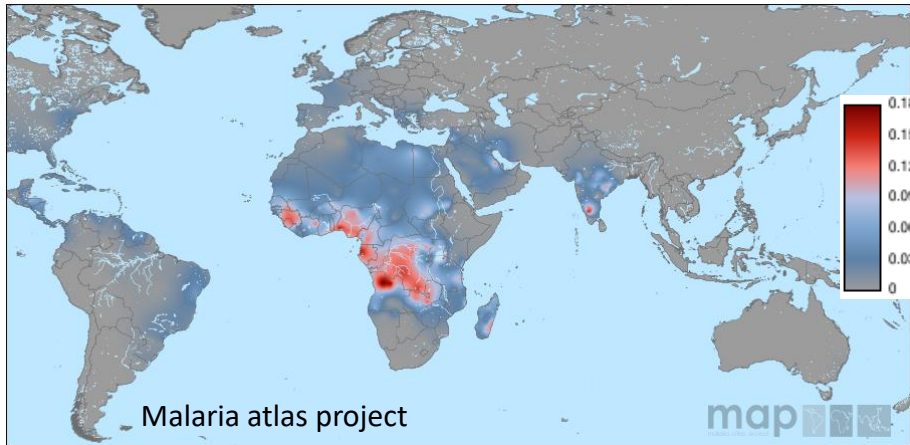


Dynamics of RBCs with altered mechanical properties in shear flow. Towards a clinical marker for sickle cell disease

Emmanuèle Helfer

Aix Marseille Univ, CNRS, CINaM, Marseille, France

Sickle cell disease: 1st genetic disease in the world

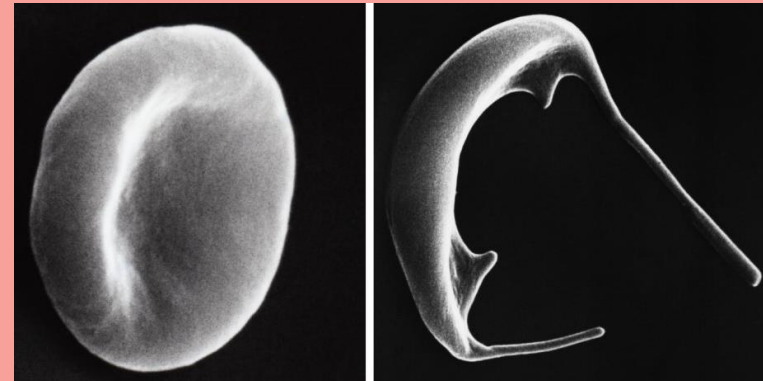


4.5 million people, 300 000 births/year

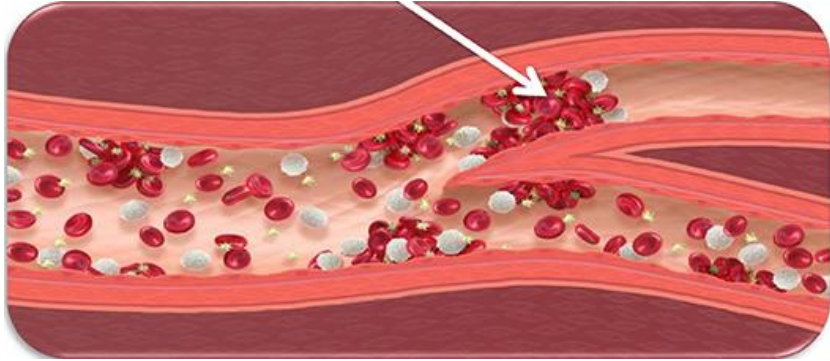
Life expectancy in developed countries
of the order of 40 years

Mutation in Hemoglobin: HbSS

- Dehydration
 - Deoxygenation
-
- Hemoglobin polymerization
 - Cell stiffening
- Partially reversible



