Kin-E-Sim is a set procedures for Igor Pro designed to predict the characteristic response of an analyte in various electrochemical methods, including normal pulsed voltammetry (illustrated below), cyclic voltammetry, etc. This document is intended to provide a new user the information they need to begin using the Kin-E-Sim program. See <citation> for further details on the implemented algorithms.

Two versions of Kin-E-Sim are provided here: KES__complete.ipf includes complete code in a single procedure file and is intended for end users. KES__Main.ipf loads the same code which is split over several procedure files. It is intended for programmers who want to examine and revise the code. Only one version can be loaded at a time.

Once Kin-E-Sim is loaded and compiled, it can be accessed from Analysis -> Kin-E-Sim -> Control Panel menu:
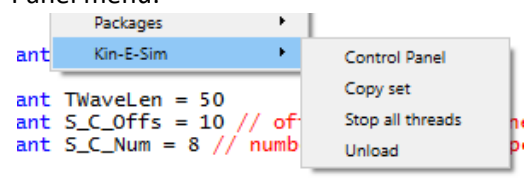
A description of the control panel and all its components is provided below. An included Igor experiment KES_Demo.pxp contains several pre-configured demo simulations, as follows.

- **Pre-loaded simulations:**
    - **Single analyte direct electrochemistry**
        - This simulation simulates NPV of a single analyte that undergoes direct electrochemistry on the electrode. As loaded, the analyte has a redox potential of -0.1 V.
    - **Singe analyte mediated electrochemistry**
        - This simulation simulates NPV of a single analyte and mediator. The analyte is unable to perform any electron transfer on the electrode and is completely dependent on the mediator for redox transitions. As loaded, both the analyte and mediator have a redox potential of -0.1 V. The concentration of the analyte is 1 mM and the concentration of the mediator is 200 μM.
    - **Single analyte mediator with two redox transitions**
        - This simulation simulates NPV of a single analyte and mediator where the mediator has two distinct redox transitions. As loaded, the analyte has a redox

potential of -0.1 V and the mediator has two redox potentials at 0.0 V and -0.2 V. The concentration of the analyte is 1 mM and concentration of the mediator is 200 µM total.

- Hint: A single mediator with two distinct redox transitions is accomplished by making two separate components and connecting them using the **alias this** function. Each component must start with a concentration value greater than 0 and the sum of the two concentrations is the total concentration of the mediator.

- **Performing a single simulation:**
  - First, use the data browser in Igor to select the folder with the title of the simulation you would like to run. Then click ↺ (reload) in the **top-left corner** of the Kin-E-Sim **control panel**. The simulation should now be loaded containing all the pre-set commands and parameters.
  - To run a single simulation using the specified parameters, press the "**do this sim**" button in the simulation panel. Note that the name of the simulation can be changed using the **base name** text box found in the simulation panel. A new window should appear that displays the amount of time needed for the simulation to complete. Once the simulation has completed, a graph will appear containing the potential profile and concentration profiles of each component present in the simulation.
  - After the simulation is completed for the first time, a new folder SimData will appear as a sub-folder of the selected simulation root folder and will contain Igor waves. The Igor wave with the same title as the simulation will contain all of the data, including the applied potential and the concentration of each component in both the reduced and oxidized states for each time point.

- **Performing a set of simulations**:
  - The **sim. set** section of both pre-loaded simulations has been set up to perform three simulations where the redox potential of the analyte is varied between -0.2, -0.1, and 0.0 V.
  - First, use the data browser in Igor to select the folder with the title of the simulation you would like to run. Then click ↺ in the **top-left corner** of the Kin-E-Sim **control panel**. The simulation should now be loaded containing all the pre-set commands and parameters.
  - To perform a set of simulations, press the "**do single set**" button in the **sim. set** panel. Once clicked, a window will appear showing the progress of the simulation.
  - After the simulation is complete, a separate graph will be built for each simulation and will show the potential profile and concentration profiles of all components. A new folder SimData will appear as a sub-folder of the selected simulation root folder and will contain sets of Igor waves. Wave names will contain numerical suffixes that reflect the order in the set (ex. simname00, simname01, etc.). Format of output waves is the same as for a single simulation.
  - New waves will also appear in the main simulation folder:
    - **simname_EappClb**: contains the list of applied potentials (no reference potentials included).

