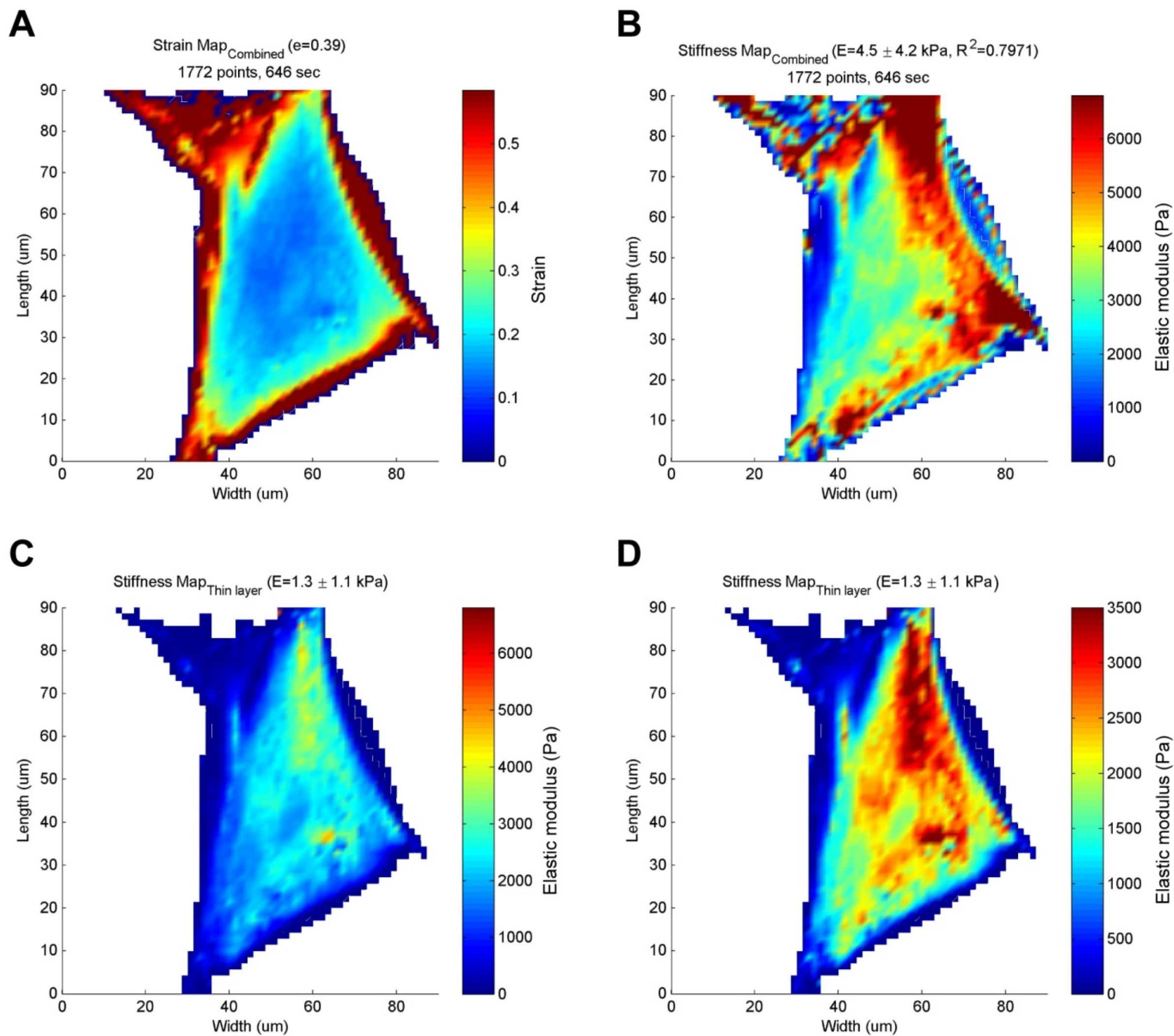
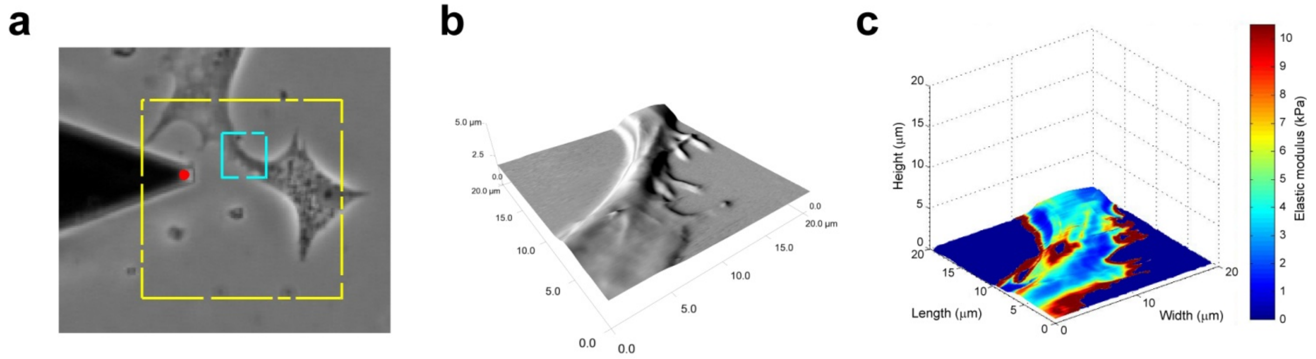
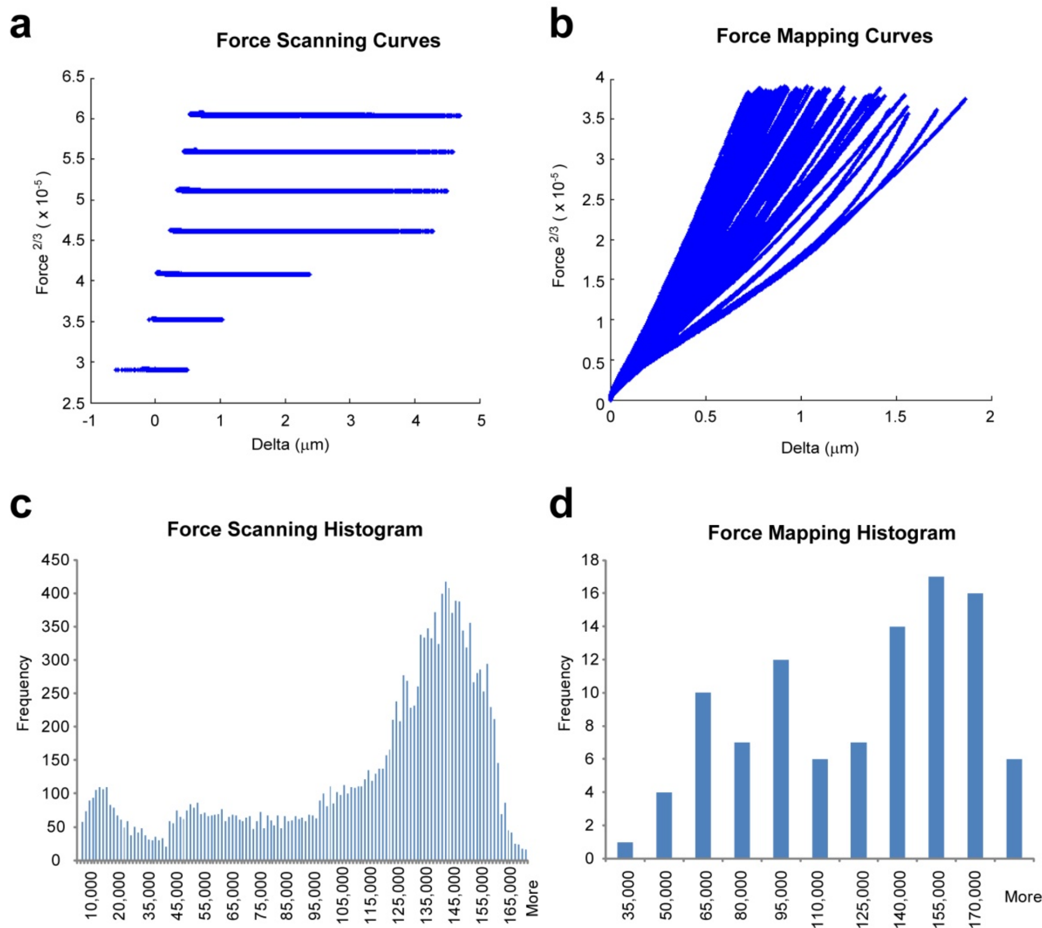