Vaso-occlusive crisis



Clogging of small blood vessels

Vital prognosis: acute chest syndrome

Sequelae: stroke, bone necrosis

Unpredictable, very painful



Palliative care

Efforts only on systematic prevention

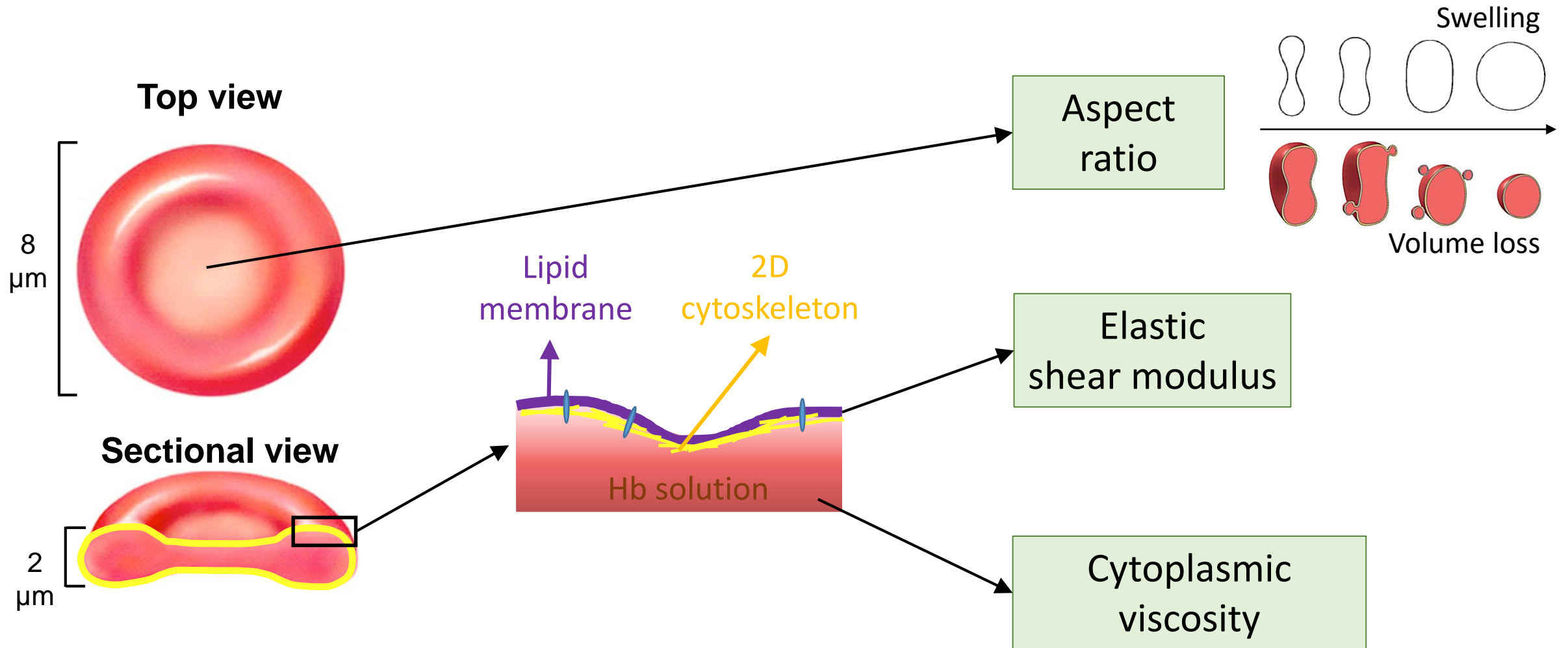
Decrease in
RBC deformability



Vaso-occlusive crises

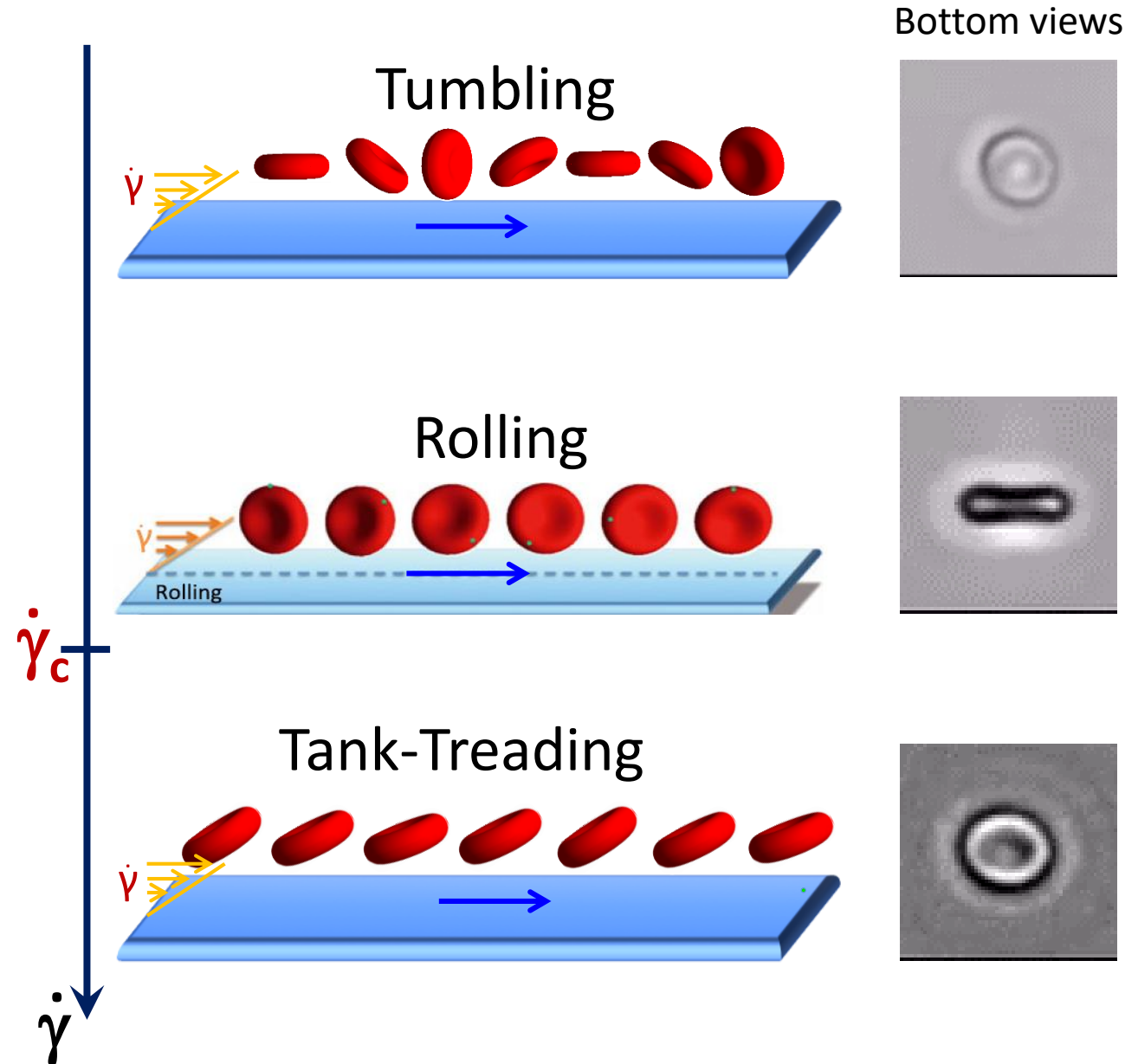
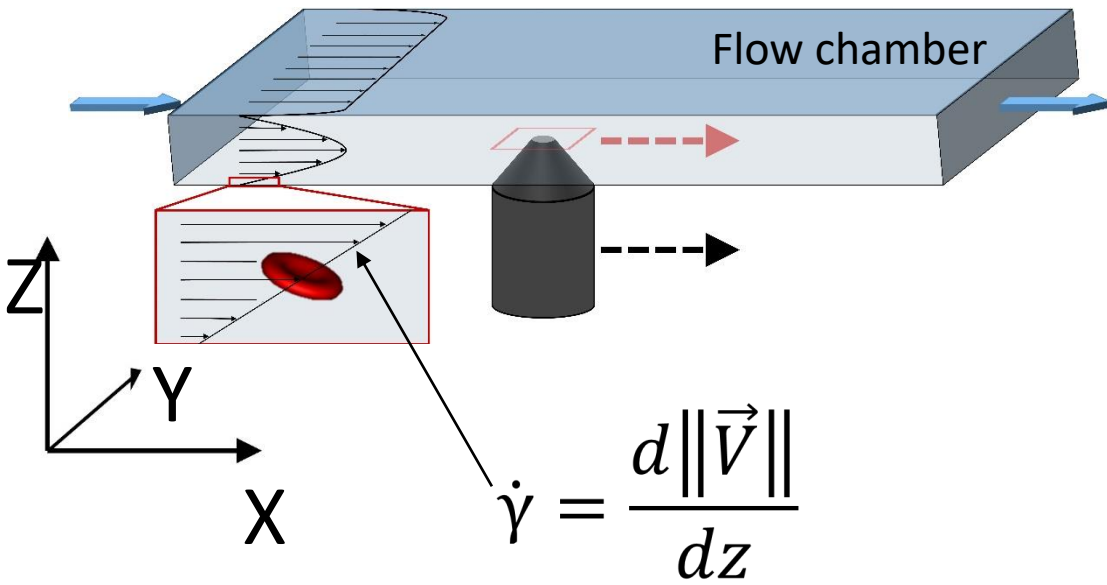
RBC mechanical marker sensitive to the imminence of a crisis?

