Supplementary Information:

A microrheological examination of insulin-secreting β-cells in healthy and diabetic-like conditions

Lukas Woolley [1], Adam Burbidge [2], Jan Vermant [1], Fotis Christakopoulos [1,*]

1. Department of Materials, ETH Zurich, Vladimir-Prelog-Weg 5, Zurich, 8093, Switzerland;
2. Nestlé Research Center, Route de Jorat 57, vers-chez-les Blanc, 1000 Lausanne, Switzerland;

$*$ Corresponding author

1 Transformation to frequency domain

The relationship between the MSD of a microsphere in a viscoelastic medium and the shear creep compliance, $J(t)$, of said fluid is given through a simple linear relation:

$$\left\langle \Delta r^2 \left(\tau\right)\right\rangle = \frac{dk_BT}{3\pi a} J(t) \qquad , \tag{S1}$$

where k_B denotes the Boltzmann's constant, T is the absolute temperature, d the dimensionality and a is the radius of the tracer particle. In principle, the transformation from the creep compliance, $J(t)$, which exists in the time domain,to the frequency-dependent viscoelastic moduli, $G'(\omega)$ and $G''(\omega)$, requires a rigorous conversion through a Fourier transformation.[1] To limit artifacts in the transformed data through the direct transformation in discrete time steps, an approximate method proposed by Mason[2] was used. This is based on a power law description of the change of the local MSD at any given time point. The power law behavior comes from the logarithmic derivative of the MSD $\alpha(\omega)$, which is in the range of $0-1$, where 0 and 1 would

correspond to a particle in a purely elastic and a purely viscous medium, respectively:

$$\alpha(\omega) = \frac{\partial ln \left\langle \Delta r^2(\frac{1}{\omega}) \right\rangle}{\partial ln \frac{1}{\omega}} \qquad . \tag{S2}$$

From that point the magnitude of the complex modulus $G^*(\omega)$ can be estimated to be:

$$|G^*(\omega)| = \frac{k_B T}{\pi a \left\langle \Delta r^2(\frac{1}{\omega}) \right\rangle \Gamma[1+\alpha(\omega)]} \qquad , \tag{S3}$$

where Γ represents the Gamma function which can be estimated to be $\Gamma[1+\alpha] \approx 0.457(1+\alpha)^2 - 1.36(1+\alpha) + 1.90$. A detailed analysis is presented in Desgupta et al.[3] where the idea of Mason[2] is expanded up to 2*nd* order. The frequency dependent elastic and storage moduli, $G'(\omega)$ and $G''(\omega)$, can than be obtained from:

$$\begin{aligned} G'(\omega) &= |G^*(\omega)| \, cos(\pi\alpha(\omega)/2) \qquad , \\ G''(\omega) &= |G^*(\omega)| \, sin(\pi\alpha(\omega)/2) \qquad . \end{aligned} \tag{S4}$$

Frequency-domain representation enables a more clear view of the different relaxation times, and Fig. S 1A-B show the apparent viscoelastic moduli, calculated from the MSD, of course subject to the limitations presented in section 2.6. The resulting values of the moduli are in agreement with those measured in other cell types.[4,5,6,7] The magnitude and frequency dependency of the storage (G') and loss (G'') moduli reflect the same information as the time dependence of the creep compliance (Fig. 5). The magnitude of G' increases upon stimulation with glucose, which can be associated with an increase of intracellular stiffness, similar to the decrease in $J(t)$. The crossover-point indicates at which frequency the response transitions from a more fluid-like character to a more solid-like character, it shifts to lower frequencies upon stimulation of the healthy cells, consistent with a stiffening and slowing down of the network. The relaxation time, calculated as the inverse of the crossover frequency, corresponds to 0.8 s and 7 s for the fasting and stimulated state, respectively. In contrast, the relaxation time is substantially larger for the PA-treated cells, corresponding to 60 s for the stimulated cells, while not being observable, in the measured frequency range, for the fasting ones. The observed increase in relaxation time

for the PA-treated case suggests that the control fidelity through cytoskeleton remodeling is deficient compared to the control. No clear plateau is observed in any condition at the measured frequency range, with the healthy starving condition showing the least pronounced one.

