Parameter Optimisation of Excitable Cell Models using CellML

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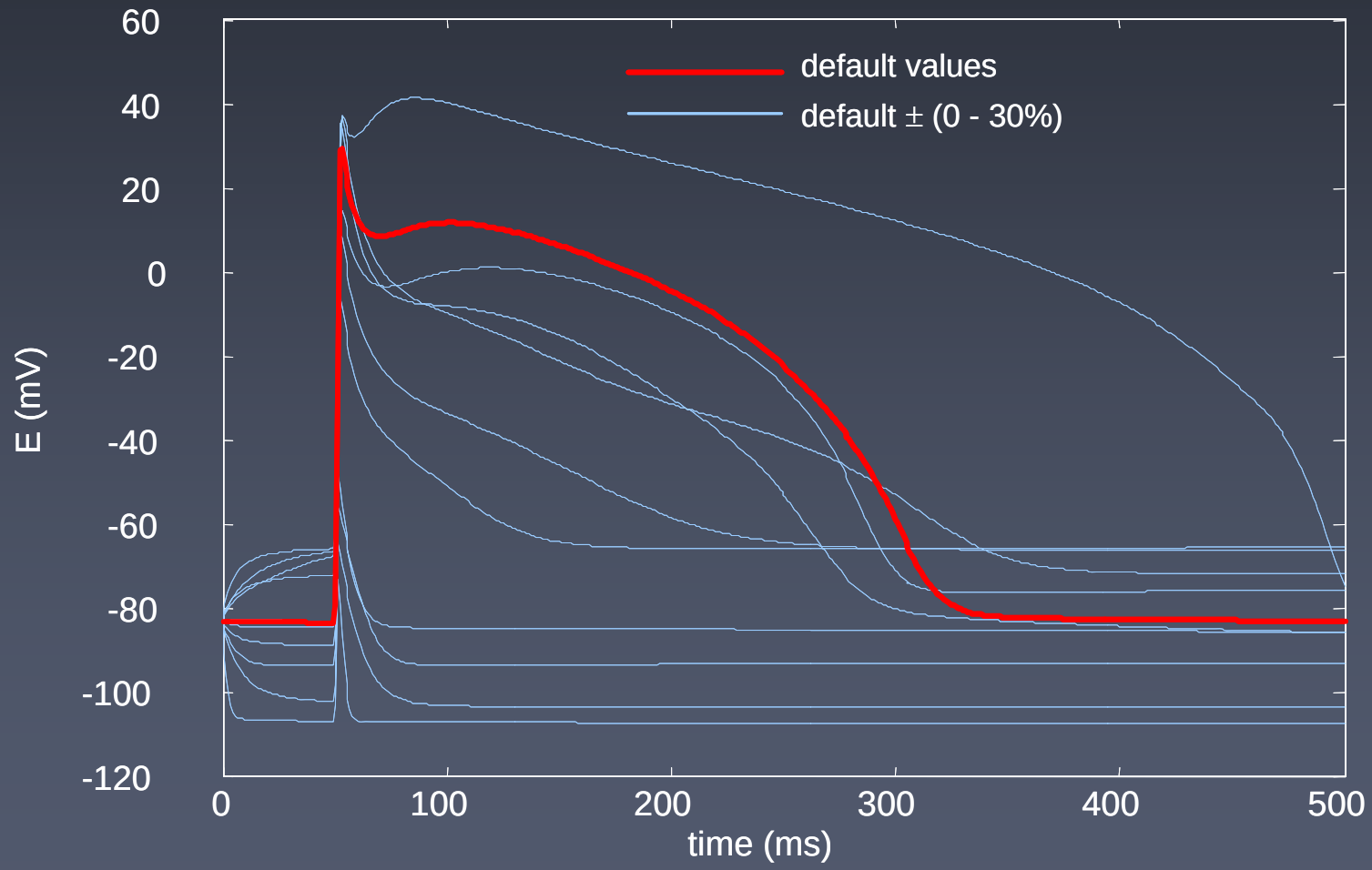
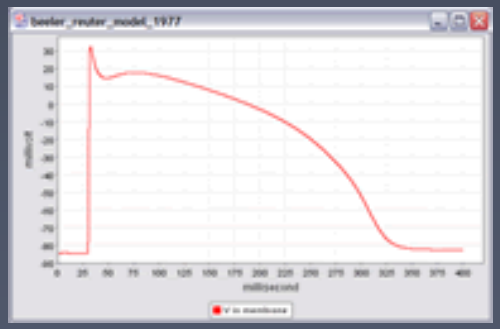
Beeler-Reuter 1977