Red blood cell deformability



➔ Need for a marker sensitive to these parameters

The mechanics of RBCs controls their motion under shear flow



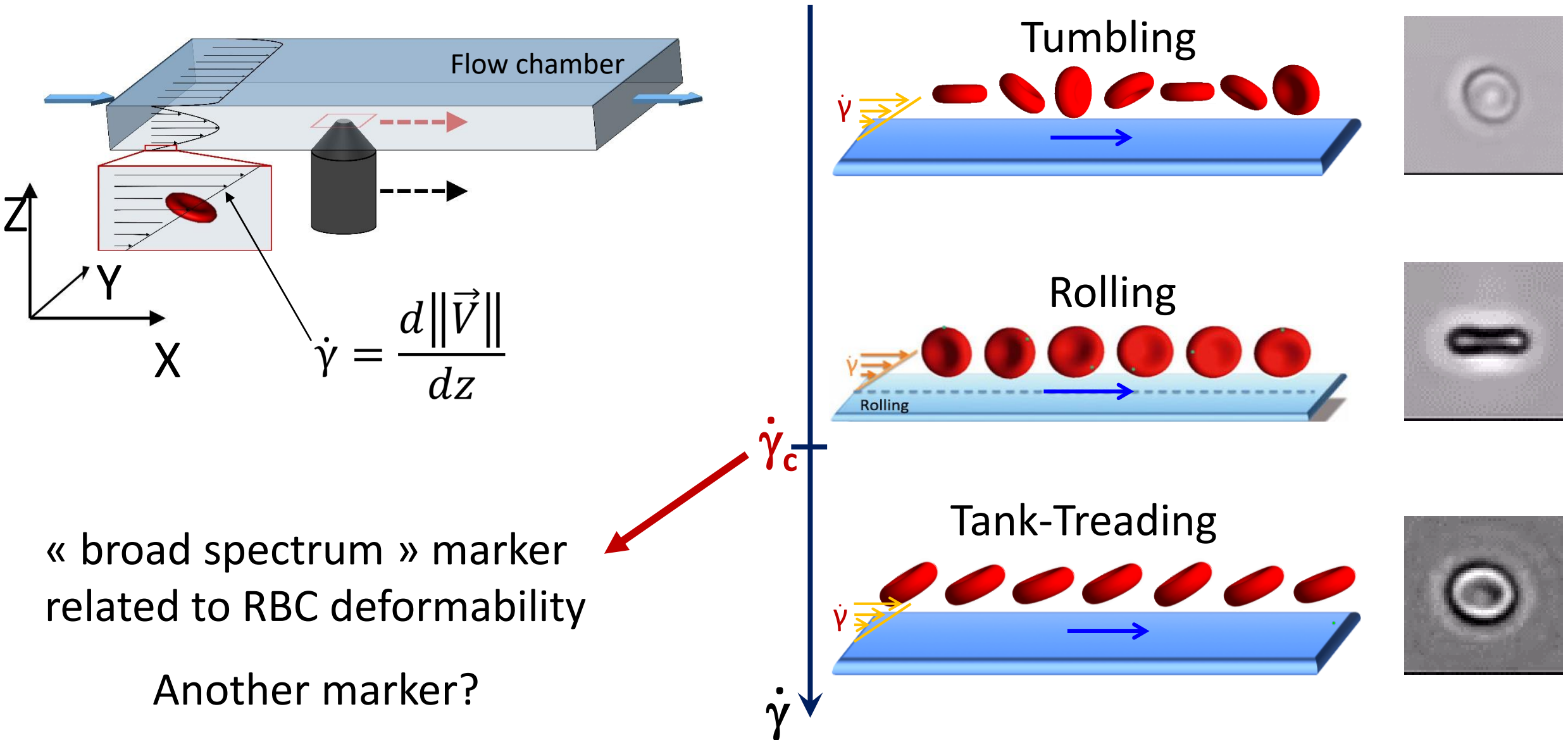
Goldsmith and Marlow, 1972

Fischer et al., Science 1978

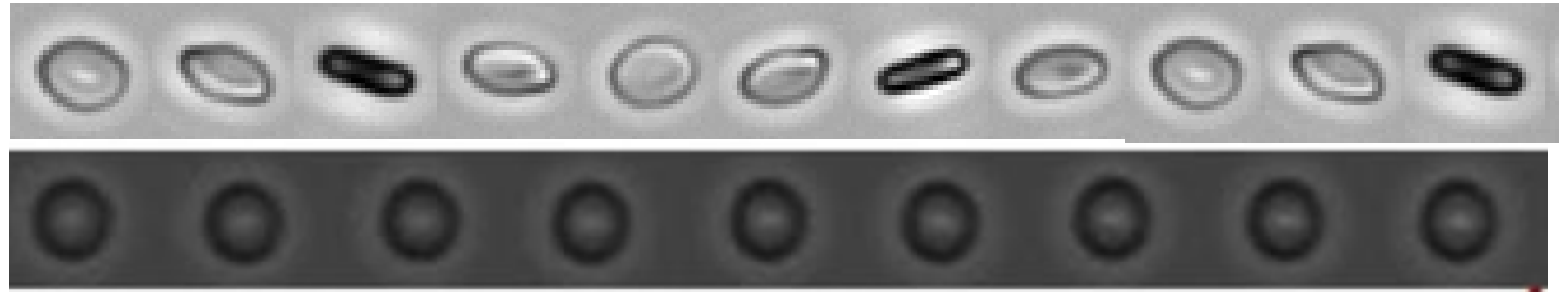
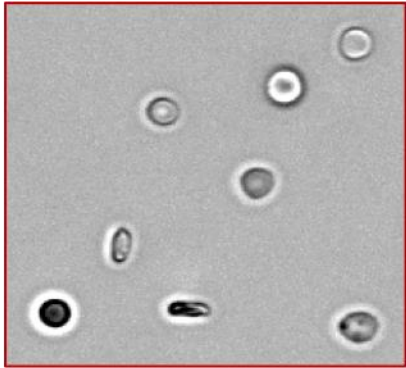
Abkarian et al., PRL, 2007

