BP 8: Poster I

Focus: Phase Separation in Biological Systems (BP 8.1 – BP 8.12); Focus: Physics of Stem Cells (BP 8.13 – BP 8.20)

Time: Monday 17:30–19:30 Location: P2/1OG

BP 8.1 Mon 17:30 P2/1OG

Erythrocytes sedimentation rate and acanthocytosis — •Alexis Darras, Thomas John, Lars Kaestner, and Wagner Christian — Universität des Saarlandes, Experimental physics, Saarbrücken, Germany

Aggregation rate of the red blood cells (RBC), or erythrocytes, is a physical parameter of blood which is often checked in medical diagnosis. The easiest and most widespread method to assess this aggregation rate is by measuring the erythrocytes sedimentation rate (ESR). It is well known that in case of inflammation, the increase in fibrinogen and other proteins results in higher aggregation and ESR than in healthy blood. However, some rare cases also lead to a slower ESR. It is notoriously the case with acanthocytosis, where patients have deformed RBC, called acanthocytes.

In this presentation, we will report new detailed measurements of ESR from acanthocytosis' patients and discuss the origin of this slower ESR. For this, we combine macroscopic tests with microscopic data of the acanthocytes aggregation. On the basis of the dynamics of colloidal gels, we will show how the change in aggregates' morphology, due to the acanthocytes, leads to slower sedimentation rate.

BP 8.2 Mon 17:30 P2/1OG

Dynamics of pressure-induced phase transitions in concentrated lysozyme solutions — •Marc Moron[1], Clementine Lovato[2], Ahmed Al-Masoodi[2], Lisa Randolph[2], Mario Reiser[2,3], Johannes Möller[3], Fabian Westermeier[4], Göran Surmeier[1], Jennifer Bolle[1], Michael Paulus[1], Metin Tolan[1], and Christian Gutt[2] — [1]Fakultät Physik / DELTA, TU Dortmund, 44221 Dortmund, Germany — [2]Department Physik, Universität Siegen, 57072 Siegen, Germany — [3]European X-ray Free Electron Laser Facility, Holzkoppel 4, Schenefeld, Germany — [4]Deutsches Elektronen Synchrotron DESY, D-22607 Hamburg, Germany

Phase transitions in concentrated protein solutions have been in the focus of research for years. For example, many diseases can be attributed to protein aggregation or liquid-liquid phase separation in human cells. Such systems can be modeled as crowded protein solutions. Lysozyme represents a well-studied model protein. We investigated the effect of hydrostatic pressure on concentrated lysozyme solutions in different environments and were able to show that besides temperature, protein concentration, cosolvents and ionic strength also the hydrostatic pressure modulates the protein-protein interaction. However, only the static properties of the lysozyme solutions were characterized. In this work, we present first pressure dependent X-ray photon correlation spectroscopy (XPCS) measurements on concentrated lysozyme solutions to study the dynamics of pressure-induced liquid-liquid phase transitions.

BP 8.3 Mon 17:30 P2/1OG

Droplets as biochemical reactors in living cells — •Sudarshana Laha[1,2], Thomas C.T. Michaels[3], and Christoph A. Weber[1,2] — [1]Max Planck Institute for the Physics of Complex Systems,Dresden — [2]Center for Systems Biology Dresden — [3]Harvard University, Cambridge

Living cells use compartments(droplets) to spatially organise molecules that can undergo fuel-driven chemical reactions. Not much is known about the mechanisms underlying such spatial control of chemical reactions and how much the properties of chemical reactions are altered by the compartments relative to homogenous systems. Here, we derive a theoretical framework to study fuel driven chemical reactions in the presence of compartments.We study two state transitions like phosphorylation via hydrolysis of ATP and enzymatic reactions. For two state transitions, we find that the ratio of phosphorylated product can be regulated by droplets by two orders of magnitude relative to the homogenous state. In the case of enzymatic reactions, we show that the initial rate of product formation can be increased by more than ten fold. We further calculate analytically the optimal conditions of designing the system. Our studies exemplify the enormous potential of phase separated compartments as biochemical reactors in living cells and enhancing the effect of enzymes. Understanding the control of biochemical reactions via compartments is key to elucidate the functionality of stress granules for the cell and is also crucial for biochemical communication among synthetic cells and RNA catalysis in coacervate protocells.

