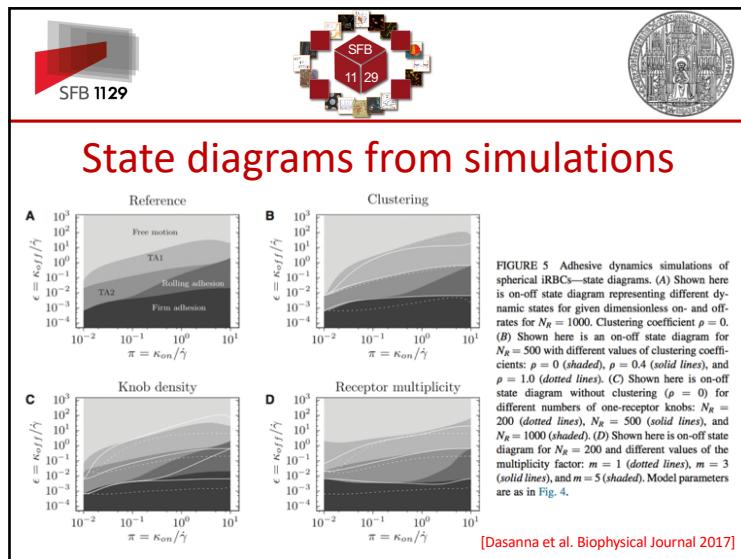
[Anal. Chem., 2014, 86 (9), pp 4379–4386]

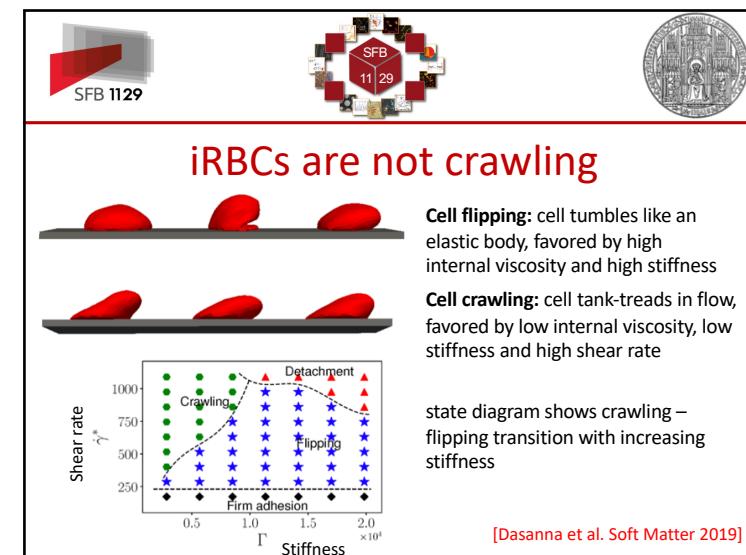
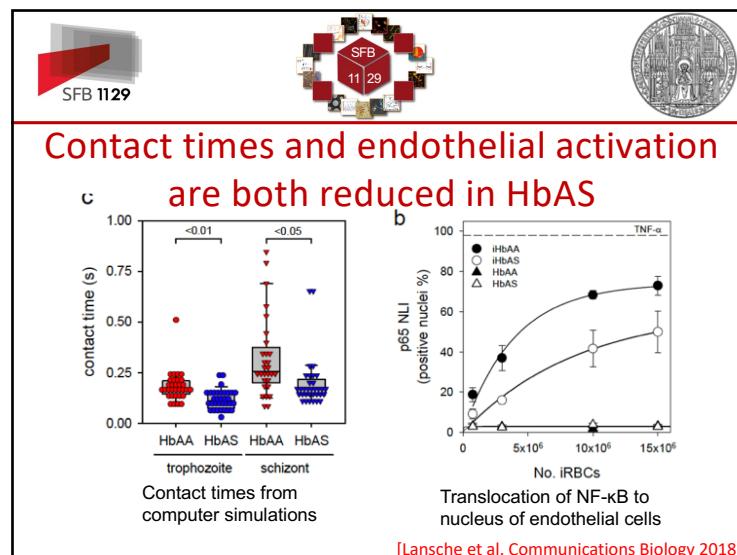
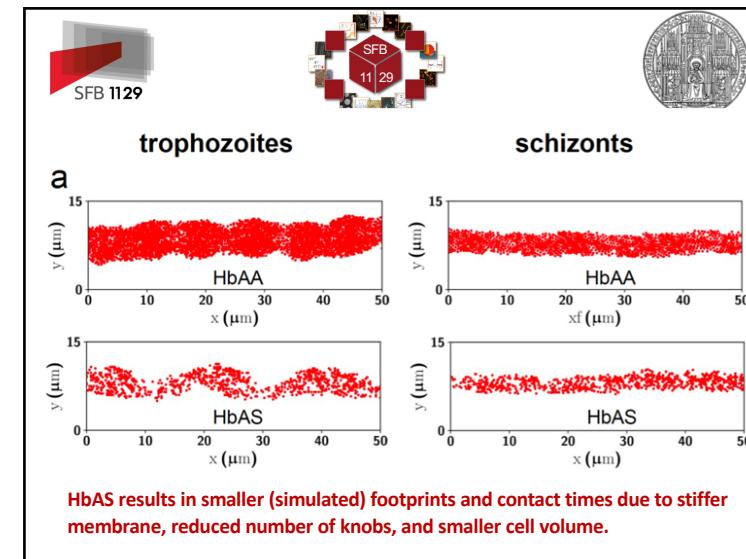
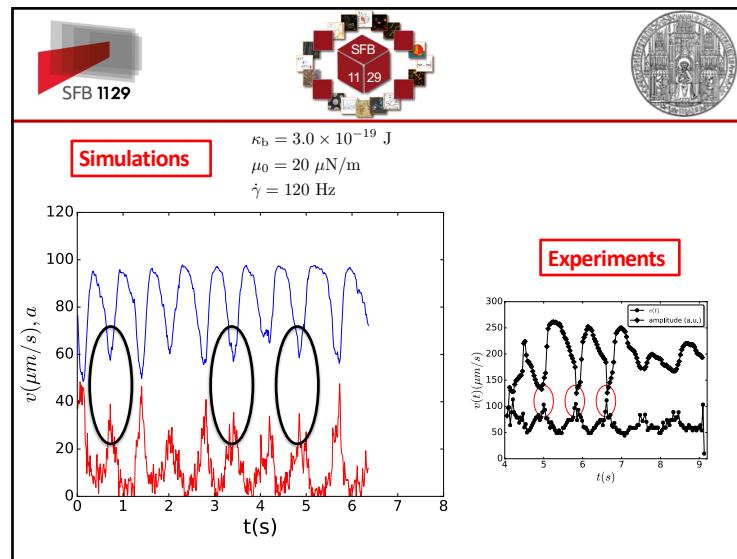
















## Two reviews on computational aspects

**F 5 Physics of the malaria parasite**

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Lecture Notes of the 10th SFB Spring School "Physics of Life" (Duisburg-Essen March 2010). All rights reserved.

**Multiscale Modeling of Malaria-Infected Red Blood Cells**

And R. Dasanna, Ulrich S. Schwarz, Gerhard Gompper, and Dmitry A. Fedosov

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M. Anderson, S. Upadhyay, Handbook of Malaria Modeling, SpringerBriefs in Mathematics 2018, 1–13.





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