Dupire et al., PNAS, 2012

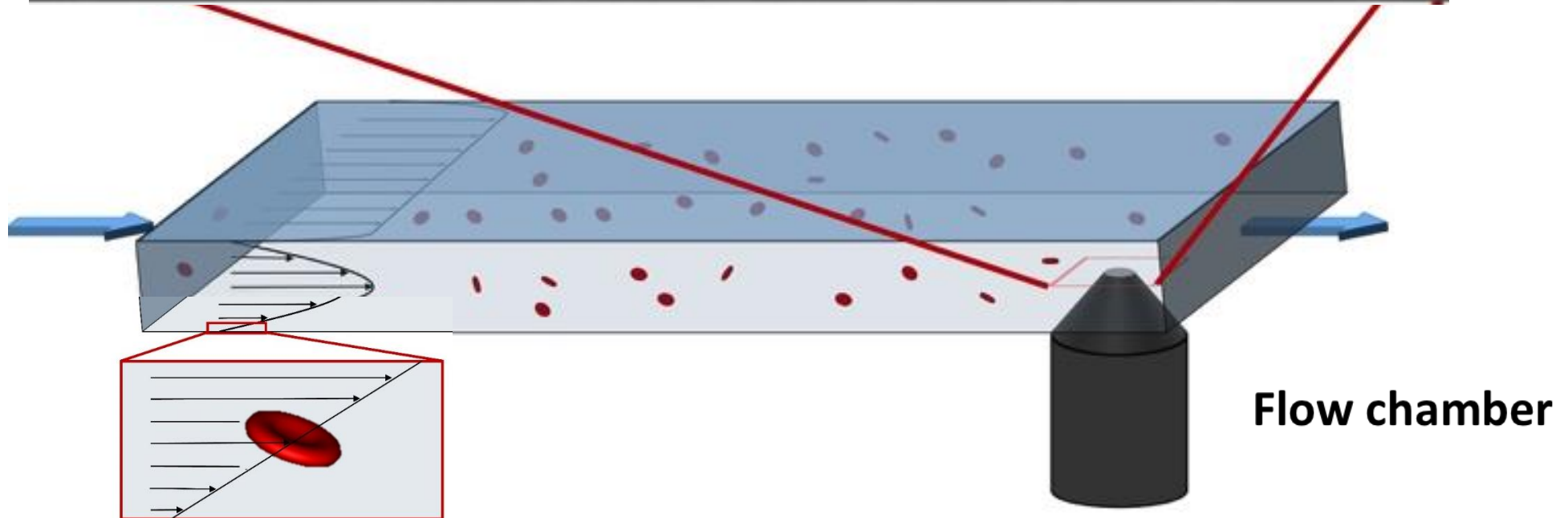
The mechanics of RBCs controls their motion under shear flow



