High-Cycle Dynamic Cell Fatigue with Applications on Oncotripsy

Erika Figueroa-Schibber

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The method of Oncotripsy (from Greek, *onco*- meaning “tumor" and –*tripsy* “to break") exploits aberrations in the material properties and morphology of cancerous cells to target them selectively using tuned low-intensity pulsed ultrasound. Compared to other noninvasive ultrasound treatments that ablate unhealthy tissue, oncotripsy has the capability of targeting unhealthy tissue with minimal damage to healthy cells in the ablation process.

We propose a model of oncotripsy that follows as an application of cell dynamics, statistical mechanical theory of network elasticity and 'birth-death' kinetics to describe processes of damage and repair of the cytoskeleton. We also develop a reduced dynamical model that approximates the three-dimensional dynamics of the cell and facilitates parameter studies, including sensitivity analysis and process optimization. The dynamical system encompasses the relative motion of the nucleus to the cell membrane and a state variable measuring the extent of damage to the cytoskeleton. The dynamical system evolves in time as a result of structural dynamics and kinetics of cytoskeletal damage and repair. The resulting dynamics are complex and exhibits behavior on multiple time scales, including the period of vibration and attenuation, the characteristic time of cytoskeletal healing, the pulsing period and the time of exposure to the ultrasound. Damage on the cells develops in the order of millions of ultrasound cycles, and the failure mechanism is explained as a fatigue process. We also account for cell variability and estimate the attendant variance of the time-to-death of a cell population. We show that the dynamical model predicts---and provides a conceptual basis for understanding---the oncotripsy effect and other trends observed in experiments.