BP 8.4 Mon 17:30 P2/1OG

Size control of Active Droplets with Non-Equilibrium Chemical Reactions — •Jan Kirschbaum and David Zwicker — Max Planck Institute for Dynamics and Self-Organization, Göttingen, Germany

Liquid droplets forming by phase separation play an important role in the spatiotemporal organization of material inside cells. However, in contrast to passive phase separation, e.g. oil-water emulsions, the interaction of cellular droplets with their inherently non-equilibrium environment is not well understood. Here, we investigate how ATP-driven chemical reactions, which switch a protein between a phase separating and a soluble form, influence the properties of droplets. Similar systems were already investigated using mass-action kinetics, but such descriptions are not thermodynamically consistent and are thus difficult to compare to experiments.

Here, we employ linear non-equilibrium thermodynamics to model the phase separation and the non-equilibrium reactions. We identify that droplet size and stability can be controlled when one reaction is driven and the enzymes controlling the rates are distributed heterogeneously. In this case, a non-equilibrium steady state with well-defined droplet radius can be reached, characterized by constant diffusive and reactive fluxes inside the system. Using the model, we determine the energy consumption and entropy production rate necessary to maintain droplets of certain sizes. For the biological example, we thus propose that enriching enzymes in droplets is one way to control their size by chemical reactions.

BP 8.5 Mon 17:30 P2/1OG

Unusual correlated dynamics in aqueous protein solutions due to thermal expansion induced shear flow — •Nafisa Begam[1], Anastasia Ragulskaya[1], Anita Girelli[1], Hendrik Rahmann[2], Fabian Westermeier[3], Christian Gutt[2], Fajun Zhang[1], and Frank Schreiber[1] — [1]Universität Tübingen, Germany — [2]Universität Siegen, Germany — [3]DESY, Germany

We study the dynamics of aqueous solutions of the globular protein bovine γ-globulin in the presence of polyethylene glycol, filled into quartz capillaries, during liquid-liquid phase separation using X-ray photon correlation spectroscopy (XPCS). Simultaneously, we probe the kinetics of the phase separation by USAXS. Microscopy measurements revealed that the solutions undergo a thermal expansion or contraction during the temperature change which induces a shear flow in the solution. To study the influence of such an intrinsic shear flow on the phase transition, we performed the measurements in the middle of the capillary, having a large shear flow, and rear of the capillary, having a negligible shear flow. Interestingly, the kinetics observed in these two cases are similar. However, in the middle of the capillary, the dynamics exhibits a strong heterogeneity, and in the rear of the capillary, the degree of heterogeneity is significantly smaller. Our findings could have a large impact in the field of condensed matter where XPCS is an important tool in studying bulk dynamics and the intrinsic shear flow is comparable to the time scale of the system dynamics.

[1] Busch et al., *Eur. Phys. J. E*, **26**, 55, (2008)
[2] Urbani et al., *J. Sync. Rad.*, **23**, 1401, (2016)

BP 8.6 Mon 17:30 P2/1OG

Bending rigidity of heterochromatin alone can induce segregation in model eukaryotic cell nuclei — Martin Girard[2], Kurt Kremer[2], John F. Marko[3], Monica Olvera de la Cruz[3], and •Aykut Erbas[1] — [1]Bilkent University - UNAM, Ankara 06800, Turkey — [2]Max-Planck Instutute for Polymer Science, Mainz 55128, Mainz, Germany — [3]Northwestern University, Evanston 60202, USA

One of the unresolved puzzles in biological sciences is the 3D packing of the meters-long DNA molecule into the confinement of micrometer-scale cell nucleus while regulating fundamental cellular activities, from

protein transcription to replication. Although the underlying 3D conformation of the genome is a complex phenomenon resulting from the dynamic interactions between nuclear proteins and negatively charged DNA, relatively simple computational models can guide us about the large-scale and long-time behavior of the chromatin. Our extensive Molecular Dynamics simulations provide an auxiliary, possibly alternative, mechanism for heterochromatin (i.e., a histone-rich version of the chromatin) localization in the cell nucleus. We showed that coalescence of heterochromatin at the nuclear center can be mimicked even for an ideal mixture scenario throughout the suppressed bending fluctuations of the heterochromatin fiber. Further, our model system also suggests that switching of the interactions between confining nuclear shell and the heterochromatin can recover the conventional segregation regime, in which heterochromatin occupies the nuclear periphery.