Detection of RBC type of motion under shear flow

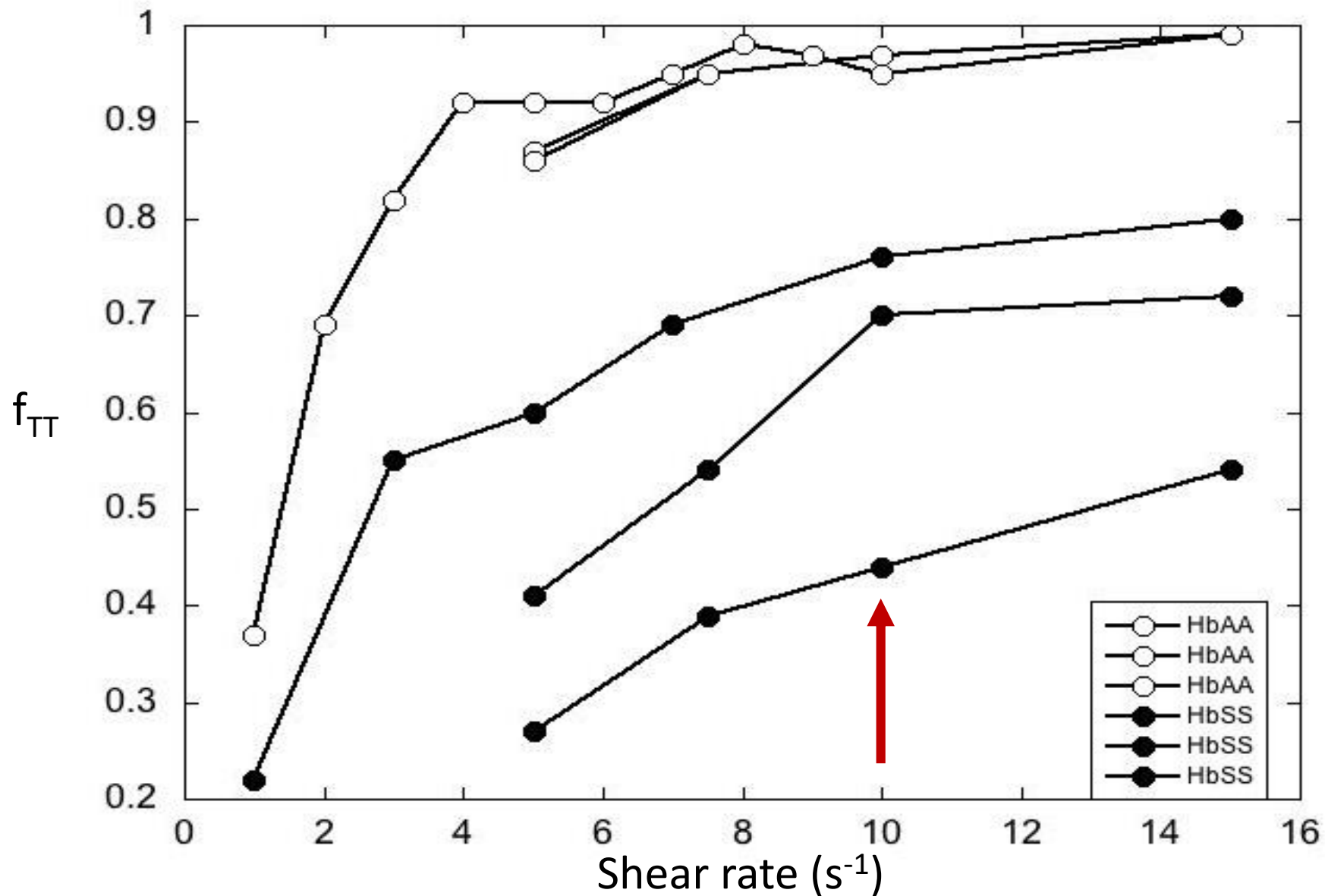


2 μ l blood



Flow chamber

Fraction of TT RBCs as function of shear rate

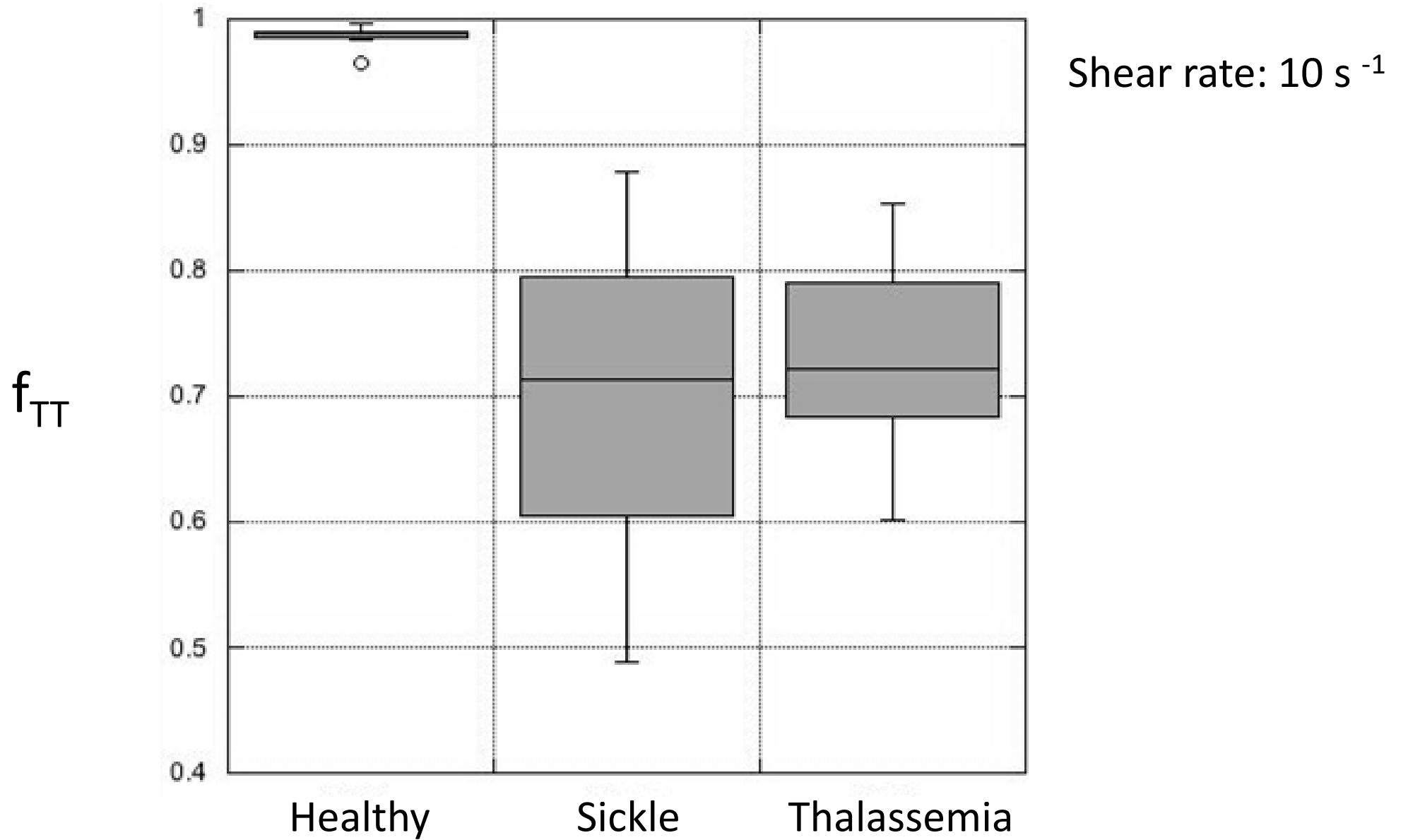


