Fitting Kinetic Data

Lecture 3 a

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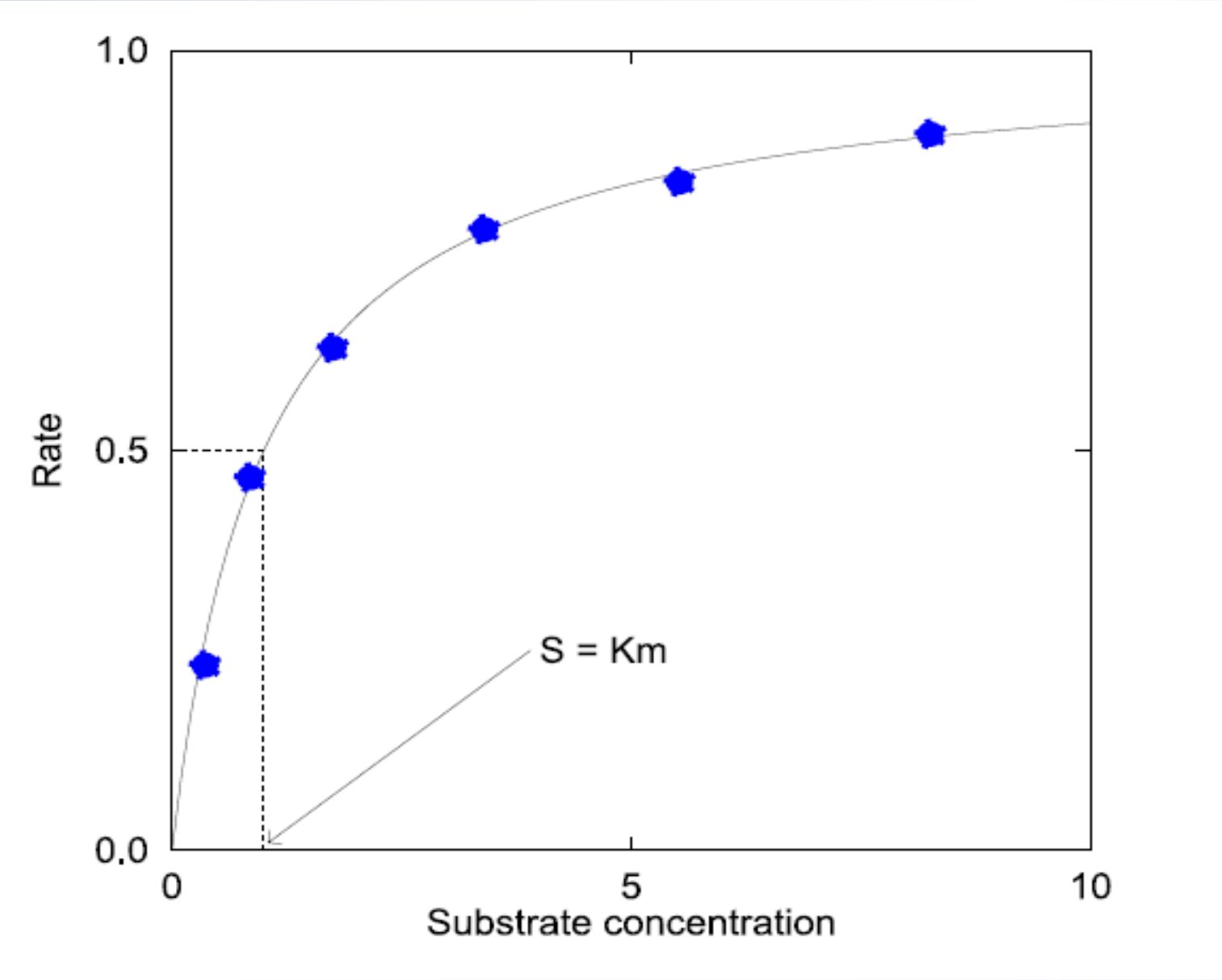
Parameter estimation from experimental data