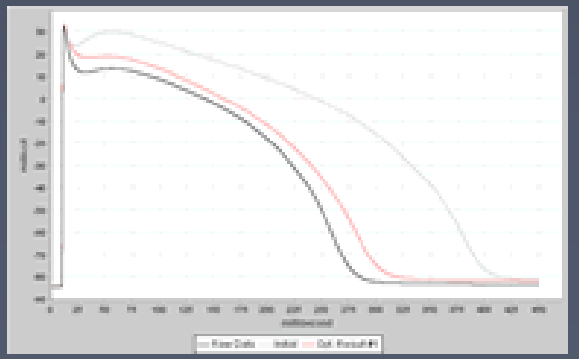
Software Overview

Parser

Solver



Optimiser



Defining Parameters

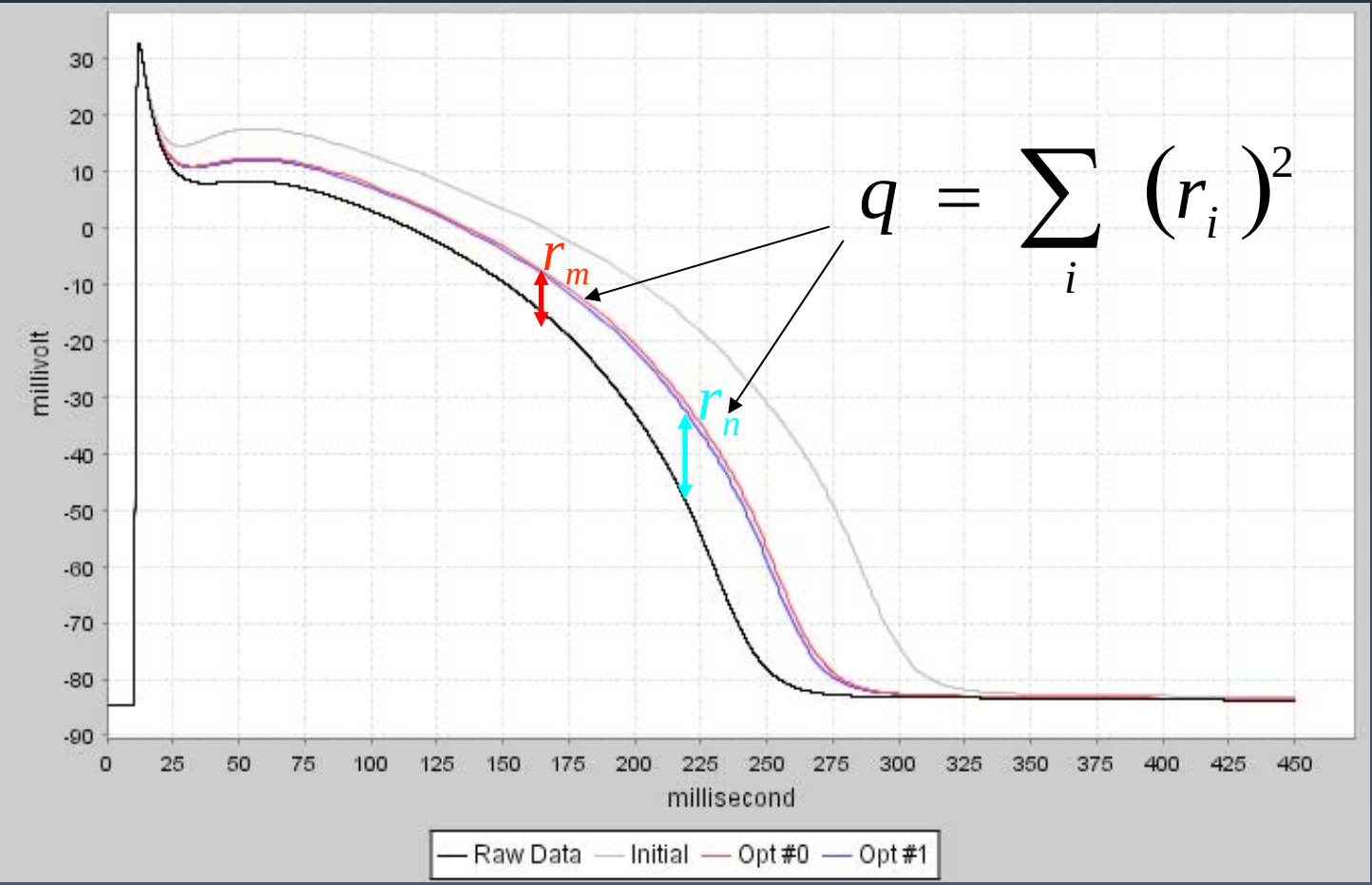
```
<variable name="g_s" initial_value="0.09" units="milliS_per_cm2" />
```

