The code should be executed in the presented order to generate required data and results.

1. **make tissues**: *script\_tissue.m* generates a collection of simulated tissues with numerically stable oxygen distribution for different fractions of vessels (vascularity 0.5%-5%), tumor cells (tumor cellularity 10%-95%), and stromal cells (stromal cellularity 5%-90%); this script calls the function *oxy\_tissue\_make\_aver.m*
2. **make classification with convex hulls:** *3D\_classification\_saturation.m* generates classification of tissues into five classes based on the average level of stabilized oxygen (0-blue-12-red-24-orange-36-yellow-48-white-60 mmHg) and represents the data in a form of five convex hulls; data for classification are read from *data\_summary.txt*, a text file generated by the *script\_tissue.m.*
3. **make optimal schedules influx:** *script\_influx.m* determines the optimal influx schedule for a given tissue and given experimental data (for each of the four ROIs) by calling *Main\_fluct\_optim\_influx.m*, and uses this schedule to determine the L2-norm as a goodness-of-fit by running *oxy\_tissue\_fluct\_influx.m*;

* the optimization file (*Main\_fluct\_optim\_influx.m*) sets up the objective function for the *patternsearch.m* optimization routine in order to determine the influx schedule for each time segment [0-4,4-7,7-10, …, 24-28] to match the simulated average level of oxygen at each time point to the experimental measurement, as an output of simulation *run\_fluct\_optim\_influx.m*;
* *Exp\_data* – experimental measurements for each ROI
* *tissue* – structure and oxygenation of simulated tissues matching initial data for each ROI generated by the *script\_tissue.m*
* Output: Opt\_data – text files with final schedules for all four ROIs *rateInflux\_opt\_influx.txt* and *rateUptake\_opt\_influx.txt*

1. **make optimal schedules uptake:** *script\_uptake.m* determines the optimal uptake schedule for a given tissue and given experimental data (for each of the four ROIs) by calling *Main\_fluct\_optim\_uptake.m*, and uses this schedule to determine the L2-norm as a goodness-of-fit by running *oxy\_tissue\_fluct\_uptake.m*;

* the optimization file (*Main\_fluct\_optim\_uptake.m*) sets up the objective function for the *patternsearch.m* optimization routine in order to determine the uptake schedule for each time segment [0-4,4-7,7-10,…,24-28] to match the simulated average level of oxygen at each time point to the experimental measurement, as an output of simulation *run\_fluct\_optim\_uptake.m*;
* *Exp\_data* – experimental measurements for each ROI
* *tissue* – structure and oxygenation of simulated tissues matching initial data for each ROI generated by the *script\_tissue.m*
* Output: *Opt\_data* – text files with final schedules for all four ROIs *rateInflux\_opt\_uptake.txt* and *rateUptake\_opt\_uptake.txt*)

1. **make optimal schedules for convex hulls:** for each ROI (black, blue, magenta, or red) tests whether tissues with numerically stable oxygen distribution within +/-3.5 mmHg from the experimental data value will well respond to optimal influx/uptake schedules, i.e., with small L2 norms.

* *codes* – contains MATLAB codes for each ROI (x=black, blue, magenta, or red): *script\_x.m* calls scripts: *script\_x\_influx.m* and *script\_x\_uptake.m*; *script\_x\_influx.m* and *script\_x\_uptake.m*: identify tissues within +/-3.5 mmHg from the experimental value and apply optimal schedules by calling *oxy\_tissue\_fluc\_x\_script.m*; as a result, the L2 norm between simulated and experimental data is calculated
* *Exp\_data* – experimental measurements for each ROI
* *Opt\_data* – optimal in flux and uptake schedules for each ROI
* *tissue* – structure and oxygenation of simulated tissues generated by the *script\_tissue.m* and the *data\_summary.txt* with summary of simulated tissue results
* Output: *tiss\_fluct\_x* – four directories (one for each ROI) with tissues for which optimal schedules are applied

1. **make convex hulls for optimal schedules:** *data\_convex\_hulls\_combined.m* generates images for each ROI with all tissues within +/-3.5 mmHg (cyan convex hull), tissues with L2<0.2 for optimal influx schedules (green convex hull), and tissues with L2<0.2 for optimal uptake schedules (black convex hull)