Supplemental Figure 1. Estimated compressive strains were calculated across a sample cell. The height of each point on the cell was determined by AFM topographical data. Probe-cell contact points were extrapolated by extending fits to the linearized Hertz model through the x-axis. These estimated contact points provided gross height and indentation measurements that could be used to calculate local compressive strains. As predicted, higher strains are observed for the outer regions of the cell where it is thinnest (A). If a thin-layer correction factor is used that accounts for the underlying rigid substrate [1], then the resulting modulus map exhibits much lower values for the peripheral regions of the cell (B vs. C). Future work will incorporate thin-layer modeling into the full analysis rather than using an a priori correction. It should be noted that the general trends observed without correction still exist: cytoskeletal elements have higher moduli than cytoplasmic and nuclear regions. This finding has been observed for other cell types, including fibroblasts [2], astrocytes [3], and kidney cells [4].



Supplemental Figure 2. Force scanning with a pyramidal tip showed a detailed mechanical property map for two touching ASCs (a, yellow box depicts maximum scan area, blue box depicts sample region). Assuming the pyramid-modified Hertz model holds for a sharp tip indenter during force scanning, this approach could help decrease convolution effects while increasing resolution. However, this image emphasizes the difficulty in capturing accurate representations of living cells. Movement of cell filopodia is revealed by discrepancies between the height image (b) and modulus map (c). The trade-off between testing duration and image quality is a common concern when imaging living samples.



Supplementary Figure 3: Force-indentation curves (Force$^{2/3}$ vs. Delta) were generated for every point across the cartilage ECM-PCM region shown in Figure 5. The force scanning data (a) show 16,384 curves (128 x 128 pts), while the force mapping data (b) show 100 curves (10 x 10 pts). The slope of each individual curve defines the Young's modulus for that point. For presentation purposes, the contact point was also extrapolated from the slope of the data. If discontinuities existed, such as for the right-most points in (a), the total indentation distance could be incorrectly estimated (i.e. 6 μm of indentation instead of 1-2 μm). Fortunately, the calculated modulus values do not depend on this extrapolated contact point, so the error is contained only to graphical aberrations as seen in the data above. Histograms depicting the frequency of Young's modulus values across the sample regions are shown for force scanning (c) and force mapping (d). The large peaks on the right represent the stiffer ECM regions, which comprise the majority of the area tested, and hence, greater frequencies. The low stiffness peak represents the inner portion of the PCM, while the transition region between PCM-ECM is represented by the range of middle-stiffness values.

Supplemental section references

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