$$i_s = g_s \cdot d \cdot f \cdot \left(V - \left(82.3 - 13.0287 \cdot \ln \chi\right)\right)$$

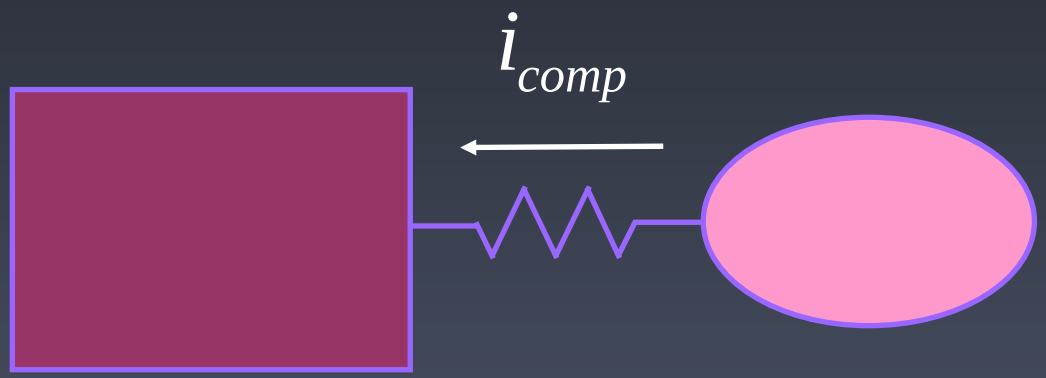
$$i_{x1} = x1 \cdot 0.8 \cdot \left(\frac{e^{0.04 \cdot (V + 77.0)} - 1}{e^{0.04 \cdot (V + 35.0)}} \right)$$

```
<cn cellml:units="microA_per_cm2"> 0.8 </cn>
```