BP 8.7 Mon 17:30 P2/1OG

Effective simulation of many interacting droplets — •Ajinkya Kulkarni and David Zwicker — Max Planck Institute for Dynamics and Self-Organization, Göttingen, Germany

It has recently been discovered that liquid droplets play an important role in organizing material inside biological cells. However, so far it is unclear how a large number of droplets behave in the heterogeneous environment of the cell. Traditionally, liquid-liquid phase separation is numerically studied using Monte-Carlo simulations, Molecular Dynamics simulations, or by solving the Cahn-Hilliard equation on a lattice. All these methods are computationally expensive since they have to resolve spatial structures on the scale of individual particles. This severely limits the system sizes that can be studied.

We propose a novel simulation method to tackle this limitation. Our method describes droplets explicitly by a position and a radius, while the dilute phase is represented by a concentration field. Assuming that droplets are far enough away from each other, they only interact by exchanging material via the dilute phase. Since the dilute phase is sufficiently described by a coarse discretization of the diffusion equation, our method is orders of magnitude faster than the traditional ones. Consequently, our method allows simulating the dynamics of many droplets on length- and timescales relevant to biological cells.

BP 8.8 Mon 17:30 P2/1OG

Hydrodynamics of pumping cell aggregates — •Max Kerr Winter and Guillaume Salbreux — The Francis Crick Institute, London, UK

Cavitation events within tissues are ubiquitous in developmental biology. In order to study such phenomena, we derive a hydrodynamic theory of cells forming aggregates and cavities by the combined action of adhesion forces and the active, polar pumping of fluid. The theory describes a coarse grained fluid consisting of cells in a medium of solutes and water. In the limit of passive, apolar cells, we investigate the steady state phase separation behaviour of the fluid in response to the strength of cell-cell adhesions. For sufficiently strong adhesions, the system separates into two phases differing by their cell density. We also study the linear stability of active, polar cells and find the system can be driven away from a uniform state by active pumping of solutes at topological defects in the polarity field. This theory takes inspiration from recent experiments with mouse embryonic stem cells (ESCs) [Shahbazi et al., Nature, 2017], where spherical ESC aggregates form cavities by the coordination of adhesion, apicobasal polarity, and active pumping.

BP 8.9 Mon 17:30 P2/1OG

Protein-free synthetic cell division controlled by metabolic activity — •Yannik Dreher[1,2] and Kerstin Göpfrich[1,2] — [1]Biophysical Engineering Group, Max Planck Institute for Medical Research, Jahnstraße 29, 69120 Heidelberg, Germany — [2]Department of Physics and Astronomy, Heidelberg University, 69120 Heidelberg, Germany

Here, we describe the protein-free division of giant unilamellar lipid vesicles (GUVs) based on the combination of two physical principles – phase separation and osmosis. We visualize the division process with confocal fluorescence microscopy and derive a conceptual model based on the vesicle geometry. The model successfully predicts the shape transformations over time as well as the time point of the final pinching of the daughter vesicles. Remarkably, we show that two fundamentally distinct yet highly abundant processes – water evaporation and metabolic activity – can both regulate the autonomous division of GUVs. Our work may hint towards mechanisms that governed the division of protocells and adds to the strategic toolbox of bottom-up synthetic biology with its vision of bringing matter to life.

BP 8.10 Mon 17:30 P2/1OG

Designing morphology of separated phases in multicomponent liquid mixtures — Milena Chakraverti-Wuerthwein[1], Sheng Mao[1], Hunter Gaudio[2], Mikko Haataja[1], and •Andrej Kosmrlj[1] — [1]Princeton University, Princeton, NJ, USA — [2]Villanova University, Villanova, PA, USA

Morphology of multiphase membraneless organelles formed via intracellular phase separation plays an important role for their functionality. Yet, very little is known how intermolecular interactions can be tuned to achieve target microstructures of separated phases. To address this, we systematically investigate morphologies of coexisting phases obtained via phase separation in Flory-Huggins liquid mixtures with 4 or more components. We demonstrate that the topology of separated phases is completely determined by their surface tensions, while their volume fractions dictate the geometry of microstructure (e.g. droplets, percolated structure). We developed a novel method based on graphs that enabled us to enumerate all topologically distinct morphologies of separated phases. Each graph is associated with a set of inequalities for surface tensions and this enabled us to reverse engineered intermolecular interaction parameters to realize all topologically distinct morphologies for 4 coexisting phases. The developed approach is general and can be applied to design morphologies with an arbitrary number of coexisting phases.