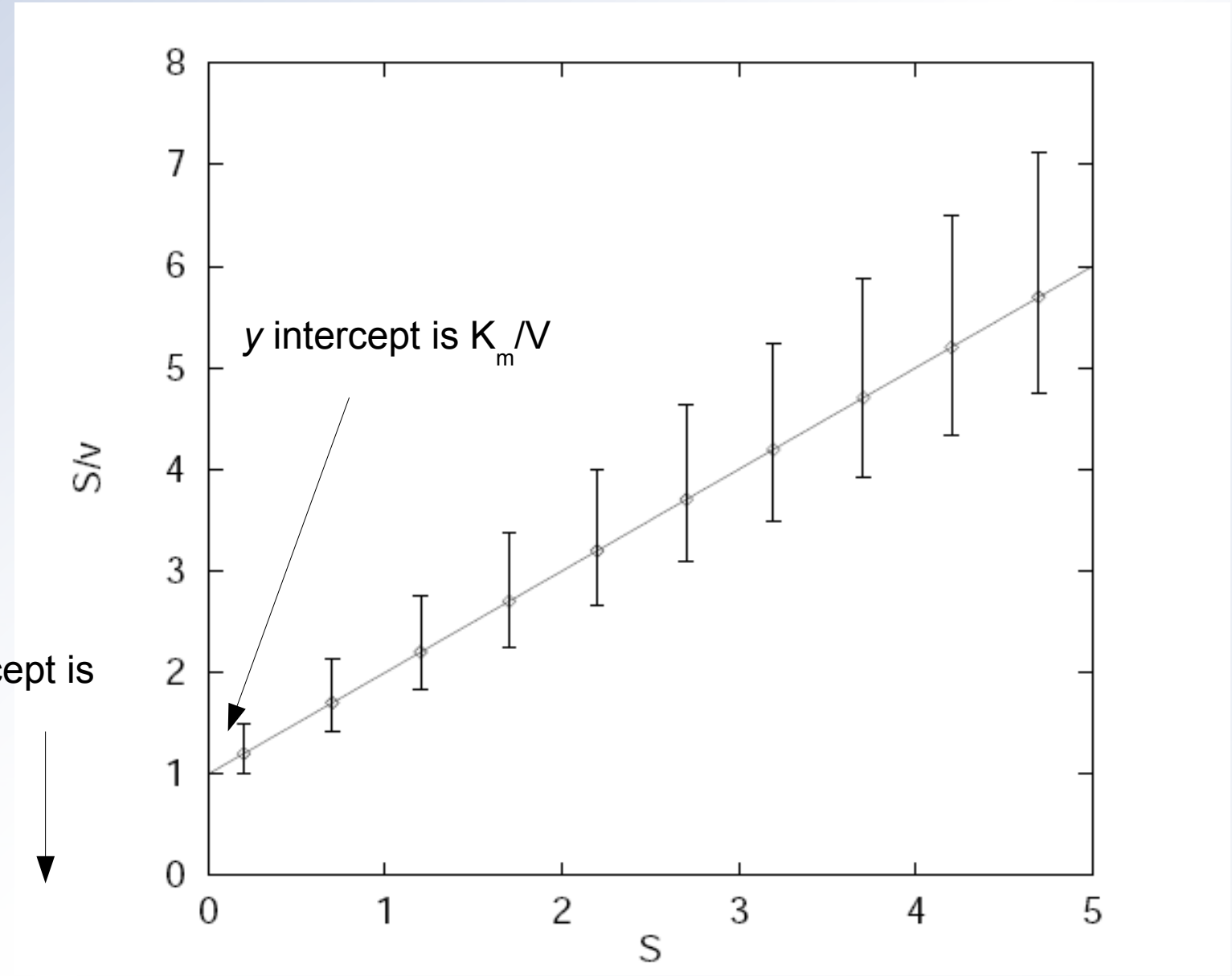
Using determination of Km and V values from experimental data as an example:

