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Supplemental Information

Emergence of Collagen Orientation Heterogeneity in Healing Infarcts and an Agent-Based Model

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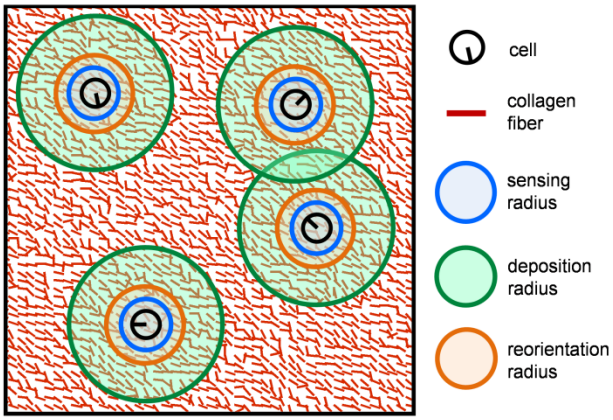

Figure S1: An agent-based model of fibroblast-mediated matrix remodeling.
The model was used to simulate fibroblasts that sense local fiber structure, orient, migrate, deposit collagen, reorient collagen, and degrade collagen. Cell sensing, deposition, and reorientation of collagen occurred over prescribed radii, which were varied in conjunction with varying remodeling rates in order to explore the sensitivity of regional heterogeneity in cell and collagen orientations to those parameters.

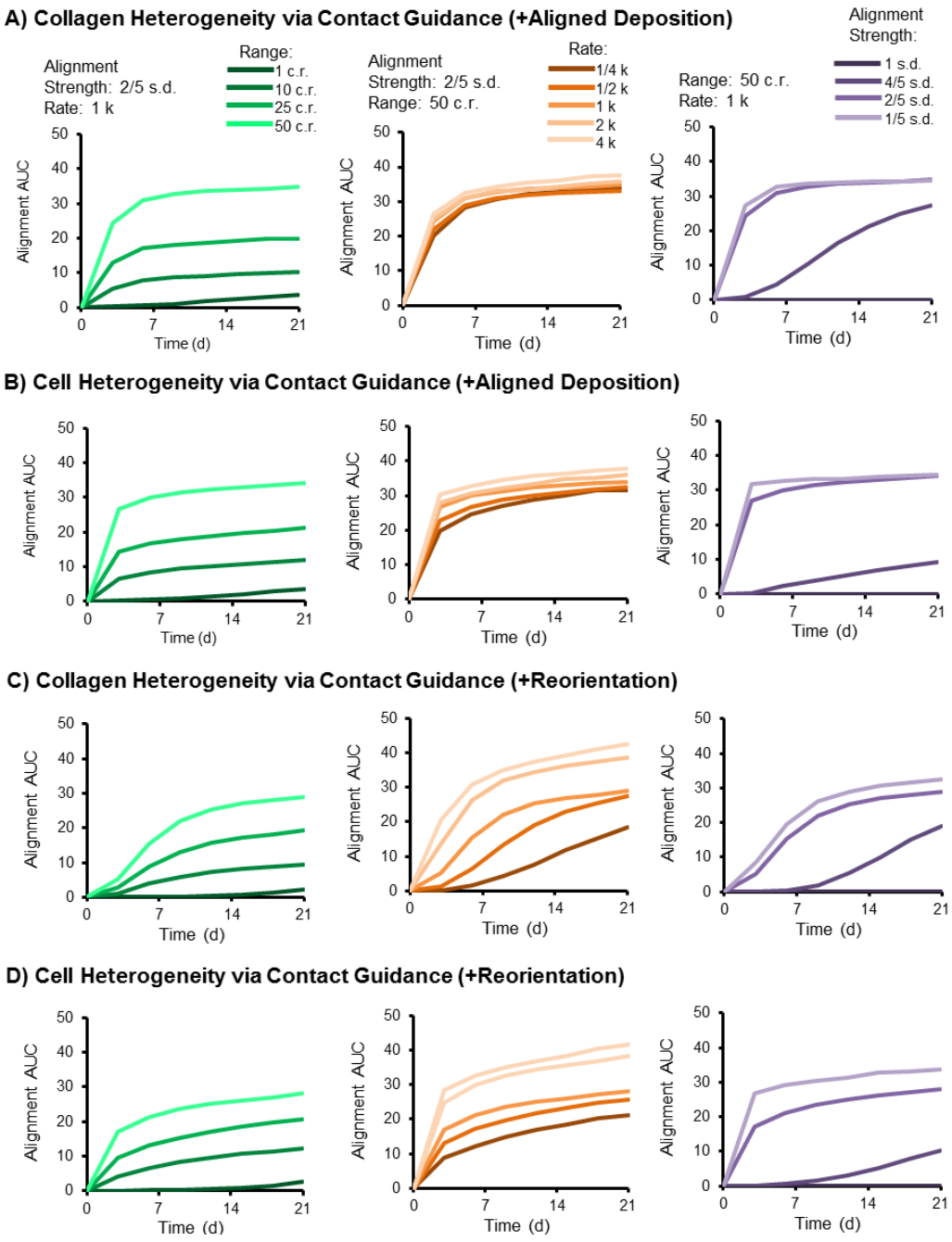

Figure S2: Orientation heterogeneity in long-range sensing simulations.
Cells were set to orient according to collagen fiber orientation distributions sampled across varying distances (i.e., sensing radius), but could only remodel fibers within direct contact (via reorientation or aligned deposition). Heterogeneity in both collagen fiber and cellular orientations (assessed as AUC from alignment vs. distance curves, see Figure 1) increased with the range of sensing (left column), the rate of remodeling (center column), and the strength of the cell alignment probability distribution (right column), but also depended upon the type of remodeling (A-B vs. C-D). Specifically, both long-range sensing with local aligned deposition and long-range sensing with local reorientation produced fiber and cell heterogeneity, aligned deposition generated heterogeneity early and remained steady through 3 weeks while reorientation emerged gradually, aligned deposition was relatively independent of remodeling rate while reorientation was highly dependent on rate, and fiber and cell heterogeneity only emerged at high cell alignment strengths.