BP 8.11 Mon 17:30 P2/1OG

Shape-instabilities in Chemically Active Multi-momponent Mixtures — •Jonathan Bauermann[1] and Frank Jülicher[1,2] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [2]Center for Systems Biology Dresden, Dresden, Germany

Recently, it has been shown that droplets can undergo splitting events in chemically active environments (Zwicker et al., Nature Physics, 2017). The authors studied the dynamics of a binary mixture in the Cahn-Hilliard theory with an additional effective flux coming from the underlying chemical reactions. Only if the system is driven out of equilibrium, a stable droplet radius can exist. We generalize this model to more components and make the breaking of detailed balance explicit in the chemical reactions by introducing an additional energy supply. This drives the system out of equilibrium and stable droplet radii can be found. If the external energy supply is strong enough, similar shape-instabilities of the spherical droplets can be found as described by the authors in the aforementioned paper. A framework like this allows not only for more complicated reaction schemes, but also gives insights into the energetics of chemical reactions in phase-separating systems.

BP 8.12 Mon 17:30 P2/1OG

Cross-diffusion induced patterns for a single step catalytic reaction — •Giovanni Giunta[1,2], Hamid Seyed-Allaei[1], and Ulrich Gerland[1] — [1]Physics Department, Technical University Munich (TUM), Garching, Germany — [2]Quantitative Biosciences Munich, Ludwig-Maximilians-Universität (LMU), Munich, Germany

There is mounting evidence that the motion of a given enzyme depends on the concentration of the corresponding substrate. Experiments performed in solution show that the higher the concentration of substrate, the higher the diffusion coefficient of the enzyme. Moreover experiments performed in steady gradients of substrate have also shown that cross-diffusive effects may be playing an important role. Here we analyze the different models proposed so far and we focus on the effects that the reaction has in shaping the substrate concentration, which in turns has an effect on the enzyme motion. We show that spatial patterns form when cross-diffusion and enhanced diffusion both contribute to the accumulation of enzymes in regions with low concentrations of substrate. In this scenario, the reaction causes gradients of substrate to get steeper, which in turns causes the enzyme to further accumulate where substrate is low. Experimental evidence of pattern formation could be used to discern between the different models proposed so far.

BP 8.13 Mon 17:30 P2/1OG

Embryonic lateral inhibition as optical modes — •Jose Negrete Jr and Andrew C Oates — École Polytechnique Fédérale de Lausanne

Spatial gene expression patterns define regions where specialised cells emerge within an embryo. Lateral inhibition is a common mechanism that creates fine grained patterns with a characteristic wavelength of

the size of 2 cells. Here we developed a generic model for patterning with lateral inhibition, and study its characteristics by making an analogy with crystal phonons from solid state physics. The tissue is redefined in terms of a Bravais lattice where the basis of the crystal contains two to three cells. The steady states are analogous to the optical modes of phonons. The model predicts that there are two different lateral inhibition states that can coexist in a certain parameter regime. Finally, our work suggests that gene expression patterns can be thought as crystal phonons, where long wavelength (Turing like) patterns corresponds to accosting modes and lateral inhibition patterns to optical modes.

Reference: Negrete Jr J and Oates AC, Phys Rev E 99, 042417 (2019)

BP 8.14 Mon 17:30 P2/1OG

A theoretical framework to describe influence of electric field on Mesechymal cell differentiation — •Jonathan Dawson[1], Ursula van Rienen[1,2,3], and Revathi Appali[1,3] — [1]Institute of General Electrical Engineering, University of Rostock, Albert-Einstein-Str.2, 18059, Rostock — [2]Life, Light and Matter, Interdisciplinary Faculty, University of Rostock — [3]Ageing of Individuals and Society, Interdisciplinary Faculty, University of Rostock

Bone regeneration is a highly complex and tightly regulated process. Concerted and controlled action of human mesenchymal stem cell (hMSC) proliferation and differentiation into osteoblasts is pivotal in bone regeneration. Multiple biochemical and physiological factors influence the osteogenic differentiation and proliferation of hMSCs. Electromagnetic field (EMF) stimulation has been successfully used for the treatment of bone disorders. However, it is still unclear how exactly EMF influences the MSC dynamics. In close collaboration with experiments, we developed a theoretical framework to understand the effect of externally applied electric fields on hMSCs. In experiments, hMSCs were cultured in a chamber exposed to low-frequency electrical field applied via a transformer-like-coupling (TLC) [Hess et al. (2012)]. Cell differentiation was measured by cell alkaline phosphate (ALP) activity. Our mean-field theory describes the dynamics of a population of ALP stained hMSCs and takes into account cell division, cell apoptosis, cell differentiation, and intracellular ALP activity. Our model can account for the differences in the experimentally observed time course behaviour of total number of cells and the total ALP activity.

