ABSTRACT FACE PAGE

1. **Presenting Author's name: _____Jacob Herrmann_____**
2. **Presenting Author's affiliation: _____Boston University_____**
3. **Presenting Author's title: _____Post-Doctoral Fellow_____**
4. **Presenting Author's email: _____jakeherr@bu.edu_____**
5. **Presenting Author's gender (optional): _____**
6. **Presenting Author's race (optional): _____**
7. **Presenting Author's ethnicity (optional): _____**
8. **Presenting Author's affiliation sector: (check one or more)**
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9. **Presenting Author's Career stage: (check one)**
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10. **Website / twitter handle / other public links (optional): _____ http://sites.bu.edu/ctmlab/__**
11. **Is this the research presented in this abstract supported by IMAG MSM-related U01 funding? Yes or No**
12. **If the Presenting Author is a trainee, who is the trainee's primary research advisor? ____Béla Suki_____**

TRAINEE POSTER AND ORAL PRESENTATION COMPETITONS:

New to the meeting this year, we are holding *both* a trainee poster competition and a trainee oral presentation competition! If the presenting author is a trainee (i.e., a student at any level or a post doctoral trainee), he/she may enter his/her abstract in the trainee poster competition, the trainee oral presentation competition, or both competitions. Trainees may also submit more than one abstract to the meeting and enter more than one abstract in these competitions. Prizes will be given to the presenters of the top-ranked trainee oral presentation and the top-ranked trainee poster (judged during the meeting by the Program Committee).

13. **If the Presenting author is a trainee, would the Presenting Author like to enter his/her abstract in the Trainee Poster Competition*? Yes or No**

*Note: Trainees who enter the poster competition are expected to stand by their poster during the scheduled poster sessions and present them to the judges.

14. **If the Presenting author is a trainee, would the Presenting Author like to enter his/her abstract in the Trainee Oral Presentation Competition**? Yes or No**

**Note: The Program Committee will select the top four abstracts from trainees who elect to enter their abstract into the trainee oral presentation competition, these four trainees will be notified by Feb. 17th, and they will deliver their oral presentations (which will be judged) on the second day of the meeting after lunch.

SELF-ORGANIZATION OF HONEYCOMBING IN AN AGENT-BASED MODEL OF LUNG FIBROSIS

[1]Jacob Herrmann*, [1]Samer Bu Jawde, [2]Dylan T. Casey, [2]Vitor Mori, [2]Jason H. T. Bates, and [1]Béla Suki
[1]Boston University, Boston, MA, USA; [2]University of Vermont, Burlington, VT, USA
email: jakeherr@bu.edu, website: http://sites.bu.edu/ctmlab/

BACKGROUND: Pulmonary fibrosis is a progressive disease involving abnormal interactions between fibroblasts and the extracellular matrix they normally regulate. We hypothesize that characteristic structural alterations occurring in fibrotic lungs (e.g. honeycombing) arise from the multiscale distributed mechanical stresses and strains developed in bulk lung tissue, alveolar septal walls, and individual collagen and elastin fibers. In previous work, an agent-based model was defined for fibroblast-mediated maintenance of collagen fiber stiffness, involving nonlinear rules for degradation (decreasing stiffness) related to mean strain, and repair (increasing stiffness) related to strain energy rate. The model exhibited a bifurcation in the behavior of a single agent-fiber pair, such that different applied forces produced one of two distinct equilibrium values in fiber stiffness. In this study, the previous 1D single-fiber model was extended into a 2D network of interconnected alveolar walls.

METHODS: Lung tissue was modeled as a 2D hexagonal network of nodes and springs, in which each spring represented an alveolar septal wall. Each spring was initialized with a randomized rest length and a linear force-elongation spring constant (or stiffness) sampled from normal distributions with coefficient of variation 0.2. Equilibrium network configurations were computed by minimizing the sum of net force magnitudes across all nodes. Tidal changes during breathing were simulated by two levels of force applied to boundary nodes of the network, representing end-expiratory pressure and driving pressure. Agent rules for degradation and repair were applied to every spring after each breath, using each spring's strain energy rate and mean strain. Simulations were conducted for 136 combinations of 17 different end-expiratory pressures and 8 different driving pressures. The primary measured outcome in each simulation was the spatial distribution of equilibrium spring stiffnesses after 400 iterations of agent-based degradation and repair.

RESULTS: For either low or high end-expiratory forces, alveolar walls were maintained to uniform stiffnesses. However for a range of intermediate end-expiratory pressure, tri-modal distributions of wall stiffness emerged (Fig. 1). Spatially, the most stiff walls were organized into ring-like structures surrounding the least stiff walls. Higher levels of driving pressure elevated the range of end-expiratory forces at which tri-modal stiffness was observed. Despite a small degree of randomized heterogeneity in initial conditions, there was no correlation between initial wall stiffness and final wall stiffness ($r^2 = 0.06$).

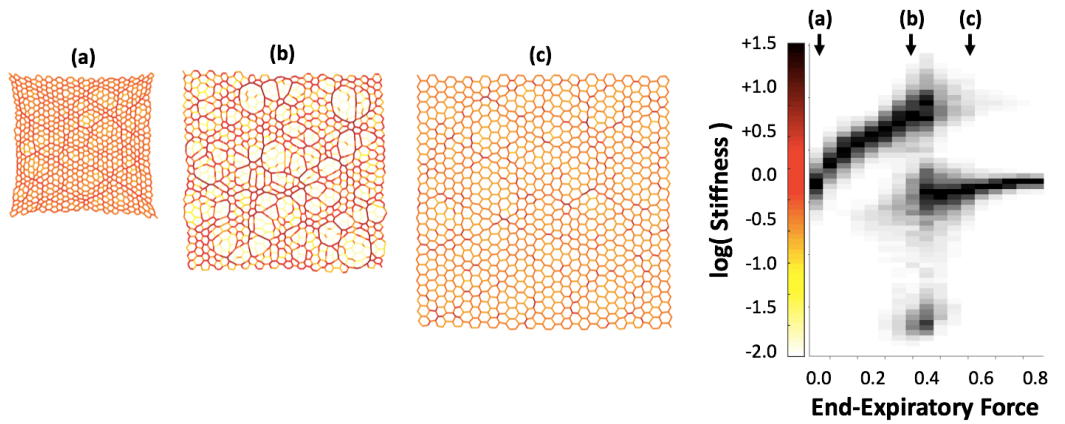

Figure 1: Final configurations of 2D spring networks representing alveolar walls colored by stiffness. Different boundary conditions for applied forces resulted in either uni-modal (a,c) or tri-modal (b) stiffness distributions. Tri-modal distributions exhibited self-organization into "honeycomb"-like patterns (b).

CONCLUSIONS: A 2D network model describing fibroblast-mediated maintainence of alveolar wall stiffness exhibited tri-modal distributions of alveolar wall stiffness. This finding is in contrast to the bi-modal predictions given by the same agent rules applied in a 1D model of individual agent-fiber interactions. Self-organizing ring-like structures resemble so-called "honeycombing" patterns that develop in pulmonary fibrosis. Although speculative, this model suggests that abnormal fibroblast behavior, or even normal fibroblast behavior under abnormal applied forces, may develop honeycombing patterns due to complex network interactions and biomechanical feedback. This may also explain why honeycombing appears first near the pleural surface, where stiffness gradients due to the stiff pleura and applied forces may be greater than in central lung tissue.