Major Instructions for the Jones and Mann implementation:
Due Date: 11/7/2017

1) Reproduce *all* figures in the paper (1A, B; 2A, B, C; 3; 4; 5A, B; 6) using Matlab.

2) Skeleton code for the base Jones model is posted on Stellar as a template for writing your implementation (last_first_jones.m). The ODEs themselves have already been implemented for you, but you are required to code in values for the reaction parameters (supplied in the Jones paper and errata) and initial concentrations (see both Jones paper and Lawson 1994). Note: You are not required to follow the template exactly or even closely, but it is highly recommended!

3) There are errors in the paper! Make all the corrections presented in the supplied Jones and Mann errata document.

4) Look at the syllabus for details on what is expected for presenting the results of your implementation. Note that the model modification is just as important as reproducing the paper's original model and figures. You should submit your **3-page** write up and .m file to Stellar and bring a paper copy of the write up to submit in class. Printing your .m file is neither required nor recommended. Figures and figure captions do not count towards the 3-page limit.

Minor instructions:

1) Save your .m file as your lastname_yourfirstname_firstauthorofpaper.m (e.g. tidor _bruce_jones.m) . Then, begin your file with:

```
function yourlastname_yourfirstname_firstauthorofpaper
```

This defines the .m file as a function instead of a script.

2) When we run your code, we should only have to press "Run" one time. That one run should generate all figures (original paper + modification plots) in separate windows so they are all displayed without re-running the program.

3) Include legends and axis labels (with units!) on all of your plots. The legends should not substantially cover any data on the plot (e.g., use the 'Location' argument to move the legend around). Each figure must also have a caption ≤ 1 paragraph long, briefly explaining the nature of the figure and its contents in your own words.

4) Note the following from Jones and Mann (p. 23369, bottom of left column): "The activity of meizothrombin is known to be about 120% that of α-thrombin (25); therefore, a relative specific activity of 1.2 is assigned to meizothrombin and 1 to α-thrombin in order to model thrombin activity in experimental results. In all other cases, a relative specific activity coefficient of 1 isassigned to the species of interest." In other words, anytime "thrombin" is plotted in the figures, **it is actually the sum of 1.2*meizothrombin and 1*α-thrombin.**

5) You may have noticed that the factor "I" introduced in Equations 8 and 20 of the Jones and Mann paper has been replaced by a simple, first-order model of degradation using the rate constant k20. Using this first-order model of decay should not affect your model noticeably, but Figures 2B and 2C (corresponding to the concentrations of factors Xa and IXa, respectively) and

Figure 3 (the reaction progress for each protein) will be significantly altered. In your submitted assignment, you should include figures produced from simulations of the provided model (i.e. with first-order degradation), **but you are expected to address this discrepancy in your write-up** and discuss possible ways to reconcile the divergent graphs, such as altering the value of k20.

6) You do not need to reproduce or show any of the experimental data, ever. You only need to show outputs produced from numerical simulation of the ODEs.

7) The modification should be biologically relevant; that is, the results should potentially say something important or interesting about the model system. Simply adjusting given parameters or performing global sensitivity analysis (though practically useful/important) does not qualify as an appropriate modification. Including new reactions and/or components known to play a role in regulating this pathway would be an example of an appropriate modification. Creativity is a component of the grade for this section!

8) You may find Matlab cannot solve the system of differential equations if you use units of molar (M). Instead, you can convert the units to something smaller (e.g., nM) so Matlab will be working with larger numbers. Alternatively, you can use Molar units, but adjust the ode solver tolerances (see Matlab tutorial slides).

9) There is a mistake in the errata for the legend for Figure 1B (yes, that's right, errors in the errata!). The circle and the diamond are reversed (so the circle refers to changing k7 and k9, and the diamonds actually correspond to changing k8 and k10).

10) When discussing the model, be sure to concisely describe the authors' key assumptions, including but not limited to: model equation formulations, assignment of parameter values, assumptions regarding the simulated environment, etc.

11) There are many facets to the knowledge required to successfully implement this paper - biology, mathematics, programming, interpretation, and creativity. You all have differing levels of skill in each of these areas. **Learning to collaborate with your classmates for mutual benefit is one of the positive side effects of this class.** Be bold in asking around and forming groups. Your code and write-up must be your own work, but beyond that, collaboration is unbridled.

Tip: Once you have completed your implementation code, a useful way to save all your figures in one place is to select File -> Publish last_first_jones.m – this will create a folder titled 'html' in your working directory containing individual files for all produced figures.

Good luck and START EARLY!!!