

HJCFIT

for Windows

Screenshots from HJCFIT

In order to fit real observations it is essential to allow for the fact that brief events are undetected. The likelihood is calculated in this program by using the method of Hawkes, Jalali & Colquhoun (1990, 1992), and Colquhoun, Hawkes, & Srodzinski (1996), to calculate the HJC distributions. These are the distributions of what is actually seen. e.g. of *apparent* open times, with exact allowance for the fact that apparent openings are often extended by missed brief shuttings. Details of the calculations can be found in [the manual](#) for DOS versions.

The welcome page

Welcome

HJCFIT
Version 0.8 (beta)
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Name of initialisation file:
AChdemo.ini

Browse for *.ini file (including autosim)
 Do not use initialization file
 Create new mechanism only
 View or modify old mechanism only
 Run DEMO fit (nicotinic, 1 set)
 Run DEMO fit (glycine, 4 sets)
 Run DEMO repeated simulations (C-K)
 Use simulated data

Printout file
hjcfit.txt

(1) Append to existing print file
 (2) Overwrite/new printout file
 (3) No printout file

Computer : PHARM48
User : dcolquho
OS :

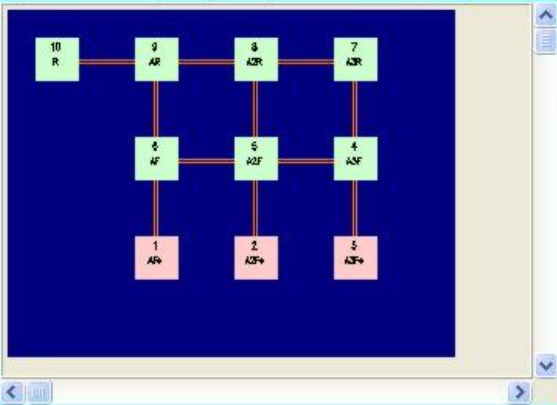
Clicking on one of the DEMO options will run a complete fit with no action from the user apart from clicking 'continue' or 'OK'.

The initial settings page

This page summarises most of the information that is needed before you can start a fit. For the demonstrations it will appear filled in correctly so all you need to do is click 'Fit'. This example shows the settings for a simultaneous fit to glycine receptor single channel recordings at four glycine concentrations ([Burzomato et al. 2004](#)).

Initial settings

Mechanism:
qmechdem.mec:Glycine flip model (mod 5 in Burzomato, 2004)



set by microscopic reversibility = 2

	Q(i,j)	Name	Cycle
1	q(4.7)	gamma3	4,7,8,5
2	q(6.9)	gamma1	6,9,8,5

of constrained rates = 6

	Q(i,j)	Name	Factor	Q(i,j)	Name
1	q(7.8)	3k(-3)	3.000	q(9.10)	k(-1)
2	q(8.9)	2k(-2)	2.000	q(9.10)	k(-1)

of fixed rates = 0 # constrained by EC50 = 0

	Q(i,j)	Name
1		
2		

Data **Browse/Change**

Number of sets = 4

	File 1
1	03012353.SCN
2	02111251.SCN
3	02100851.SCN
4	02080652.SCN

View Details

Set = 1 **Change**

Ligand: Concentration
glycine 10.0000 [micromolar]

One channel only

Critical shut time (ms) = 4.0

Use CHS vectors

Bad shutting ends group

Set intervals: bad if longer than:
10000 [shut times (ms)]
40 [open times (ms)]

Resolution = 30.0 [microsecond]

Prev. set **Next set**

Initial guesses **Change**

File:
Extreme guesses for flip model (Burzomato 2004)

	Q(i,j)	Rate name	Value
1	q(1.6)	alpha1	5000.00
2	q(6.1)	beta1	500.00
3	q(2.5)	alpha2	2700.00
4	q(5.2)	beta2	2000.00
5	q(3.4)	alpha3	800.00
6	q(4.3)	beta3	15000.00
7	q(4.7)	gamma3	300.00
8	q(7.4)	delta3	120000.01
9	q(4.5)	3k(-3)F	6000.00
10	q(5.4)	k(+3)F	450000000.00
11	q(5.8)	gamma2	1500.00
12	q(8.5)	delta2	12000.00
13	q(5.6)	2k(-2)F	4000.00
14	q(6.5)	2k(+2)F	900000000.00