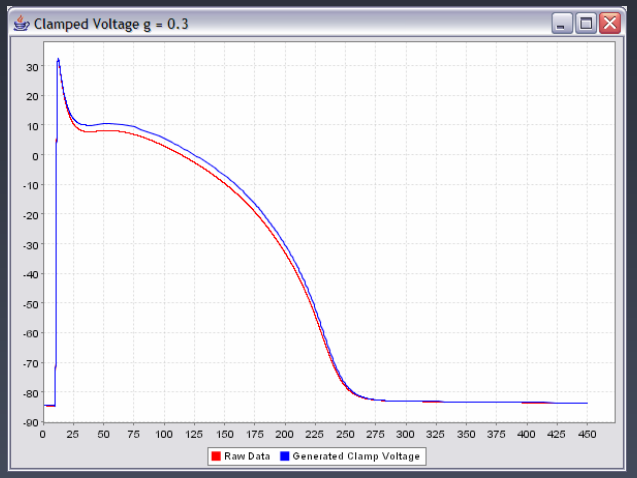
Objective Function – Direct



Objective Function – Data Clamp



Ionic Model **Real Cell Data**



Raw data and clamped potential

$$i_{comp} = g\left(V_{\text{model}} - V_{\text{data}}\right)$$

$$q = \sum \left(i_{comp}\right)^2$$

i_{comp}

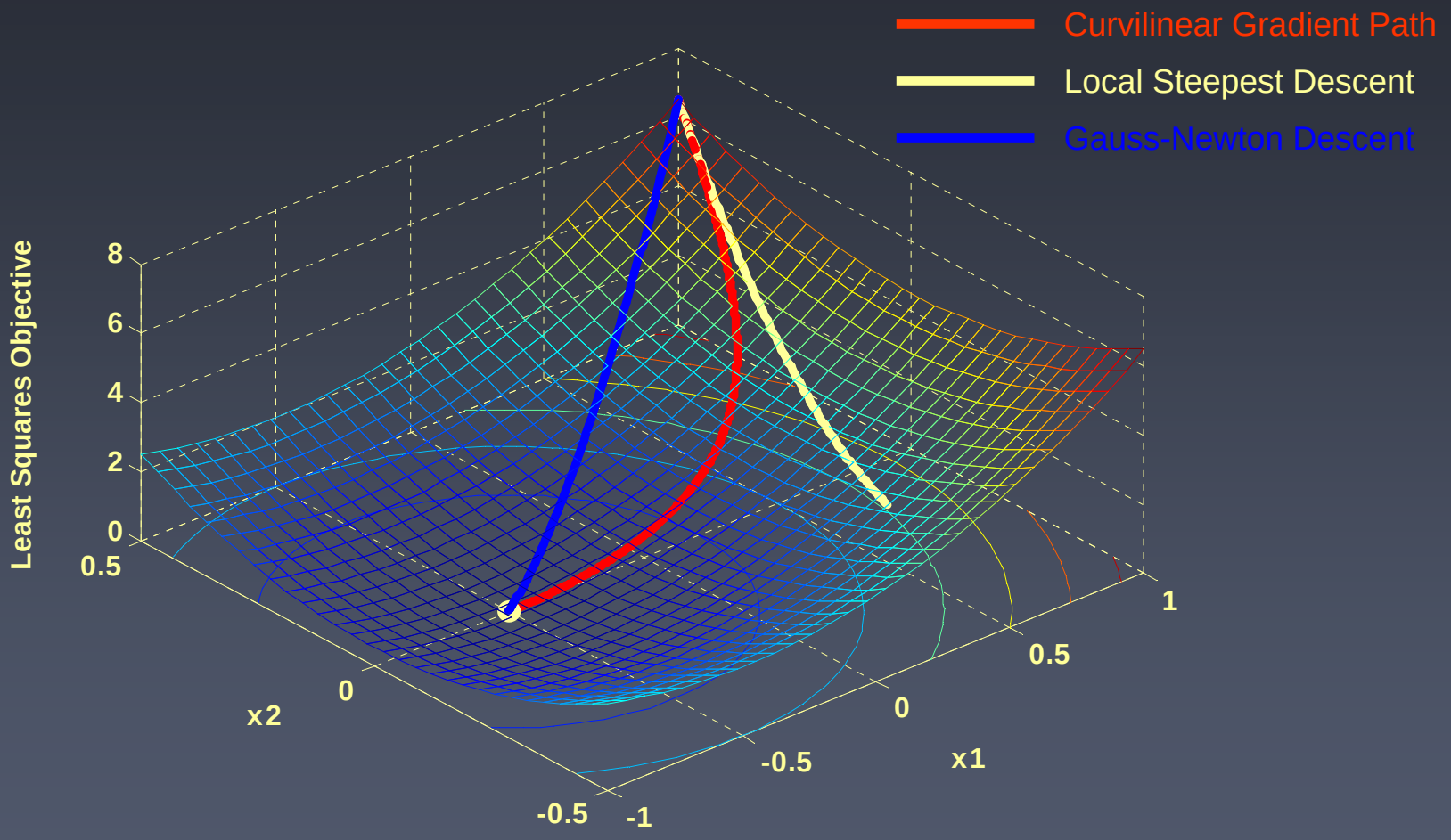
Identifiability Analysis

- Least square
- Locally identifiable if Hessian (**H**) is non singular
- $\mathbf{H} = \mathbf{J}^T\mathbf{J}$, where **J** is the Jacobian of objective function.
- Reciprocal condition number (*rcond*)

Parameter Identifiability Analysis on Ionic Current Conductance

Model	# Parameters	*rcond* (Direct)	*rcond* (Data Clamp)
Beeler-Reuter (1977)	4	6.313E-9	1.050E-8
Drouhard-Roberge (1987)	4	1.348E-4	4.951E-5
Luo-Rudy (1991)	6	9.880E-5	2.639E-4
Shannon *et al* (2004)	22	4.098E-13	2.067E-9
Earm-Nobel (1990)	11	6.567E-5	6.173E-5
Lovell *et al* (2004)	15	2.330E-7	2.205E-3
Hodgkin-Huxley (1952)	3	9.507E-2	7.178E-2

Parameter Optimisation



Curvilinear Gradient:

$$L(\alpha) = \left(e^{-\mathbf{H}\alpha} - \mathbf{I}\right)\mathbf{H}^{-1}\mathbf{a}$$