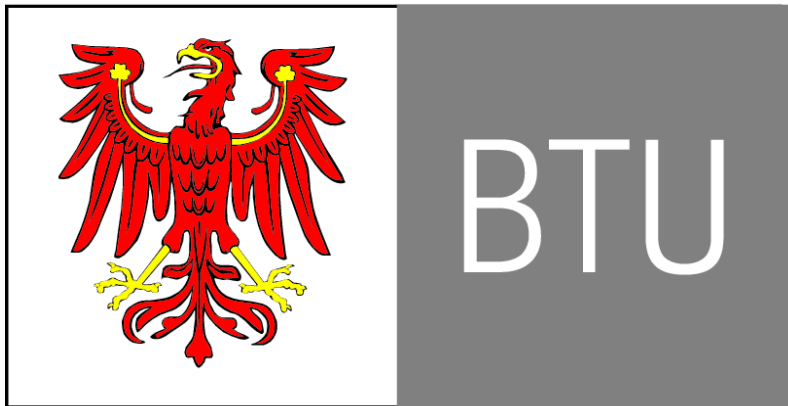


Workshop on modelling and visualisation
of biological and chemical systems

Simulation of Chemical Reactions with GroIMP and XL



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Outline

- 1.Motivation
- 2.Introduction to chemical kinetics
- 3.Specification of chemical systems in GroIMP
- 4.Discussion

Motivation

- Plant growth depends on
 - Structural constraints
 - Lighting
 - Nutrient distribution
- Simulation of nutrient distribution consists of
 - Transport
 - Chemical Kinetics

Chemical Kinetics

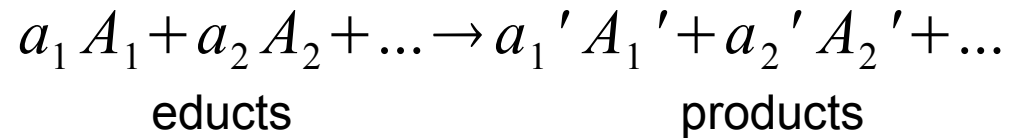
- Describes change of concentration over time
- Experimental determination of reaction rates
- Simulation by transforming chemical reactions into differential equations
- Depends on conditions:
 - Physical state (solid, liquid, gas)
 - Concentration (according to collision theory)
 - Temperature
 - Catalysts, pH-Value, ...

Investigation of Kinetics of a Chemical Reaction

1. Determination of reaction rate by measurement of substrate concentrations at different times; calculation of rate constants.
2. Finding a relation between measured reaction rates.

Rate of Reaction

- General chemical reaction:

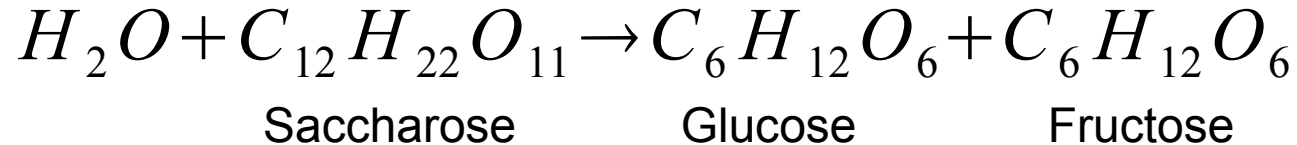


- Rate of reaction:

$$v = \frac{d\xi}{dt} = -\frac{1}{a_1} \frac{dn_1}{dt} = -\frac{1}{a_2} \frac{dn_2}{dt} = \frac{1}{a_1'} \frac{dn_1'}{dt} = \frac{1}{a_2'} \frac{dn_2'}{dt}$$

First Investigations

- In 1850 by *Ludwig Wilhelmy*:
inversion of saccharose acid solutions



- Observation of reaction by polarimeter
- Result:

$$\frac{dc}{dt} = -k c$$

- k is the rate coefficient, proportional to concentration of acid (acid is catalyst)