- **simname_SetClb**: reports the value of the varied variable (in this case, the redox potential of the analyte) for each simulation.
- **simname_OxC00_NPV**: contains the concentration of component 0 at each applied potential for all three experiments. This data can be transposed into a vertical column and plotted versus **simname_EappClb** to visualize the Nernstian profile.

Altering simulation parameters: Kin-E-Sim is a flexible framework that can simulate any experimental method that can be programmatically described. This is accomplished by passing a list of parameters (defined in Method Settings wave) to several template functions (simulation prep, process and plot). Users can write their own prep and process function or re-define any of parameters as long there is consistency between parameters and functions. Notice that for a function to be recognized by KieESim, it must have exact same order and type of parameters as defined in the template or the example.

Altering reaction schemes: Kin-E-Sim was originally developed to simulate changes in homogeneous solution in response to applied potentials. However, it can simulate any combination of multiple reactions on the electrode, in the solution, or the mixture of two types of reactions. This includes branching, isomerization and multi-step reactions, that can be defined using component aliases. Method parameters and setup functions may be irrelevant for simulations involving homogenous reactions only.

Multi-threaded simulations: Kin-E-Sim is multithreaded (MT) simulation. This is accomplished differently depending on whether a single or multiple simulations are carries out.

- Single simulation: multiple threads can be used for RK integration. Notice, however, that MT carries an overhead that my make parallel integration more time consuming than a single threaded. Compare results of using 0-1 cores vs 2+ cores on your particular computer.
- Sets of simulations:
  - If single simulation is set to a ST mode (nthreads < 2), simulations in the set will be carried out in parallel. This is the recommended mode.
  - If single simulation is set to a MT mode (nthreads > 1), simulations in the set will be carried out sequentially.

Control Panel:
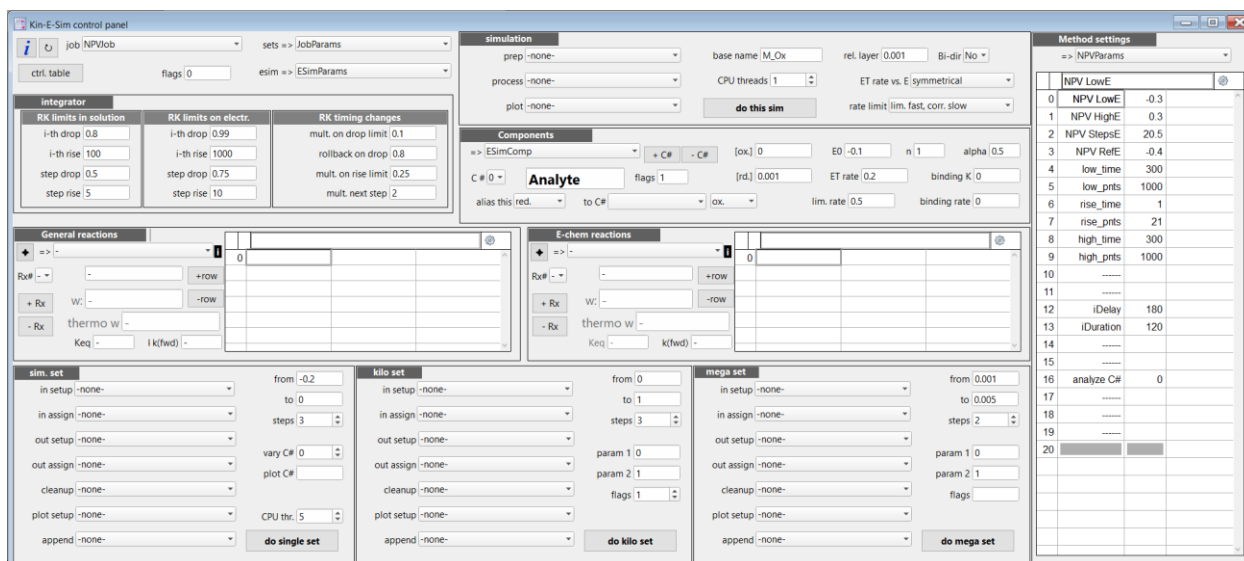
- **Top-left corner**
  - i : Shows the current version of Kin-E-Sim kinetic simulator
  - ↻ : Reloads selected job
  - **job**: Allows for the selection of a user-defined job set that specifies all values, methods, and waves for the simulation. Job sets are stored in text waves. Multiple job waves can be made to easily switch between experiments.
  - **sets =>** : Defines parameters of single simulation or simulation sets.
  - **ctrl. table**: Creates a table showing the names and contents of all parameter waves for the selected job.
  - **flags** : miscellaneous flags.
  - **esim =>** : Defines configuration of electrochemical system and parameters of the numerical integrator.

