A Lesson in Cartilage Therapy: Do Chondrocytes Utilize Mechanical Energy from Exercise for Cell Maintenance and Growth?

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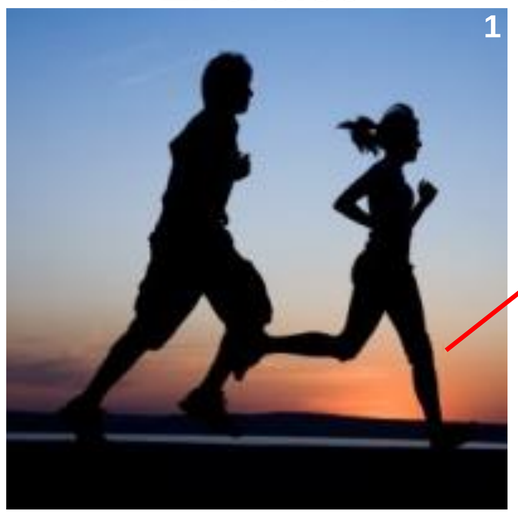
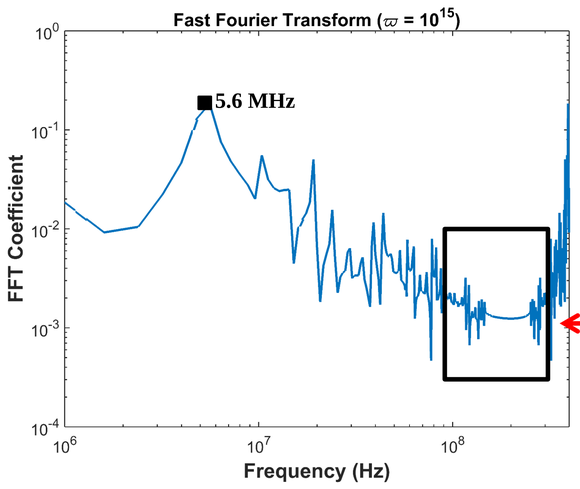
Introduction:

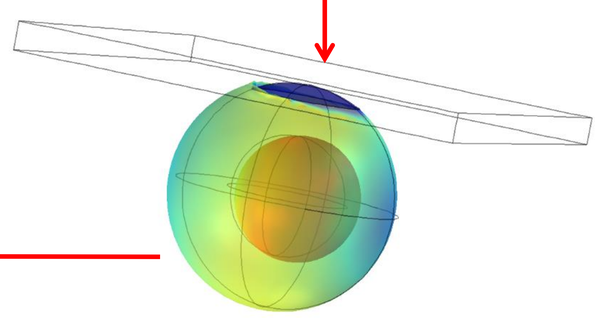
Exercise



causes impact on cartilage



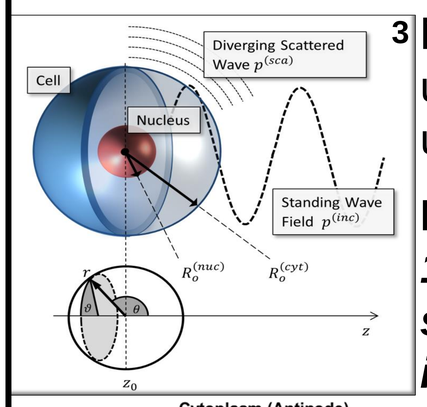
Impact causes high frequency vibrations in cells