- Old approach – linear transformations
- New approach – non-linear fitting

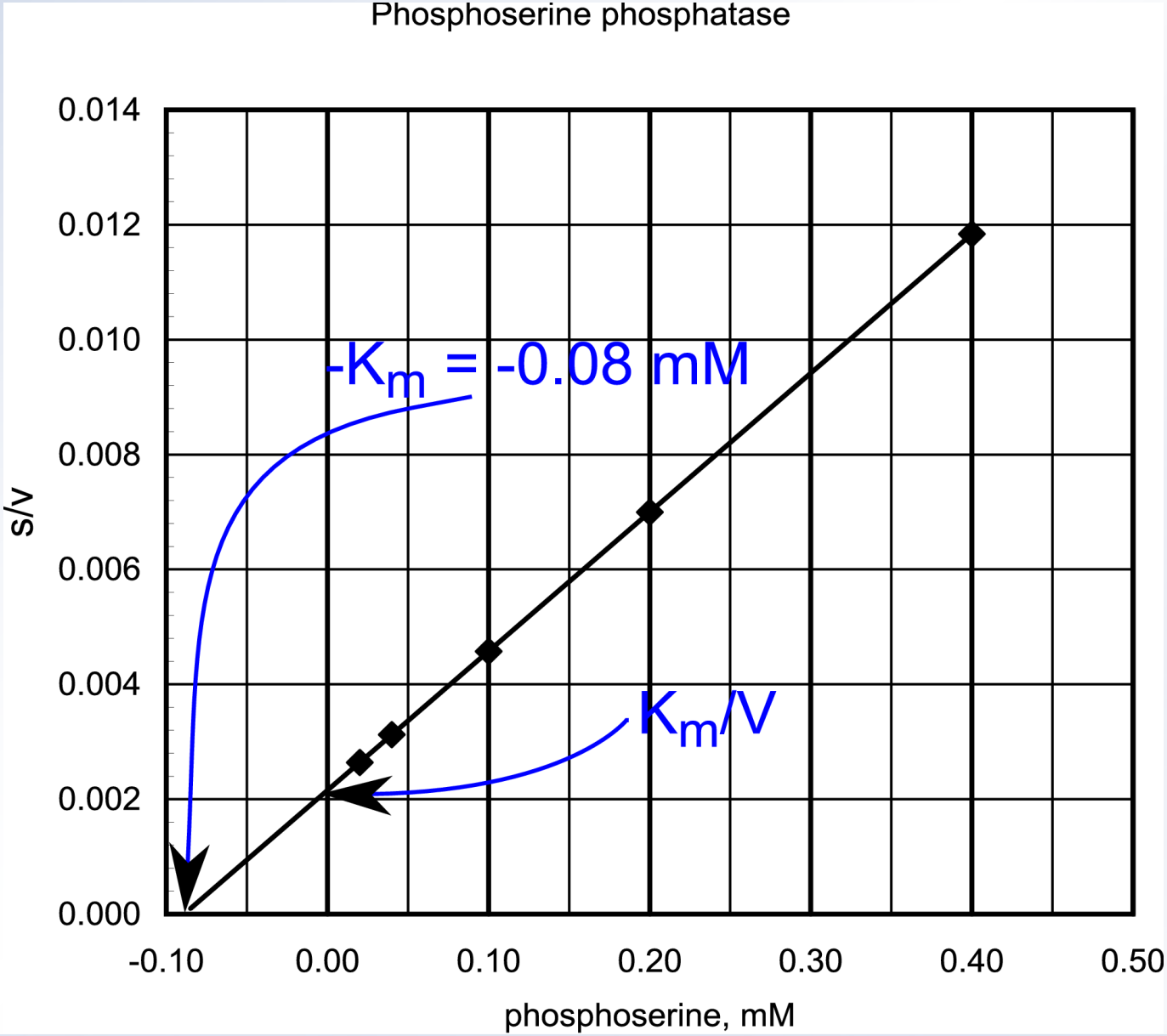
An enzyme kinetics experiment



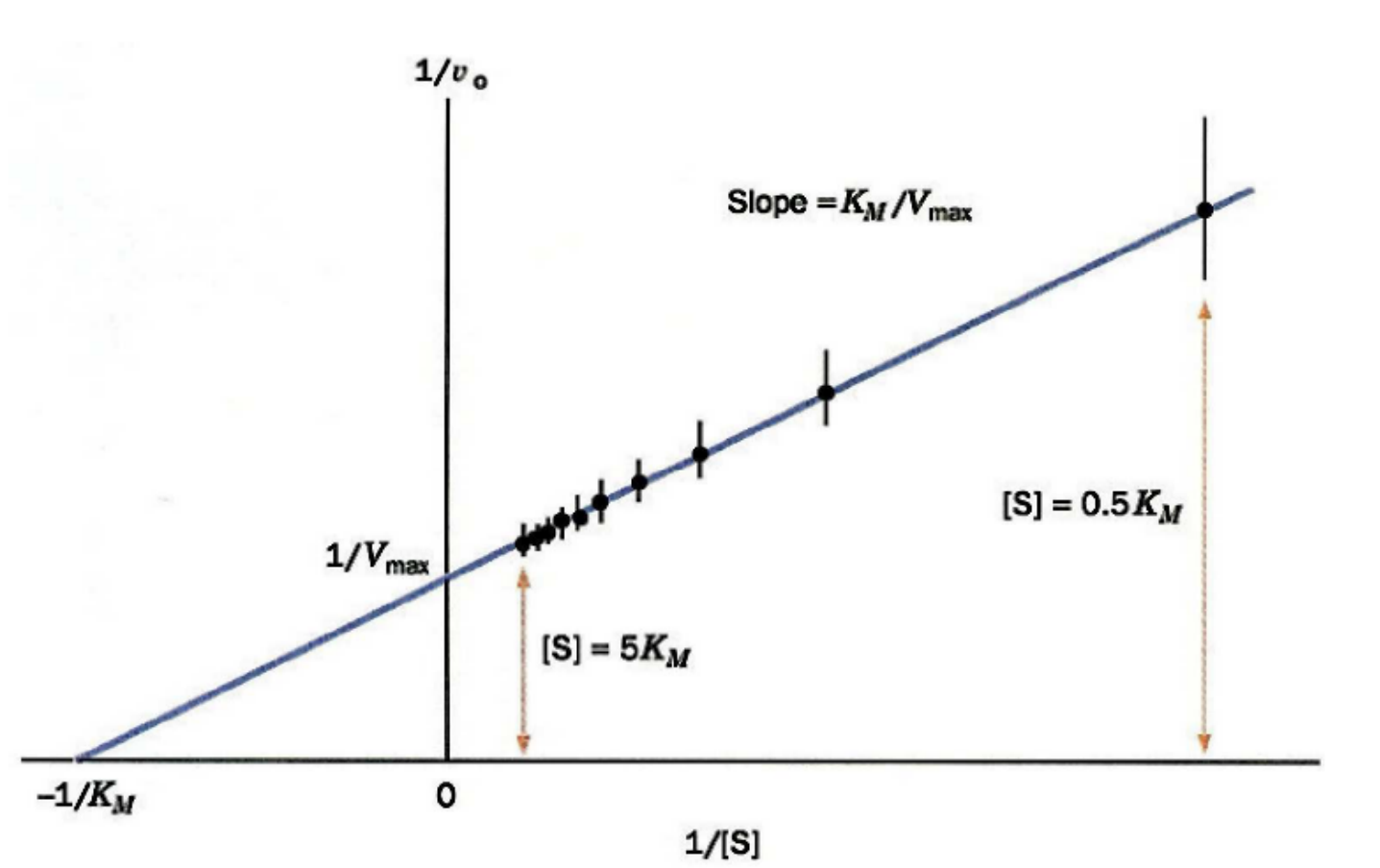
Hanes plot



Hanes plot showing intercepts



Lineweaver-Burk plot

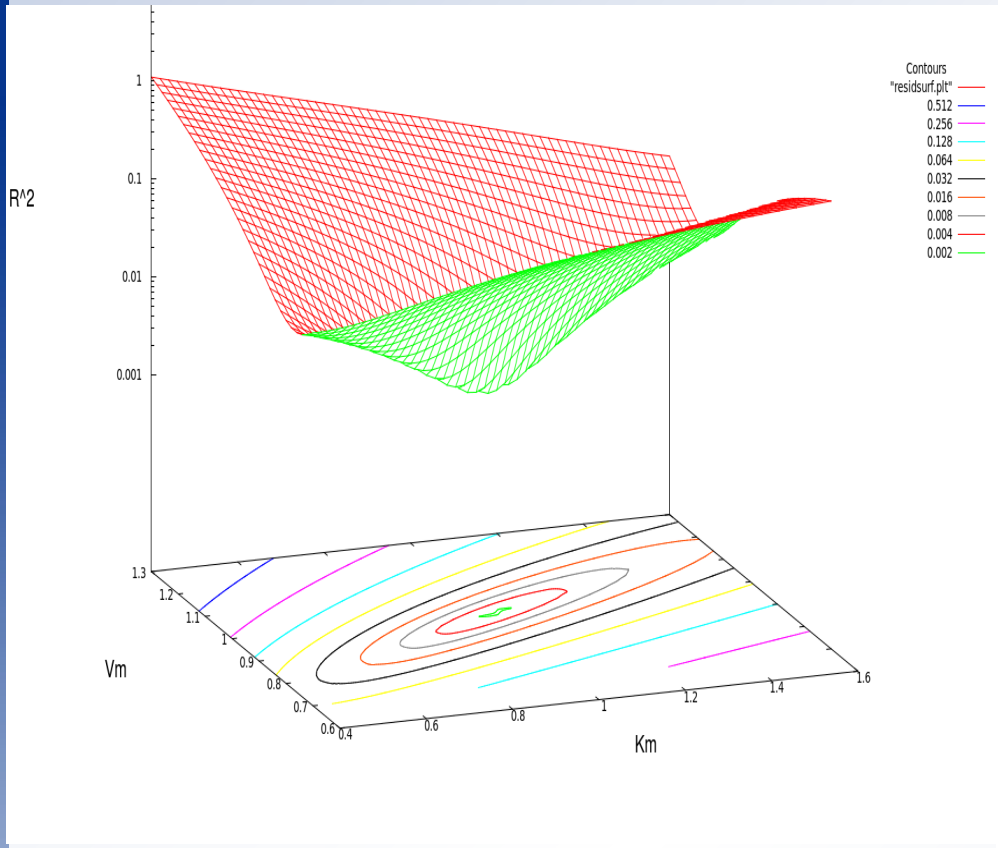


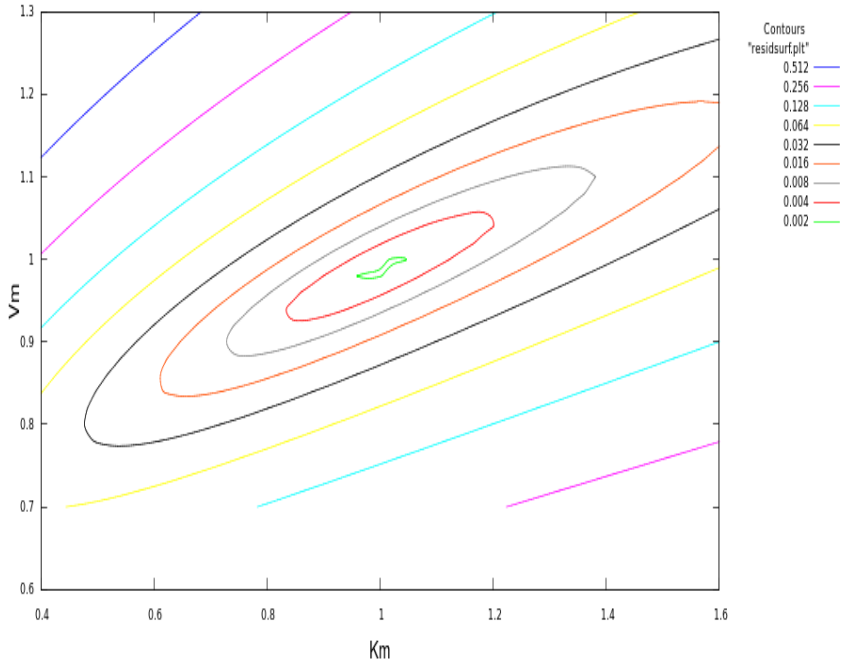
Demonstration of non-linear fitting

- Finding the 'best-fit' hyperbola through a set of points.
  (./runviewlogcont; ./runviewcontmap; gnuplot / load 'enzfitter.gnu')

- The aim is to minimise the sum of the squares of the deviations of the experimental points from a hyperbola by iteratively adjusting K_m and V.

Dependence of the sum of squares on K_m and V





Finding the optimum

- For non-linear problems, solutions are obtained iteratively starting with initial estimates.
- Nonlinear solvers use various strategies to move 'downhill' to the solution.
- If there is more than one dip in the surface, and initial estimates are poor, the solver may find the nearest minimum and miss the best solution. Try using different initial estimates.
- There may be no satisfactory solution if:
  - Two or more parameters are strongly correlated so that changing one parameter can be compensated by changing one or more others.
  - The experimental points contain no information about one or more parameters.

Problem

- The file enz2.dat contains data for the kinetics of phosphoserine phosphatase.
- Determine the Km and V for the enzyme with respect to its substrate phosphoserine, either by:
  - Examining file 'enzfitter.gnu' and performing the equivalent analysis on this data, or
  - Using the Excel file 'enzfitter.xls' and modifying it with this data. You need to have the solver add-in activated in your copy of Excel.