

## BM5063 Systems Medicine

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### Problem Set 6

#### Instructions

1. You are not expected to submit answers to these problems

#### Questions

1. Reanalyze the inflammation and onset of fibrosis numerically by considering Hill's activation functions for the effect of growth factors on fibroblasts and macrophages.
2. Experiments that deplete macrophages show conflicting effects on fibrosis. In some contexts, fibrosis is prevented whereas in others it is enhanced. Show, using the numerical model of the previous question, that the deciding factor is the timing of depletion.
  - (a) What happens when  $M$  is set to zero with fibroblasts below their unstable fixed point?
  - (b) What happens when  $M$  is set to zero with fibroblasts above their unstable fixed point?
3. ECM is produced by myofibroblasts. ECM degradation is controlled by proteins called MMPs and TIMPs, where MMPs enhance the degradation of ECM and TIMPs inhibit the degradation of ECM. MMPs are produced mainly by macrophages apart from a small baseline level that is produced by the tissue. TIMPs are produced by both macrophages and myofibroblasts
  - (a) Write down equations describing the levels of ECM due to these interactions.
  - (b) Analyze this system with the help of the phase diagram.
  - (c) Do it numerically.