Maximum values for: **Change**

association rates = 1.000e+009
all other rates = 1.000e+006

Save to ini file **Save to mec file**

All checked; proceed now:

Fit

Show data and specified model (no fit)

Fitting

At the end of the nicotinic receptor demonstration fit we see that it took 36 seconds. On my current (2013) Windows 7 laptop it takes only 16 seconds to converge.

```

n= 600 L= 39823.81
  alpha2      beta2      alpha1a      beta1a      alpha1b      beta1b      k(-1)a      k(-1)b      k(+1)b
2126.809    52240.395    5952.527    56.672    56177.010    89.022    1520.427    9468.641    414334672.387
n= 610 L= 39823.81
2126.792    52245.573    5953.954    56.712    56165.167    88.943    1521.237    9466.415    414577908.117
n= 620 L= 39823.81
2127.931    52266.955    5954.444    56.663    56157.124    89.005    1520.379    9464.655    414274783.361
n= 630 L= 39823.81
2126.882    52242.831    5952.766    56.691    56168.679    88.991    1520.887    9467.180    414475265.637
n= 640 L= 39823.81
2126.882    52242.831    5952.766    56.691    56168.679    88.991    1520.887    9467.180    414475265.637
Return with averaged vertices
Simplex finished at:11:52:25
Duration of fit: 0 days 0 hours 0 min 36 sec
number of evaluations = 643
Max log(likelihood) 39823.81
  
```

Mechanism File:qmechaem.mec Name:Two unequal bindings [C&S AKI 1985] Rate file:Guess Z,

After calculation of errors, the values for the rate constant estimates are displayed.

Results of fit with errors:

	Q(i,j)	Name	Initial guess	Final value	CV(%)	SD	Constraint/Fix	Factor
1	q(1,4)	alpha2	1500.00000	2126.94727	6.36105	135.29623		
2	q(4,1)	beta2	50000.00000	52245.02344	5.41894	2831.12793		
3	q(2,5)	alpha1a	2000.00000	5952.98145	3.50784	208.82097		
4	q(5,2)	beta1a	20.00000	56.70864	16.20897	9.19189		
5	q(3,6)	alpha1b	80000.00000	56161.18359	9.06040	5088.42773		
6	q(6,3)	beta1b	300.00000	88.96288	15.52129	13.80819		
7	q(4,6)	k(-2)a	1000.00000	1521.30078				1.000
8	q(6,4)	k(+2)a	1.00000e+008	1.00000e+008			fixed	
9	q(4,5)	k(-2)b	20000.00000	9465.86621				1.000
10	q(5,4)	k(+2)b	1.00000e+008	4.14602e+008				1.000
11	q(5,7)	k(-1)a	1000.00000	1521.30078	11.20655	170.48526		
12	q(7,5)	k(+1)a	1.00000e+008	1.00000e+008			MR	
13	q(6,7)	k(-1)b	20000.00000	9465.86621	5.59308	529.43372		
14	q(7,6)	k(+1)b	1.00000e+008	4.14602e+008	15.27087	6.33133e+007		

To copy/paste highlight the required area in the table with the mouse(left button) and then click the right button

Exit Store mec. with fitted rates Do plots

Plots to see the quality of the fit

After fitting has converged, the quality of the fit can be judged by displaying six types of graph. The distribution of the apparent open times is shown in the histogram. The blue line superimposed on (not fitted to) the histogram shows the HJC distribution of apparent open times that is predicted by the fit. The fact that it describes the observations well shows that the mechanism used is adequate to describe the data. The red dashed line shows the predicted 'true' distribution of open times, calculated from the fitted rate constants with no missed event correction (by the simpler methods of [Colquhoun & Hawkes, 1982](#)).