- **Simulation**
  - **prep**: function that generates the potential waveform or performs other pre-simulation steps.
  - **process**: function that performs step-wise simulation and integration.
  - **plot**: function for post-processing of a single simulation, including preparation of a report graphs.
  - **base name**: Name of the current simulation provided by the user. Multiple wave names will be derived from this name.
  - **CPU threads**: The maximum number of CPU threads the program may use during the simulation.
  - **do this sim** : A button used to start a single simulation.
  - **rel. layer**: The layer thickness in centimeters
  - **Bi-dir**: Allows the user to run the simulation as unidirectional or bidirectional (reversible) modes. Exact interpretation depends on the potential waveform.
    - **No**: Simulation will run in unidirectional mode and perform the simulation once using the potential profile described under the method settings.

- **Yes**: Simulation will run in bidirectional mode and perform two simulations, the first following the potential profile as described under the method settings, and the second following the potential profile in the opposite direction.
  - **ET rate vs. E**: Specifies electron transfer rate on the electrode as a function of applied potential relative to redox potential of this component.
  - **rate limit**: Allows the user to select whether the simulation is run using the complete model or the reduced model.

- **Integrator** : Parameters of Runge-Kutta integration
  - **RK limits in solution/electrode:** limit of changes in concertation of any component relative to that at the beginning of the step.
    - **i-th drop**: maximal reduction in the concentration during incremental RK step.
    - **i-th rise**: maximal rise in the concentration during incremental RK step.
    - **step drop**: maximal reduction in the concentration during complete RK step.
    - **step rise**: maximal rise in the concentration during complete RK step.
  - **RK timing**
    - **time X on drop limit**: reduction in simulation step if maximal allowed concentration decrease limit has been violated in the preceding attempt.
    - **time rollback on drop**: additional reduction is simulation step if boundary conditions were violated.
    - **time X on rise limit**: reduction in simulation step if maximum allowed concentration rise limit has been violated in the preceding attempt.
    - **next step time X**: Increase in the next simulation step after successful completion of this step.

- **Components** : This section is used to define the components that make up the simulated reaction, including all mediators and analytes.
  - **=>** : Drop down menu to select the wave containing the list of components and their properties, including interactions with the electrode.
  - **C #** : Drop down menu to select ID of an individual component in this set, followed by its literal name
  - **+ C#** : add a component
  - **- C#** : remove the currently selected component
  - **[ox.]**: The initial molar concentration of the oxidized state of the component
  - **[rd.]**: The initial molar concentration of the reduced state of the component
  - **E0**: The redox potential of the component in volts
  - **n**: The electron transfer coefficient of the component
  - **alpha**: The α of the component
  - **ET rate**: The intrinsic rate constant for the electron transfer at the electrode ($k°_{el}$)
  - **Binding K**: The equilibrium constant that controls the population of the component in solution versus bound to the electrode surface (only used for the complete model)
  - **Binding rate**: The rate constant that control the rate at which the component binds to the electrode surface (only used for the complete model).

- o **lim. rate**: The maximum effective rate constant for the electrolysis (only used for the simplified model).
- o **flags**: determines if the simulated concentration profiles of this component should be processed further. Input is 0 or 1.
- o **alias this**: Allows two or more components to be treated as the same species. Used for mediators or analytes that have multiple redox potentials or are involved in other equilibria.
    - **none**: no alias is provided for this component
    - **ox**: the oxidized form of this component is the same species as another component in the component list.
        - **To C#**: Allows the user to select the alias component and its oxidation state
    - **rd**: the reduced form of this component is the same species as another component within the component list.

