**ERiQ Computational Model Instructions**

\*\*All .m files need to be in the same folder directory in Matlab

* **ERiQ.m**
  + This file is not run, it is only called by the ode solver
  + This calls separate functions for each equation. These are each their own .m files labeled ‘f\_.m’
    - Separated for organization and ease of optimization
* **ERiQ\_event.m**
  + Does not run, but needs to be called in the ODE solver as options to terminate the system if MFUNCT reaches 0.5.
* **ERiQ\_ODE.m**
  + Full aging simulation
  + Use this file to run the odesolver on ERiQ.m
    - It uses initial conditions established via homeostasis (our original conditions should be in a comment)
    - The code will establish variables for you – i.e. MFUNCT, ATP, AKT, etc.
    - The code will auto-plot these major nodes
  + Global constants will be colored in light blue – these affect ALL functions in the folder
    - P53\_Act and MDR can be changed to affect changes
    - **To Run the Local Sensitivity Analysis**
      * Each ‘f\_.m’ function is multiplied by a global “SA” value that is set at 1 for normal conditions within the ERiQ\_ODE.m code
        + Labeled ‘\_SA’ (i.e. NFKB\_SA = 1)
      * Changing this SA value will manipulate the function the name corresponds to.
        + i.e. NFKB\_SA = 1.1 🡪 a 10% increase in NFKB activity
        + i.e. NFKB\_SA = 0.9 🡪 a 10% decrease in NFKB activity
      * \*\*To change ROS levels, please use ROS\_SA2 and NOT ROS\_SA
      * Rerun ERiQ\_ODE.m for new values
        + ‘Parameters’ table will list new values for you
        + Record values in Excel for ease of SOF calculation
        + Don’t forget to reset the ‘\_SA’ global value back to 1 before looking at the next sensitivity analysis.
* **ERiQ\_Pulse**
  + Simulation of ERiQ pulses in MDAMAGE and MFUNCT (not full aging simulation)
  + Will plot two figures representing the responses to these pulses, simply run the whole script
  + \*\*Should you wish to change strength of the pulse
    - Rerun individual assessment of the simulation between t = [0 3000] and t = [3000 6000] where the new pulse occurs in the second time range; plot these on the same figure
      * Use conditions found in Y(end) of the first time range as base for the initial conditions used in the odesolver in the second time range
      * The pulse is reflected by reducing or increasing the value of a specific initial condition in the second range
        + I.e. at end of t = [0 3000], MDAMAGE = 0.0724. To reflect a pulse increase of 0.5, the initial condition for MDAMAGE during t = [3000 6000] would be 0.0724+0.5 = 0.5724.
        + You can change these as you see fit, but you need to update the initial conditions to reflect new pulse
* **ERiQ\_homeostasis.m**
  + Generates plot of varying MDR values and effect on lifespan/MFUNCT
  + Can run as is; change MDR values (for Ys 1 through 7) for different simulations
* **ERiQ\_simulation.m**
  + Compilation of all .m files in one script that can be published as PDF or html
  + Does not run – will yield error. For supplemental file production only
* **ERiQ\_SA.m**
  + Used to run multi-parameter local sensitivity analyses. This file is NOT run, similar to how ERiQ.m is not run – it just establishes the equations
  + P53 vs MDR
    - Run script ERiQ\_SA\_p53\_MDR to use loop and generate 3d plot
      * Can edit the range of values used here for parameter analysis – but if changed, make sure you also update the plot axis ticks accordingly
  + NFKB vs MDR
    - Run script ERiQ\_SA\_NFKB\_MDR to use loop and generate 3d plot
      * Can edit the range of values used here for parameter analysis – but if changed, make sure you also update the plot axis ticks accordingly
* **ERiQ\_Global\_Analysis\_RUN.m**
  + Script to run a global sensitivity analysis
  + Script calls the function ERiQ\_Global\_Analysis.m. Do not run that function, only use the file labeled RUN.
  + Run this script to perform a global Monte Carlo sensitivity analysis that perturbs each parameter in the same simulation
    - N = 1000, but can be changed in code
    - Gaussian distribution, mean = 1, std = 0.033
      * Represents max 10% increase or decrease
      * For higher increase, change standard deviation
  + Saves 2 tables
    - GSA = actual random SA parameters chosen
    - GSA\_percent = % change in parameter change and final values
    - Can copy these tables into Excel for further analysis
* **ERiQ\_treatments.m**
  + Generates plots for lifetime inhibition of NFKB, AKT, mTOR and Autophagy
  + Follow comments to change these inhibition concentrations
    - Follows the idea of sensitivity parameter changes
* hline.m and vline.m
  + Funtions from MathWorks to place vertical line at specific point on x-axis. Needed for pulse plots
    - Simply need to be in the same folder directory, do not change