Chondrocytes deform

Figure 1. Effect of chondrocytes stimulation by exercise

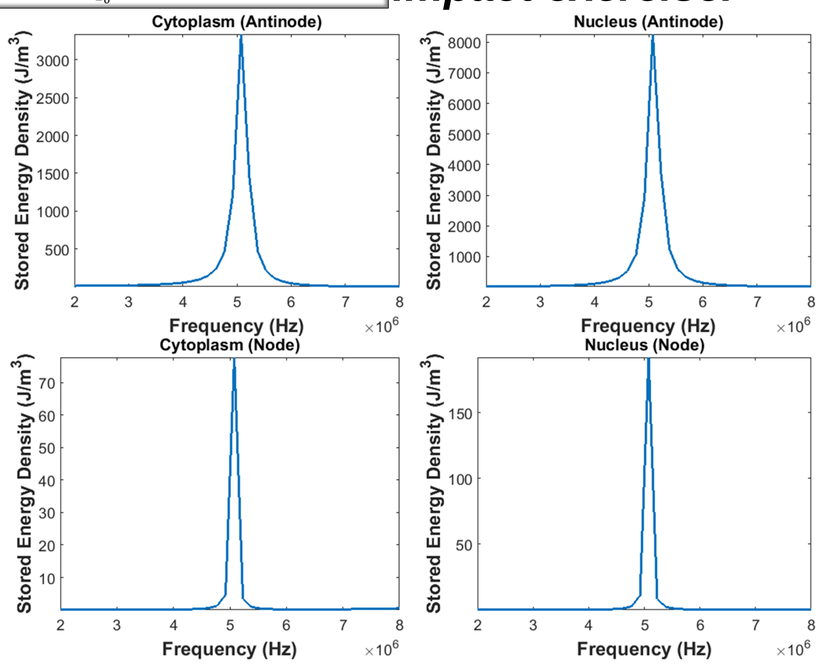
Connecting impact to ultrasound:

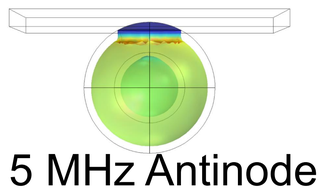


Model a chondrocyte in a standing ultrasound field at different frequencies using **Acoustics Module**.

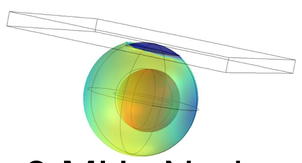
Model findings:

1. Resonance frequency from US study matches ringing frequency of impact exercise.





5 MHz Antinode



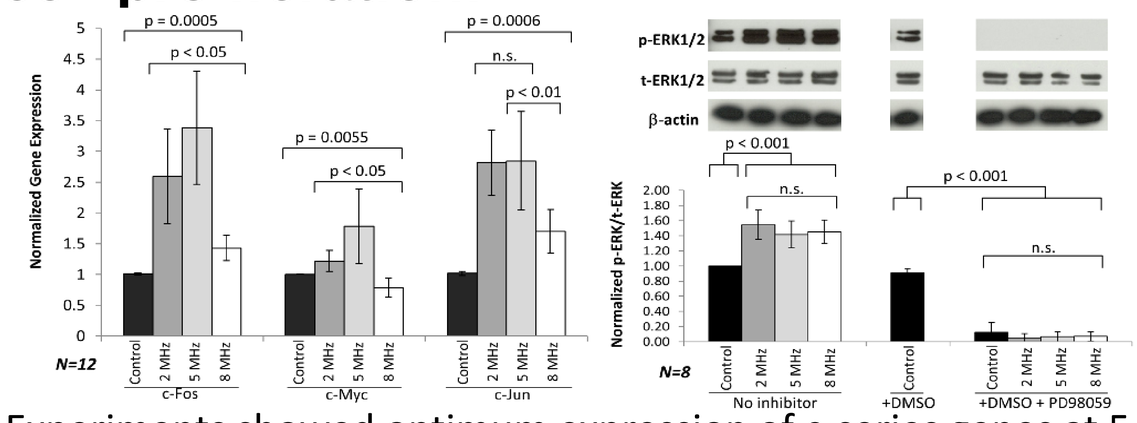
8 MHz Node

2. Only at resonance does mechanical energy couple into nucleus – storing 2x more than in cytoplasm.

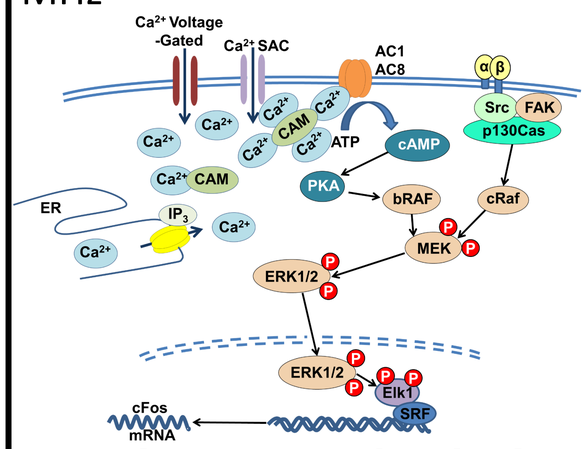
3. Impact causes periods of high mechanical energy density in nucleus.