Chemical Equilibrium

- In 1863 application to chemical equilibrium by *C. M. Guldberg* and *P. Waage*
- Chemical equilibrium is result of compensation (of forward and backward reaction)



$$v_f = k_f [A]^a [B]^b$$

$$v_r = k_r [C]^c [D]^d$$

- In equilibrium:

$$v_f = v_r$$

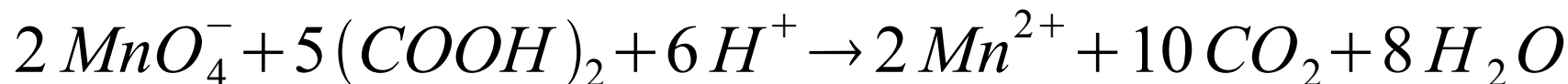
$$k_f [A]^a [B]^b = k_r [C]^c [D]^d$$

- *Van't Hoff*:

$$K = \frac{k_f}{k_r} = \frac{[A]^a [B]^b}{[C]^c [D]^d}$$

Further Investigations

- 1865 to 1867: Investigation of reaction between potassium permanganate and oxalic acid by *A. V. Harcourt* and *W. Esson*



$$v = k [\text{MnO}_4^-][(\text{COOH})_2]$$

- Conclusion:
Stoichiometric reactions do not allow inference of chemical kinetics!
- → Theory of consecutive reactions

Experimental Methods of Chemical Kinetics

- Reaction under same conditions in different vessels in parallel
- Extraction of small samples during the reaction
- Measurement of physical properties during the reaction:
 - Colour, absorption
 - Index of refraction, optical rotation, polarization
 - Volume, pressure, temperature

Order of Reaction

- Experiment yields values of concentration for different times
- Rate of reaction is a function of concentrations:

$$\frac{dc_1}{dt} = f(c_1, c_2, \dots, c_n)$$

- Rate of reaction depends on the product of concentrations:

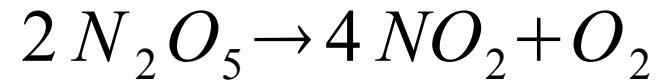
$$\frac{dc_a}{dt} = -k c_A^a c_B^b \dots c_N^n$$

- Order of reaction is the sum of the exponents, so

$$a + b + \dots + n$$

Example 1

- Decomposition of nitric pentoxide:

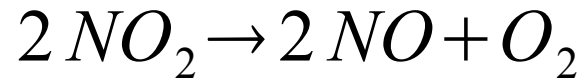


$$\frac{d[N_2 O_5]}{dt} = -k_1 [N_2 O_5]$$

\Rightarrow 1st order reaction

Example 2

- Decomposition of nitrogen dioxide:



$$\frac{d[\text{NO}_2]}{dt} = -k_2[\text{NO}_2]^2$$

\Rightarrow 2nd order reaction

Example 3

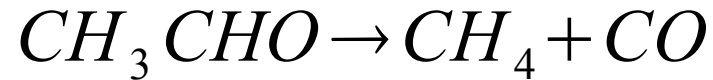


$$\frac{d[C_2H_5Br]}{dt} = -k_2[C_2H_5Br][(C_2H_5)_3N]$$

\Rightarrow 2nd order reaction

Example 4

- Decomposition of acetaldehyde:



$$\frac{d[CH_3CHO]}{dt} = -k_{1,5}[CH_3CHO]^{3/2}$$

\Rightarrow 1.5th order reaction

Conclusion

- There is no relation between the form of the stoichiometric equation and the reaction order of a chemical reaction.

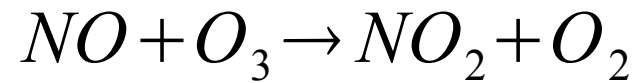
Reaction Molecularity

- Neither stoichiometric equation nor the reaction rate can provide reliable information about the real chemism of a reaction.
- Often reactions have many intermediary steps
- Single steps of a complex reaction are called elementary reaction

Reaction Molecularity (2)

- unimolecular:
spontaneous decomposition of a molecule
 - bimolecular:
collision of two molecules
- Reaction molecularity only meaningful for elementary reactions

Example of a bimolecular reaction



$$\frac{d[NO]}{dt} = -k_2[NO][O_3]$$

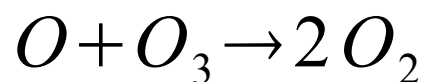
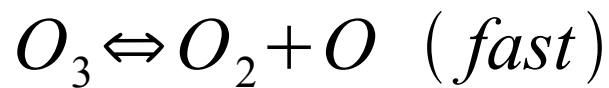
Reaction Mechanism

- Chain of consecutive elementary reactions
- Example: $2 O_3 \rightarrow 3 O_2$
- If this would be an elementary reaction, then it must hold:

$$\frac{d[O_3]}{dt} = -k_2 [O_2]^2$$

- The experiment shows: $\frac{d[O_3]}{dt} = -k \frac{[O_3]^2}{[O_2]}$

- Explanation:



