Nonlinear Fibroblast Mechanics: A story of history

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Cell mechanics is a key player in development, disease and many other biological processes. Living cells exhibit a complex nonlinear response to mechanical cues, which is not understood yet. A stiffening as well as softening is observed, depending on the stimulus and the experimental technique. Here, we apply large amplitude oscillatory shear (LAOS) to a monolayer of fibroblast cells using the cell monolayer rheology technique [1][2]. We find that the nonlinear cell response not only depends on the amplitude and the frequency of oscillations. Moreover, it is highly susceptible to a mechanical preconditioning. Cell response can exhibit hallmarks of nonlinear viscoelasticity, elastoplastic kinematic hardening or inelastic fluidization for the same steady state oscillations. Experimental results indicate that a preconditioning changes cytoskeletal network structure in a rate dependent way. Network alterations can be driven by passive filament reorganizations, filament rupture and the binding/unbinding of crosslinking proteins. We speculate that the pronounced strain path dependence of nonlinear cell response might obscure the underlying universality of nonlinear cell mechanics on a microscopic scale. Our results highlight the interplay between viscoelastic and inelastic contributions to the cell mechanical response.

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