- **Method settings:** User selects an Igor wave containing the method parameters. These parameters are used by the preparation function to generate a potential waveform.
    - o **NPVParams**
        - **NPV LowE**: the initial potential in volts of the NPV steps
        - **NPV HighE**: the final potential in volts of the NPV steps
        - **NPV StepsE**: the number of steps to perform from **NPV LowE** to **NPV HighE**
        - **NPV RefE**: the reference potential in volts
        - **low_time**: the time in sec that **NPV RefE** will be applied.
        - **Low_points**: the number of data points to be recorded during **NPV RefE**.
        - **High_time**: the time in sec that each applied potential from **NPV LowE** to **NPV HighE** will be applied.
        - **High_points**: the number of data points to be recorded during each applied potential from **NPV LowE** to **NPV High E**.
        - **Rise_time**: asdf
        - **Rise_points**: asdf
        - **iDelay**: the amount of time in sec to wait during each potential step before integration of component concentrations begins.
        - **iDuration**: the amount of time in sec over which components concentrations will be integrated during each potential step.
        - **Analyze C#**: the component that should be processed further.

- **Echem reactions:** This section defines the electrochemical reactions that take place in solution between mediators and analytes.
    - o 🔽: Pressing this button creates the waves needed to set up the reactions
    - o **Rx#**: Drop down menu used to select reactions to be edited, followed by the literal name of the reaction.
    - o **+ Rx**: add a reaction to the list
    - o **- Rx**: remove the currently selected reaction.

- o **Keq**: The equilibrium constant of the electrochemical reaction. This read-only value is calculated based on the E0 of the components involved in the reaction.
- o **k(fwd)**: The forward rate of the reaction (user input)
- o **w** and **Thermo w.**: Read-only names of waves used internally to describe current reaction.
- o **Reaction table**:

  - ▪ Each row is used to describe how a single component is changed during a reaction. Rows can be added for reactions that involve multiple components by pressing the "+ row" button or removed by pressing the "- row" button.
  - ▪ Columns:
    - • **->|#..** : ID of the reactant component
    - • **->|Ox..** : stoichiometric coefficient of the oxidized form as a reactant
    - • **->|Rd..** : stoichiometric coefficient of the reduced form as a reactant
    - • **..#|->** : ID of the product component
    - • **..Ox|->** : stoichiometric coefficient of the oxidized form as a product
    - • **..Rd|->** : stoichiometric coefficient of the reduced form as a product
    - • *Hint*: A stoichiometric coefficient of "0" is used for non-participating forms of reactants or products.
    - • *Example*: In the table shown above, components 0 and 1 are participating in an electrochemical reaction. As written, one mole of oxidized component 0 reacts with one mole of reduced component 1 to form one mole each of reduced component 0 and oxidized component 1.

- • **General reactions**: Used to set up non-electrochemical reactions that take place in solution. This section can be used to simulate the conversion of one component into another, or the reaction between two or more components to form new components.
  - o See **Echem reactions** for an in depth explanation of each element of this section not listed below:
  - o **Keq**: The equilibrium constant of the general reaction. This value is set by the user.

- • **sim. set**: This section is used to automate a series of simulations that change a single variable such as the E0, concentration, ET rate, or lim. rate of a component. A set yields a 1D variation in the model.
  - o **In setup**: Method that performs preparation of the set; called ones per set.
  - o **In assign**: Method that performs assignment prior to each simulation.
  - o **Out setup**: Method that prepares output set data; called once per set.
  - o **Out assign**: Method that saves the results of each simulation.
  - o **Cleanup**: Method for general maintenance at the completion of the set.

- **Plot setup**: Method to prepare graphical report; called once per set.
- **Append**: Method append results of the simulation to the graphical report.
- **From**: The initial value of the variable to be changed
- **To**: The final value of the variable to be changed
- **Steps**: The total number of simulations to be performed. This also controls how much the variable is varied between each step.
- **Vary C#**: Identifies the component that will be altered during each step.
- **Plot C#**: Identifies the component to be appended to the graphical report.
- **CPU thr.**: Sets the maximum number of threads that may be used during the simulation.
- **Do single set**: Press this button to perform the simulation set.

- **kilo set**: This section is used to automate a series of simulations that alter a second variable. All **sim. set** simulations are repeated for each value of **kilo set** variable, which yields a 2D variation in the model.
  - Values of **param 1, param 2** and **flags** can be used and interpreted by the assignment methods.

- **mega set**: This section is used to automate a series of simulations that alter a third variable. All **kilo set** simulations are repeated for each value of **mega set** variable, which yields a 3D variation in the model.
  - Values of **param 1, param 2** and **flags** can be used and interpreted by the assignment methods.