BP 8.15 Mon 17:30 P2/1OG

Arrhythmogenicity Test Based on a Human Induced Pluripotent Stem Cell (iPSC)-Derived Cardiomyocyte Layer — •Konstantin Agladze — Moscow Institute of Physics and Technology, Dolgoprudny, Russian Federation

In vitro screening for potential side-effects of drugs on human induced pluripotent stem cell-derived cardiomyocytes is cutting-edge technology in pharmaceutical industry. The using iPSC-CM is considered as a part of comprehensive battery for an accurate and complex mechanistic-based assessment of the proarrhythmic potential of drugs. Induced pluripotent stem (iPS) cells from a healthy individual were differentiated into a cardiomyocyte monolayer that was identified by immunocytochemistry and the patch-clamp technique also considering of the potential impact of the developing phenotype of the iPSC-CMs. To study the occurrence of reentry as a precursor to arrhythmias, a standard obstacle was created in the cell layer. With the aid of optical mapping, the measure of arrhythmogenicity was determined, as defined by the probability of a reentry occurrence for the particular frequency of stimulation. A change in the potassium current corresponding to LQTS type 2 at frequencies matching high heart rates was demonstrated visually and quantitatively. Also, the efficiency of this method for quantifying both the effectiveness and ineffectiveness of drugs for a particular donor and for determining the donor*s cardiovascular disease risk zone was tested.

BP 8.16 Mon 17:30 P2/1OG

The role of geometry and cell-cell communication in the migration of anterior visceral endoderm cells — Jonathan Fiorentino[1,2,3] and •Antonio Scialdone[1,2,3] — [1]IES, Helmholtz Zentrum München, Germany — [2]IFE, Helmholtz Zentrum München, Germany — [3]ICB, Helmholtz Zentrum München, Germany

The migration of Anterior Visceral Endoderm (AVE) cells during early mouse embryonic development is crucial for the establishment of an anterior-posterior axis. AVE cells might move in response to a shallow gradient of a molecular cue. Prior to migration, they form multicellular rosettes, structures in which five or more cells meet at a central point, whose functional role is still unknown.

Relying on the Local Excitation Global Inhibition model (LEGI), which considers the presence of a local and a global molecular reporter as the mechanism of gradient sensing, we explore the hypothesis that rosettes' formation enhances cell-cell communication, increasing the cells' ability to measure external signals.

We extend the LEGI model to a 2D system where all the cells or only a subset of them can exchange molecular signals. We characterize the gradient sensing ability of cells adopting different geometric configurations, which suggests that the spatial arrangements of AVE cells in the embryo likely maximize their ability to measure weak gradients of external signals. Furthermore, we identify the transcriptional differences between AVE and VE cells and the active signalling pathways through the analysis of single-cell RNA-sequencing data collected from mouse embryos at the migration stage.

BP 8.17 Mon 17:30 P2/1OG

A multidisciplinary approach to defining the identity and dynamics of adult gastric isthmus stem cells — •Seungmin Han[1,2], Juergen Fink[2], Jong Kyoung Kim[3], Benjamin Simons[1,2], and Bon-Kyoung Koo[4] — [1]WT-CRUK Gurdon Institute, Cambridge, UK — [2]WT-MRC Cambridge Stem Cell Institute, Cambridge, UK — [3]DGIST, Daegu, Republic of Korea — [4]Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA), Vienna, Austria

The gastric corpus epithelium is the thickest part of the gastrointestinal tract and is characterized by rapid tissue turnover. Several markers have been proposed for gastric corpus stem cells in both isthmus and base regions. However, the identity of isthmus stem cells (IsthSCs) and the interaction between distinct stem cell populations is still usnder debate. Here, based on unbiased genetic labeling and biophysical modeling, we show that corpus glands are compartmentalized into two independent zones, with actively-cycling stem cells maintaining the pit-isthmus-neck region and slow-cycling reserve stem cells maintaining the base. Independent lineage tracing based on Stmn1 and Ki67 expression confirmed that rapidly-cycling IsthSCs maintain the pit-isthmus-neck of corpus glands. Finally, single-cell RNA-seq analysis is used to define the molecular identity and lineage relationship of a single, cycling, IsthSC population. These observations define the identity and functional behavior of IsthSCs.