population of at least 250 cells

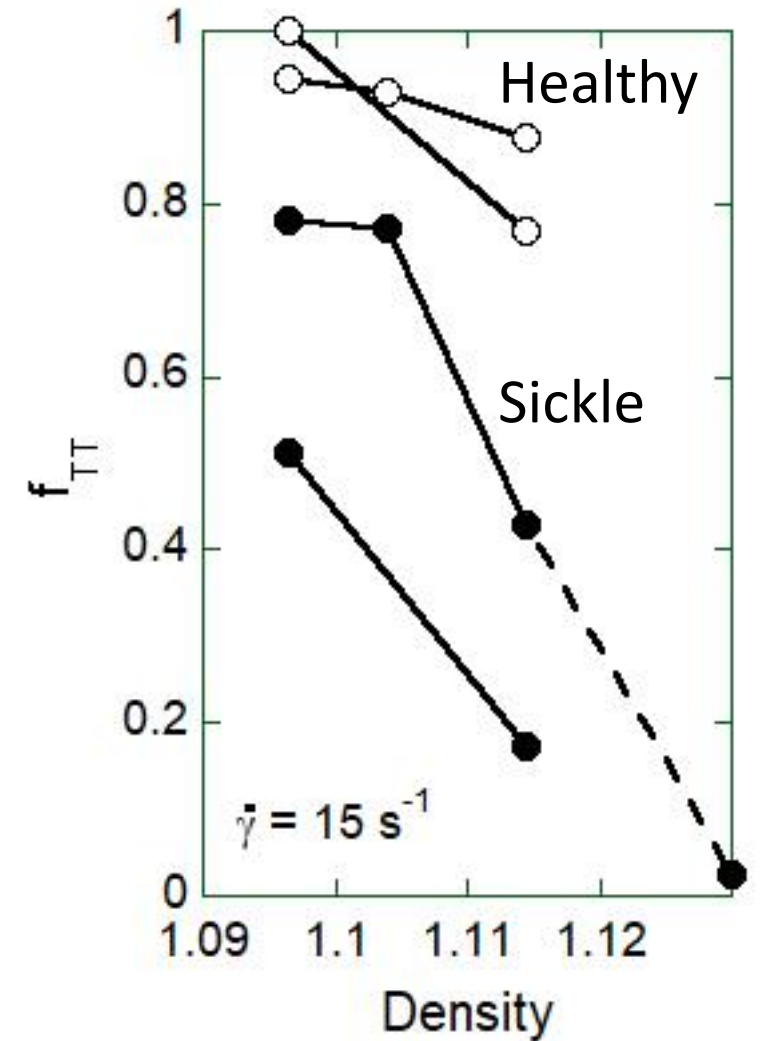
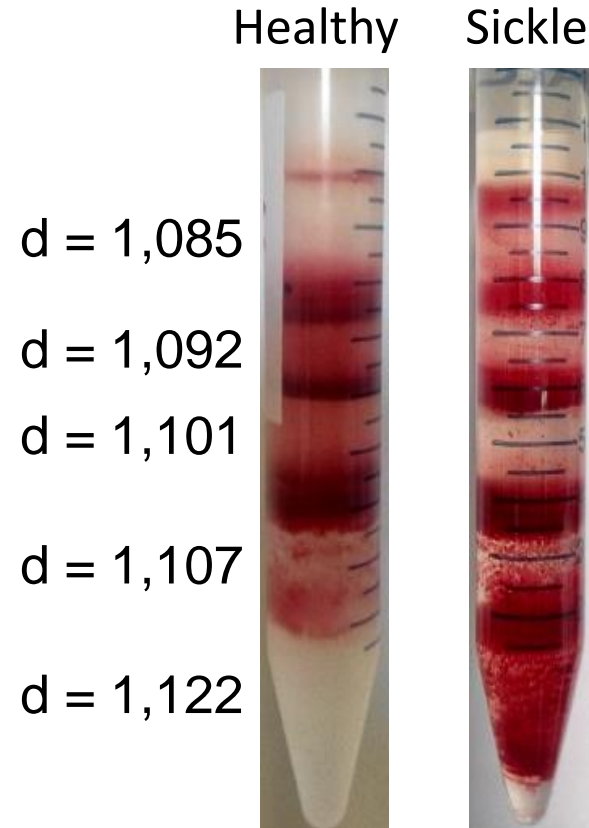
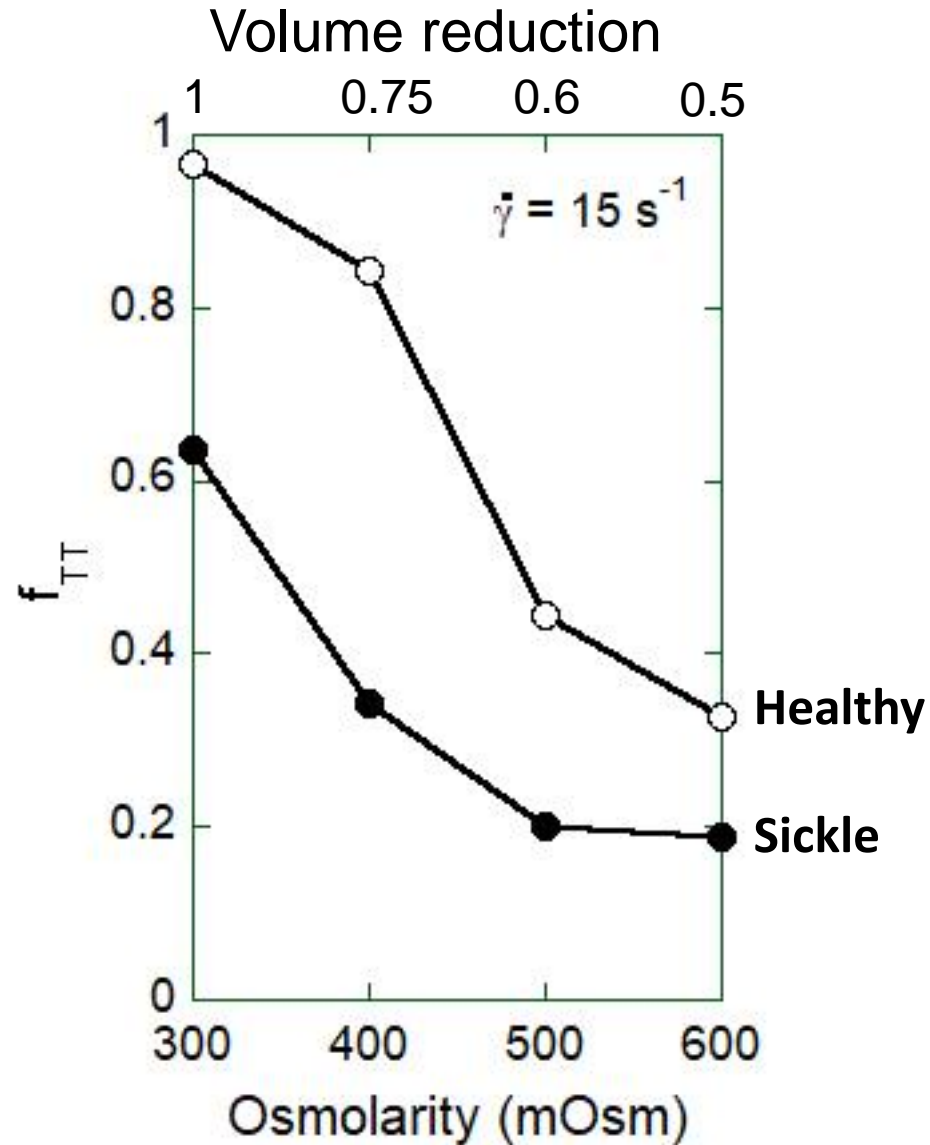
HbAA Healthy

