Questions for Professor Benny Geiger

Q: Are minor fluctuations of pH in the cell vicinity implicated in the cell response to mechanical triggers?

A: As per the effect of minor pH fluctuations - I am not aware of a systematic recent study, but could refer to 2 relevant observations. Long ago we have isolated ventral membranes of cultured cells and noticed that switching the pH of the medium from \sim 7.0 to \sim 6.0 increased dramatically the adhesion of the ventral membrane of the cells to the substrate, visualized by interference reflection microscopy (see Fig 4

in https://www.weizmann.ac.il/immunology/Geiger/sites/mcb.Geiger/files/Avnur_J%20Mol%20Biol_12_81 _51_0.pdf). The effect was used for isolation of attached ventral membranes, but also suggested that close contacts (not focal adhesions, particularly) can involve ionic interactions.

Q: Do you think that the concept of tensegrity (as popularized by D. Ingber <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4112545/</u>) is a good approximation for cellular biomechanics?

A: Surely the concept introduced by Don Ingber had an impact on the research community and contributed to the early development of the field of mechanobiology. As I see it, the tensegrity concept, beyond telling us that the cell in elastic, maintaining a balance between contractile and rigid elements, raises interesting question about the dynamic molecular processes that regulate the interplay between the different mechanical networks within the cells, and their reorganization upon internal or external perturbation.

Q: Thinking about even more complex systems – mechanics in tissues. How much these properties of adhesion complexes you described (e.g., vinculin conformational changes in response to forces) may change when moving from adherent cells to tissues, where cells are exposed to more of 3-D type interactions with not only cell adhesion to substrates but also cell-cell adhesions and interactions with other cells within the tissue?

A: Focal adhesion-like strictures (with vinculin and all the others, do exist (of course) in real tissues, but their configuration was hardly addressed, mainly due to the limited information on local forces and rigidities is intact tissues, and the difficulty of data collection in 3D. which will be essential. If I had to choose a system to study in vivo, I would have probably tried smooth muscle, where such structures are rather prominent.