Generation of AFM cellular datasets and classification by ML

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Background incl. aims
Mechano-biological measurements have the potential to distinguish healthy cells from pathological cells. Since 2007, a number of articles have shown that metastatic cancer cells have a Young's modulus (or elastic modulus) measured by atomic force microscopy (AFM) on living cells that is significantly lower than that of benign cells. However, cells are not inert and purely elastic materials, but dynamic and viscoelastic systems.

Methods
In order to measure these viscoelastic properties in living cells, we carried out dynamic mechanical analysis (DMA) measurements using AFM. After indenting a cell, we apply a strain and record the stress. The strain is proportional to the pulsation and therefore to the 6 frequencies we chose (from 1 to 200 Hz), and the stress is proportional to the phase shift of this pulsation. Knowing the strain and stress, we can then calculate G' (shear storage) in phase with the strain and G'' (shear loss) in phase with the strain rate. In our study, we sought to classify a population of cancer cells from a population of non-cancer cells. On each cell, 16 force curves (FC) and 19 characteristics/FC, corresponding to the viscoelastic properties and constituting a part of the mechanome, were calculated.

Results
All the FCs were then classified using machine learning (ML) tools with a statistical approach based on a fuzzy logic algorithm, trained to discriminate between non-malignant and cancerous cells (training basis, up to 51 cells/cell line). The proof of concept was carried out on non-malignant (RWPE-1) and cancerous (PC3-GFP) prostate cell lines.

Conclusion
After developing an algorithm to automate AFM measurements, we were able to measure 141 cells in dynamic mechanical analysis and demonstrated the ability of our method to correctly classify between 68 and 74 % of cells (31 cells in the test base/cell line).

Keywords:

AFM, DMA, viscoelasticity, ML, classification

Reference:

(Cross et al. 2007), (Wang et al. 2021), (Proa-Coronado et al. 2019), (Hedjazi et al. 2015)