**Local Sensitivity Analysis**

**Simulation of variation of model parameters**

The variation of model parameters with “multiplication factor” for all four circuits is carried out using the following files as stated in the **MATLAB Main File** column. The associated ODEs shown in Figure 1 of the main text for each circuit are coded in the following files as stated in the **ODE File** column. All the simulation results for each circuit are saved into a .mat file as stated in the **MAT File** column.

|  |  |  |  |
| --- | --- | --- | --- |
| **Circuit** | **MATLAB Main File** | **ODE File** | **MAT File** |
| TX Circuit | Transcription\_Local\_SA.m | TX\_ODE.m | txmetricupdate.mat |
| TL Circuit | Translation\_Local\_SA.m | TL\_ODE.m | tlmetricupdate.mat |
| HY-1 Circuit | Hybrid\_TY1\_Local\_SA.m | HY\_TY1\_ODE.m | hy1metricupdate.mat |
| HY-2 Circuit | Hybrid\_TY2\_Local\_SA.m | HY\_TY2\_ODE.m | hy2metricupdate.mat |

**Simulation of circuit analysis**

Using the MAT file for each circuit, the distribution metric (Figure 3 in the main text), histogram (Figures 4 in the main text and S5 in the Supplementary information) and sensitivity polar plot (Figures S1-S4 in Supplementary Information) can be analysed and plotted using the following files.

|  |  |
| --- | --- |
| **Circuit** | **MATLAB File** |
| TX Circuit | Transcription\_MetricAnalysis.m |
| TL Circuit | Translation\_MetricAnalysis.m |
| HY-1 Circuit | Hybrid1\_MetricAnalysis.m |
| HY-2 Circuit | Hybrid2\_MetricAnalysis.m |