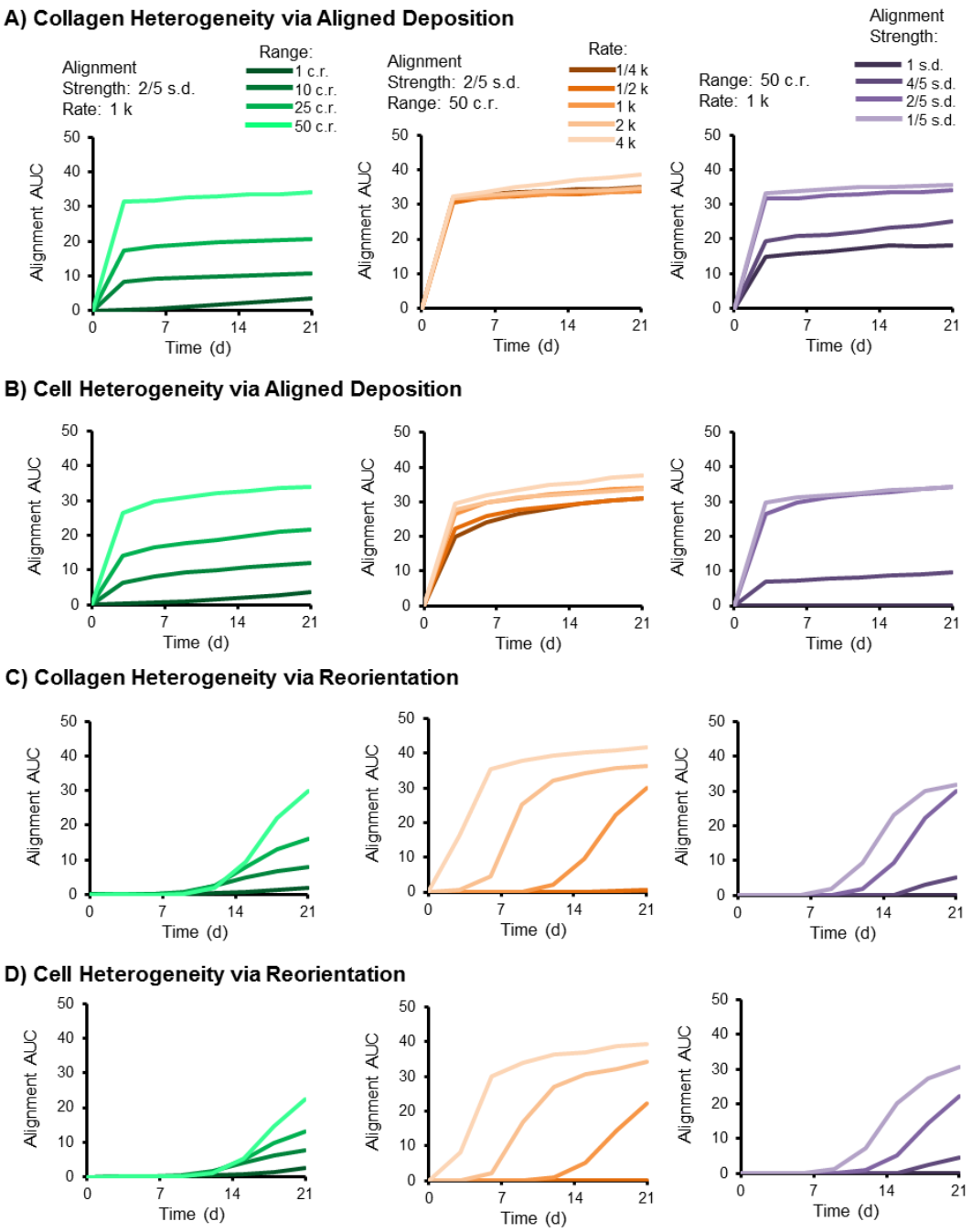

Figure S3: Orientation heterogeneity in long-range remodeling simulations.
Cells were set to remodel fibers across varying distances (i.e., reorientation radius or deposition radius), but could only sense orientation of collagen fibers within direct contact. The degree of regional heterogeneity in collagen fiber & cell orientations (assessed as AUC from alignment vs. distance curves) increased with the range of remodeling (left column), the rate of remodeling (center column), and the strength of the cell alignment probability distribution (right column), but also depended upon the type of remodeling (A-B vs. C-D). Specifically, both long-range aligned deposition and long-range reorientation produced fiber and cell heterogeneity, aligned deposition generated heterogeneity early and remained steady through 3 weeks while reorientation emerged gradually, aligned deposition was relatively independent of remodeling rate while reorientation was highly dependent on rate, and cell heterogeneity only emerged at high cell alignment strengths.