Documentation of fit tool for opsins modelling with the 22HH model

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# Intro

A Hodgkin-and-Huxley type model was proposed to be a good alternative for opsin modelling. The model consists of two state pairs. The first one represents the opening and closing of the channel. The other represents the light dark adaptation of the channel conductance, acting thus as a conductance regulator. For the rationale behind the model and structure we refer to:

Schoeters R, Tarnaud T, Martens L, Joseph W, Raedt R, Tanghe E. Hodgkin and Huxley Opsin Model for Computationally Efficient Optogenetic Neurostimulation in Cells and Networks. bioRxiv [Internet]. 2020 Nov 10 [cited 2020 Nov 17];2020.11.10.376939. Available from: <https://doi.org/10.1101/2020.11.10.376939>

Below we elaborate on the fit-tool itself and the code written in MATLAB.

# Content

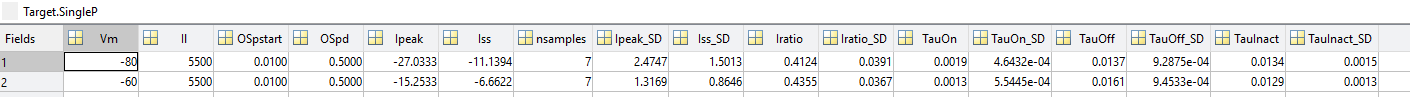
* Compile\_script.m:   
  create standalone application (see comments inside script)
* runfitH134Rexp.m:   
  create input file or start fit of ChR2H134R opsin based on experimental data. Example of changed hyperparameters (test version with lowerd time limit, particles, starting points etc : get to know procedure)
* run22fitHMM.m:   
  create input file or start fit of MerMAID opsin based on experimental data. Example of changed hyperparameters
* runfit22HH\_LIS:   
  run fit22HH (fit tool master function) while adding extra metadata and save output. Possibility to send email when done, start profiler and save figures.
* Inputs folder:   
  Place where input file is stored prior starting fit. Input file contains target filename and location as well as additional settings. If using subfolders, do not forget to include subfolder name when passing to fit22HH or runfit22HH\_LIS
* Results folder:   
  place where results are stored
* Targets folder:   
  place where target file is located
* Functions folder:   
  Contains all functions used during fitting procedure

# Functions

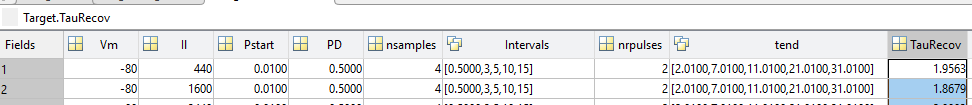
## Fit22HH

The master function of the fitting procedure. It requires an Input structure which contains the targets filename. Also, possible to add extra settings through varargin (or via a single cell containing all parameter name and value pairs). As output, the fitted parameters are given of each step with additional metadata.

Important is the Target structure which should at least contain a SingleP field (Target.SingleP, single pulse experiments). If data of two pulse experiments is available, Target.TauRecov can be added as well. The features are stored as follows:



Standard deviations (e.g., Ipeak\_SD) are not mandatory. Use of the depends on selected cost-function method. Preferably, Vm (voltage clamp value) is in mV, Il in W/m2, time constants in seconds as well as pulse start and duration (OSpstart, OSpd with OS = optical pulse). Units of current features (Ipeak, Iss) si free of choice (but the same for all) but the range of gChR2 should be chosen accordingly. If data is available on TauRecov: it should be stored as follows:



After loading the target data. The hyperparameters are determined through the **declare\_parameter** function. Changes given via settings/varargin are made accordingly. Depending on chosen options, some checkups are performed prior start of fit. Next, doubles in target file are combined and the target file is sorted (sort is not mandatory but improves plot quality). Next the relationships can be plotted via **plotFeature**.

Prior start of the first fit, the target data and weights are stored in the correct format and altered if needed, **genXYFB** (see intermediate fit through approximation). The new time constant targets are plot via **plotTau**. Next the intensity and voltage dependencies are loaded from the **load\_functionDB**. Depending on the selected fitOrder the intermediate fit is created (i.e., first estimation of parameter values see paper for more details.). The result of this intermediate fit is visualized with the **runODE** function. Finally, a final optimization is performed (**final\_opt**) including all parameters on a limited parameter space.

## Subfunctions

Functions are ordered based on occurrence in fit22HH. Extra info can typically be found inside the function

### Declare\_parameters

Contains the default settings of the fitting procedure. Settings are altered via settings cell which contains a name-value pair. For more details on parameters we refer to declare\_parameters function and parameters\_ReadMe.txt

### adjFields

Function that merges structures and changes default fields.

### plotFeatures

create a plot of the I and V dependencies of the features.

### genXYFB

reorganize target data. Determine weights (if necessary, depends on selected methods), make changes to target features (needed when higher powers are used or in case of TauRecov see paper). Light dependencies of Tau off and recov are averaged out (model is not able to represent these)

### PlotTau

Create a figure of the TauO and TauDA training data

### Load\_functionDB

Database that contains multiple functions which can be used as dependencies. If new relationship defined it can be added here or given as input through the settings. Check here on format of dependencies.. Defined sets (with multiple possibilities) probably won’t work anymore. Change made on how we loop through dependencies (see final\_opt). names list need to have the same length. !*Some adjustments need to be made if testing multiple dependencies in one fit as in current format it is possible that during the intermediate step a same fit is made multiple times …)!*

### fitORDER

Not a function but important to elaborate on. To fit the steady state values, already an approximation of the timeconstants is required (see paper). Either these are approximated via the training time constants tauon, off, inact,… or a fit of tauO and tauDA is made first. The latter method is preferred when datapoints of the timeconstants and current features do not coincide (see paper Williams). The former method subordinates TauO to the (and more specifically tauoff,model) to the already fitted steady state values. (see constraint paper to make current return back to baseline after optical pulse)

### fitTau

function that fits tauO and tauDA to target data generated in genXYFB

### objfun\_Tau

weighted normalized costfunction used in fitTau with ‘fmincon’ SolverMethod

### nonlinconTau

function defining nonlinear constraints in Taufit (see paper)

### fitGODA\_IpIssBased

fit steady state dependencies (Oinf, DAinf) based on current features (Ipeak, Iss and Iratio, last one if specified)

### fitGODA\_allfeatBased

same purpose as above only used when fit order set to GODA-tDA-tO. Meaning steady-state values fit prior time constants (see explanation fitORDER)

### nonlincon

nonlinear constraints function used in fitGODA\_allfeatBased, fitGODA\_IpIssBased and final\_opt

### runODE

recreate voltage clamp experiments with intermediate or final fitted model.

### States\_Vclamp

Differential equations that need to be solved

### Final\_opt

Final optimization. An overall costfunction is defined: **objfun\_CT**, comparing currentraces (needs to be validated) or **objfun\_FB (**feature based costfunction see paper), includingthe complete model and the trimmed parameter space based on intermediate fit. The features are determined as would be done on experimental date (via **Extrac\_feat**). No more approximations (except if requested see Taurecov, through method\_tr but currentraces is prefferd).

### EstimTauRecov

Rescale taurecov obtained by model with b. However Taurecovmodle is approximated.

### Outfun and stopPSO

Functions to stop the particle swarm optimization algorithm when stuck in singularity.