HbSS Sickle

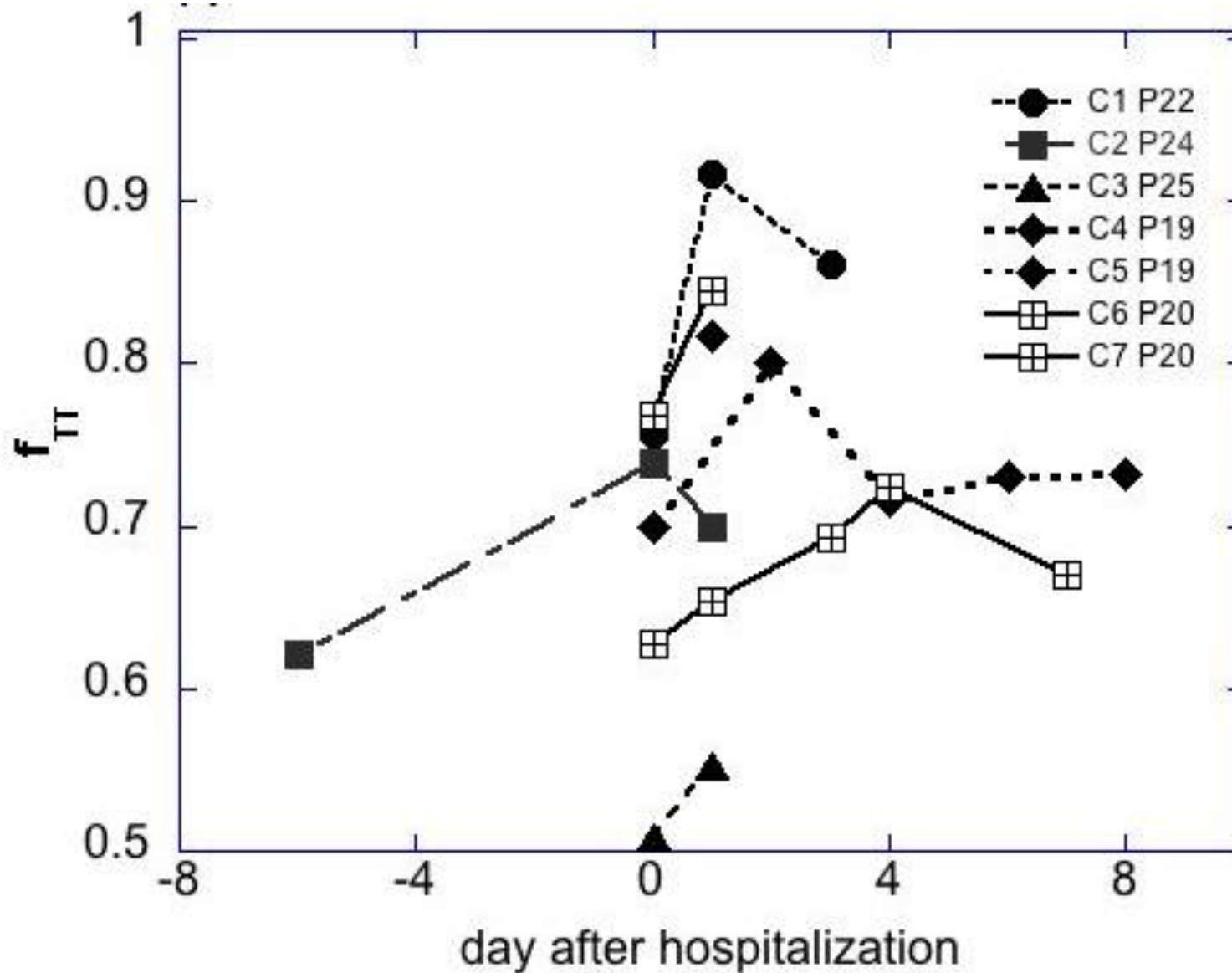
Fraction of TT RBCs SCD and thalassemia



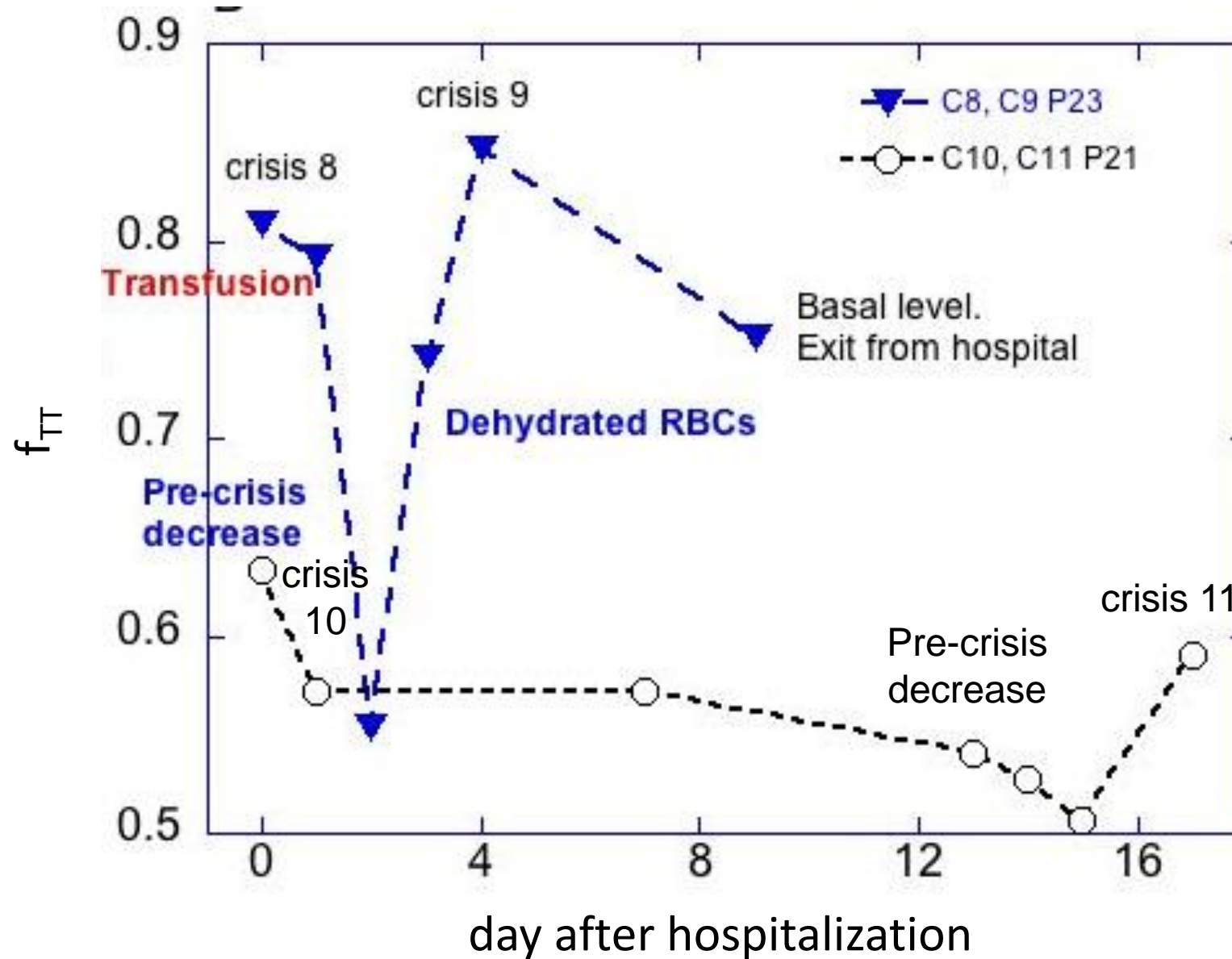
The fraction of TT RBCs is related to cell hydration and density



