Dynamic real-time deformability cytometry: High-throughput single cell rheology in complex samples

Bob Fregin[1, 4], Fabian Czerwinski[1], Doreen Biedenweg[2], Salvatore Girardo[3], Stefan Groß[2, 4], Konstanze Aurich[2], Oliver Otto[1, 4]

[1]*University of Greifswald, ZIK HIKE, Greifswald, Germany*

[2]*University Medicine Greifswald, Greifswald, Germany*

[3]*Technical University of Dresden, Biotechnology Center, Center for Molecular and Cellular Bioengineering, Dresden, Germany*

[4]*University Medicine Greifswald, Deutsches Zentrum für Herz-Kreislauferkrankungen (DZHK), Greifswald, Germany*

In life sciences, the material properties of suspended cells have attained significance close to that of fluorescent markers but with the advantage of label-free and unbiased sample characterization. Until recently, cell rheological measurements were either limited by acquisition throughput, excessive post processing, or low-throughput real-time analysis. Real-time deformability cytometry [1] expanded the application of mechanical cell assays to fast on-the-fly phenotyping of large sample sizes, but has been restricted to single material parameters as the Young's modulus.
For comprehensive cell rheological measurements of elasticity and viscosity on a millisecond time-scale we developed dynamic real-time deformability cytometry (dRT-DC) [2]. Utilizing Fourier decomposition, dRT-DC is capable to disentangle cell response to complex hydrodynamic stress distributions found in almost all microfluidic systems.
We demonstrate that reconstruction of cell deformation from odd Fourier components only, provides a measure that is governed by the steady state flow inside the channel but not by entrance or exit effects.
This system is capable to determine viscoelastic properties of suspended cells at a rate of up to 100 cells/s. As a first application we show a rheological characterization of all major blood cell types including the label-free discrimination of B- and CD4+ T-lymphocytes.

[1] O. Otto et al. Nat. Meth. 12, 199-202 (2015).
[2] B. Fregin et al., Nat. Commun. 10, 415 (2019).