The following is a brief summary of the files contained within the code; when to invoke them, and what they are used for.

***Global\_test.m***

* This is the main header file, where the initial conditions for the entire optimization are stored. From this header, a pool of MATLAB workers is initiated, the files are compiled (using the *mex* command), and the initial conditions, and bounds are set.
* The program is run from this header file

***WT\_REDUCED\_CHANNEL\_Sim\_Exp\_Norm.m***

* This file contains the objective function for the drug-free WT channel model, and is where the parallelization takes place. Each protocol is sent to a MATLAB worker, and the result of the simulation is compared to the experiment
* “Total\_Error” at the bottom of the script is the objective function to be minimized

***WT\_Drug\_Sim\_Exp\_FLEC.m***

* This file contains the objective function for the drug-channel interaction, is where the parallelization takes place, and where the objective function is defined (similar to WT\_REDUCED\_CHANNEL\_Sim\_Exp\_Norm.m above)

***Global\_test\_SEQ.m***

* This file is the main header file, when sequential optimization is required.
* From this header, a pool of MATLAB workers is initiated, the files are compiled (using the *mex* command), and the initial conditions, and bounds are set.

***WT\_Drug\_Sim\_Exp\_FLEC\_SEQ.m***

* This file is similar to WT\_Drug\_Sim\_Exp\_FLEC.m, except that the optimization is run sequentially, first with 1 protocol, then 2 protocols etc.

***fminsearchbnd.m***

* This is the bounded Nelder Mead algorithm

***Global\_Variables.h***

* This file contains the global variables used in the C++ code, where the protocols are simulated

**WT\_Flec\_implicit.h**

* This file is the WT drug channel model, where the differential equations describing the kinetic transitions of the different states of the Na channel model are described
* The input parameters to be optimized are further defined here

***main\_SSA.cpp; main\_ACT.cpp; main\_RFI.cpp; main\_RUDB.cpp; main\_TAU.cpp***

* The above protocols are used in the WT drug-free fitting

***main\_BLOCK.cpp; main\_FDUDB1.cpp; main\_FDUDB2.cpp; main\_CELL.cpp***

* The above protocols are used in the drug-binding fitting
* Note, that FDUDB is split into two protocols, so that it can be sent to two MATLAB workers to speed up the simulation (1Hz for FDUDB1; 2, 5, and 10Hz are simulated with FDUDB2)