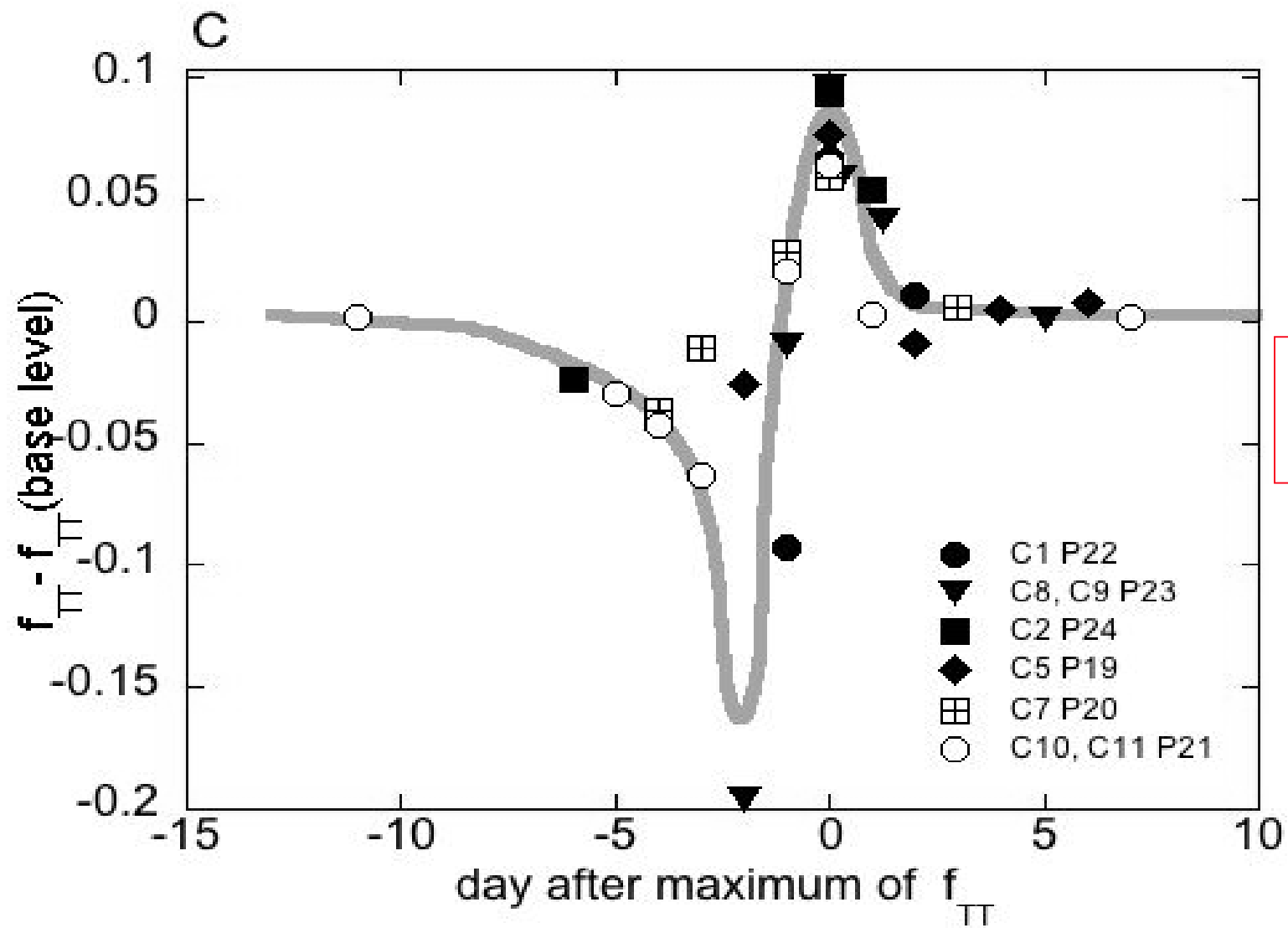
TT fraction during the course of a vaso-occlusive crisis



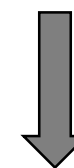
Sequence of two crises



f_{TT} trend evolution during vaso-occlusive crises



European patent application
EP 18305914.6



Clinical trial
from sept. 2018

Conclusion

The fraction of tanktreading RBCs is

- sensitive to genetic diseases that affect RBC deformability
- a perfect candidate for predicting vaso-occlusive crises in SCD



Low cost device that can be installed at the patient's bedside

Other applications: in-vitro test for drug evaluation...

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**Marseille
Medical
Genetics**

Marseille Medical Genetics

Aix-Marseille Université, INSERM

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A*MIDEX project (n° ANR-11-IDEX-00001-02)



CNRS Pre-maturation



THANK YOU FOR YOUR ATTENTION!