BP 8.18 Mon 17:30 P2/1OG

Trajectories of cell shape and state during cellular fate transitions — •Wolfram Pönisch[1,2], Agathe Chaigne[1], Irene Aspalter[1], Guillaume Salbreux[3], and Ewa Paluch[1,2] — [1]MRC Laboratory for Molecular Biology, University College London, London, UK — [2]Department of Physiology, Development and Neuroscience, University of Cambridge, Cambridge, UK — [3]Francis Crick Institute, London, UK

To form complex organisms, cells specialize to perform different tasks, a process called differentiation. The required cellular fate transitions are often accompanied by cell shape changes and there are strong indications that cell shape and state are coupled.

Here, we present a pipeline to quantify and analyze cell shapes during cellular fate changes. We will present how the high-dimensional morphometric features of cell shapes for different cellular states can be quantified and projected to a low-dimensional space with the help of dimensional reduction techniques. To identify clusters of cells and classify cells based on those clusters, we use a variety of machine learning algorithms. We can then study the trajectories of cell shape and cell state markers while cells transition between distinct states.

We use our pipeline to investigate the coupling between cell shape and fate during the exit from naïve pluripotency in mouse embryonic stem cells. We find that cells can be classified into two unambiguously distinguishable clusters, and investigate the shape and state trajectories of cells, transitioning from a spherical shape towards a spread morphology.

BP 8.19 Mon 17:30 P2/1OG

Challenging the cancer stem cell hypothesis: Markov model-based evaluation of Glioblastoma cell plasticity — Thomas Buder[1], Andreas Deutsch[2], and •Anja Voss-Böhme[1] — [1]University of Applied Sciences Dresden — [2]TU Dresden

For glioblastoma (GBM) and other cancers, intra-tumoral phenotypic heterogeneity has been proposed to rely on cancer stem cells (CSC) postulated to reside at the apex of a hierarchical organization and to sustain tumor progression and heterogeneity by generating differenti-

ated progeny. Analyzing flow cytometry data of glioblastoma multiforme cell lines under normaxia and hypoxia with the help of stochastic Markov process models, we show that GBM phenotypic heterogeneity arises from non-hierarchical, reversible state transitions, instructed by the microenvironment and predictable by mathematical modeling. We introduce a method for automated parameter estimation and prognosis from time-course cell proportion data which supports the analysis of the hierachical pattern underlying the transition structure. This method is implemented in a freely available R package, Cell Trans.

(1) A. Dirkse, A. Golebiewska et al. Nature Comm. (2019).
(2) T. Buder et al. Front. Onc.(2019).
(3) T.Buder et al. Bioinformatics and Biology Insights (2017).

BP 8.20 Mon 17:30 P2/1OG

The morpho-rheological phenotype of hematopoietic stem cells as a novel marker for transplantation — •Angela Jacobi[1,2,3], Ahmad A Nawaz[1,2], Martin Kräter[1,2], Martin Bornhäuser[3], and Jochen Guck[1,2] — [1]MPL, Erlangen, Germany — [2]BIOTEC, TU Dresden, Dresden, Germany — [3]University Hospital Carl Gustav Carus, TU Dresden, Dresden, Germany

Hematopoietic stem cells (HSCs) are transplanted after chemotherapy to reconstitute all blood cells. Unfortunately, analysis of their surface protein expression by standard flow cytometry does not yield functional information. Morpho-rheological properties of HSCs, determined predominantly by the cells cytoskeleton, play an important role for their function and can serve as a label-free marker for their identification. Numerous methods to measure morpho-rheological properties of cells are currently available, but most of them are limited in the ability to screen large heterogeneous populations in a robust and efficient manner, a feature required for successful translational applications. With real-time deformability cytometry (RT-DC) mechanical properties of cells in suspension can be screened continuously at rates of up to 1,000 cells/s, similar to conventional flow cytometers, which makes it a suitable method for HSC screening. Based on RT-DC measurements, we establish here a specific morpho-rheological fingerprint of HSCs that allows to distinguish them from all other blood cell types. We further show that this morpho-rheological phenotype allows for sorting of HSCs from heterogeneous human bone marrow samples, which could find practical application in HSC transplantation.