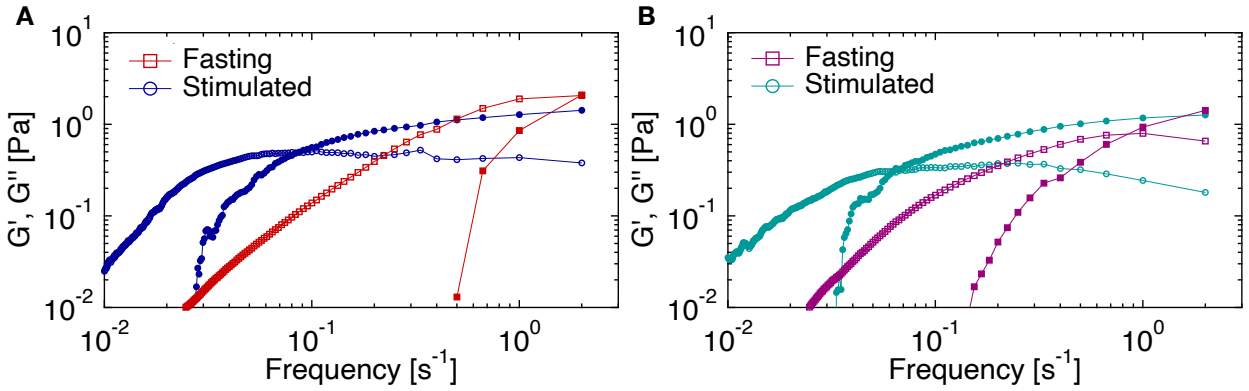

Figure S 1: Frequency-domain representation: Storage modulus (G', solid symbols) and loss modulus (G'', open symbols) as a function of frequency for (A) control and (B) PA-exposed cells. Square and circle symbols correspond to fasting and glucose-stimulated conditions, respectively.

2 Ergodicity breaking and noise-terms

The autocorrelation function of all the evaluated conditions show a slight negative correlation between two following frames, indicating some elasticity in the probed system (Fig. S 2A). The histograms of Fig. S 2B-C show the velocity distribution of the evaluated conditions. Seemingly, the excess curtosis does not change drastically between the different cases, further supporting the claim that the condition can be evaluated and compared to each other and professedly without having a considerably different non-thermal noise contribution between the analyzed conditions.

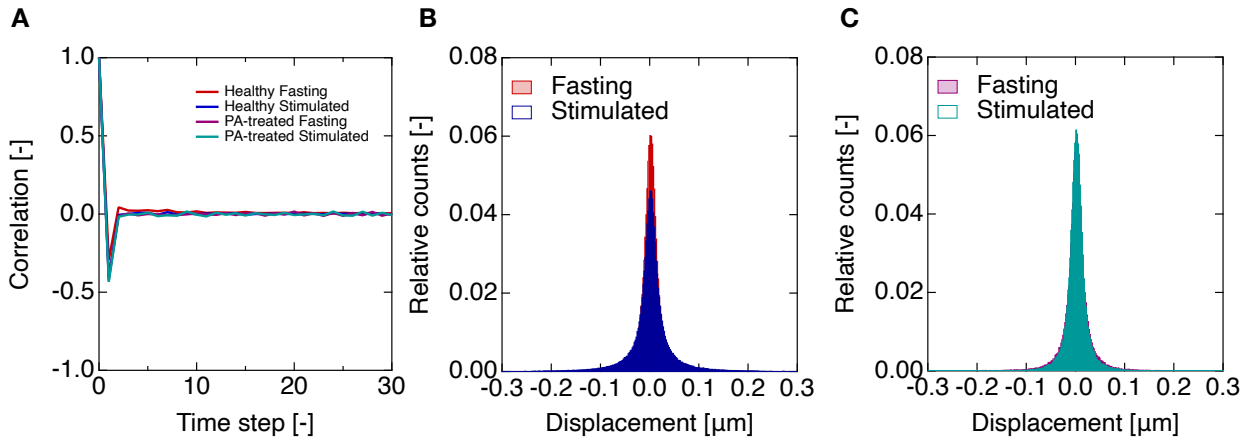

Figure S 2: (A) Normalized autocorrelation function of individual tracks for different cases. Velocity histograms for control (B) and PA-treated (C) cells for both fasting and stimulated conditions, normalized by the total count of steps.

References

[1] M. Baumgaertel and H. H. Winter. Determination of relaxation and retardation spectra from dynamical mechanical data. *Rheologica Acta*, 28:511–519, 1989.

[2] Thomas G. Mason. Estimating the viscoelastic moduli of complex fluids using the generalized Stokes-Einstein equation. *Rheologica Acta*, 39:371–378, 2000.

[3] Bivash R. Dasgupta, Shang You Tee, John C. Crocker, B. J. Frisken, and D. A. Weitz. Microrheology of polyethylene oxide using diffusing wave spectroscopy and single scattering. *Physical Review E - Statistical Physics, Plasmas, Fluids, and Related Interdisciplinary Topics*, 65(5):051505–1–051505–10, 2002.

[4] Soichiro Yamada, Denis Wirtz, and Scot C. Kuo. Mechanics of living cells measured by laser tracking microrheology. *Biophysical Journal*, 78(4):1736–1747, 2000.

[5] Brenton D. Hoffman, Gladys Massiera, Kathleen M. Van Citters, and John C. Crocker. The

consensus mechanics of cultured mammalian cells. *Proceedings of the National Academy of Sciences of the United States of America*, 103(27):10259–10264, 2006.

[6] John C Crocker and Brenton D. Hoffman. Multiple-Particle Tracking and Two-Point Microrheology in Cells. *Methods in Cell Biology*, 83:141–178, 2007.

[7] Denis Wirtz. Particle-tracking microrheology of living cells: Principles and applications. *Annual Review of Biophysics*, 38:301–326, 2009.