Figure 2. Effect of chondrocyte stimulation by US

Linking mechanical energy in nucleus to cell proliferation:



Experiments showed optimum expression of c-series genes at 5 MHz[3]



Model cAMP/PKA/ERK Pathway

Postulate I: US increases pERK transport rates to/from nucleus

Result: Model does not support experiments.

Postulate II: Mechanical energy in nucleus strains chromatin and increases $k_1 = k_0 e^{-(f-f_r)^2}$

$$ELKPP + SRF \overset{k_1, k_{-1}}{\longleftrightarrow} ELK1PP \cdot SRF \overset{k_2}{\rightarrow} ELK1PP \cdot SRF + cFos$$

Result: Model matches experiments qualitatively

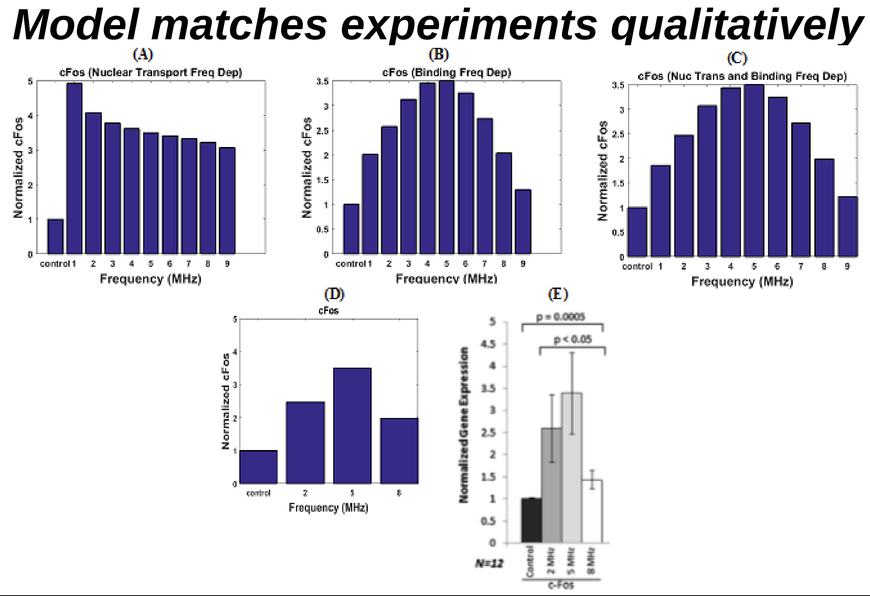


Figure 3. US effects on signaling pathway

Conclusions:

1. *Exercise causes chondrocytes to vibrate at primary resonance.*
2. *Only at resonance does mechanical energy couple in nucleus.*
3. *In vitro expression of c-genes, stimulated at different frequencies, confirms optimal cell activity at resonance.*
4. *Combining our two postulates provides strong evidence that mechanical energy can directly affect gene expression.*
5. *Chondrocytes benefit from exercise by linking mechanical energy to cell metabolics.*

References:
1. http://porchiaswish.com/blog/the-profound-effects-of-daily-running-on-anxiety-levels/
2. http://www.nyboneandjoint.com/articles/articular-cartilage-damage/
3. Louw, T.M., et al. Mechanotransduction of ultrasound is frequency dependent below the cavitation threshold. Ultrasound Med Biol. 39(7):1303-19, 2013.

Excerpt from the Proceedings of the 2015 COMSOL Conference in Boston