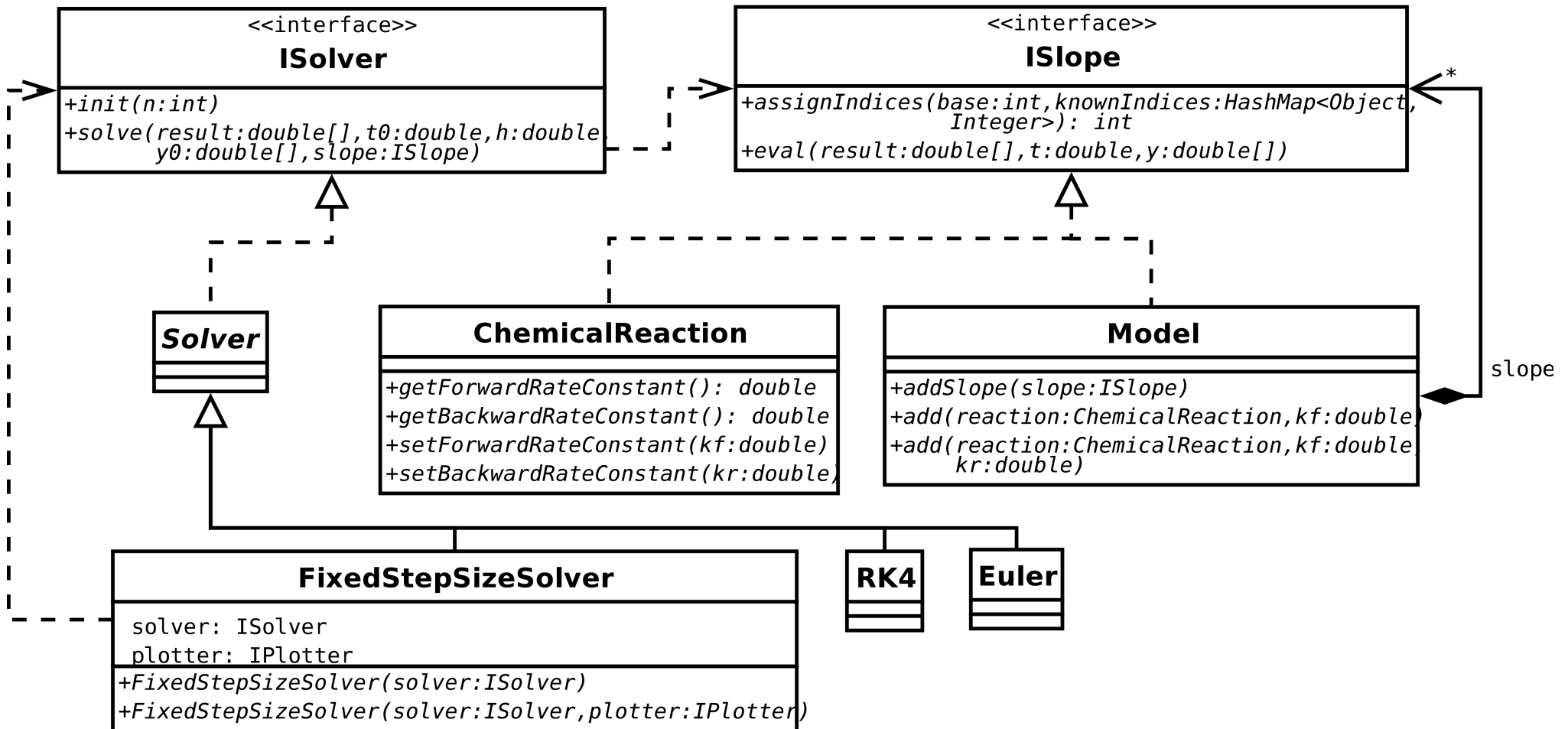
$$[O] = K \frac{[O_3]}{[O_2]}$$

$$\frac{d[O_3]}{dt} = -k_2' [O][O_3] = -k_2' K \frac{[O_3]^2}{[O_2]}$$

Simulation of Chemical Systems

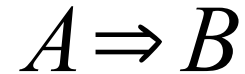
- Results are the concentrations of substrates as a function of time
- Performed by numerical integration
- Chemical equations must be translated into differential equations
- Automatic translation does only work for elementary reactions

Simulation Framework



Simple Example

- Three substrates: A, B, C
- Two reactions:



- Differential equations:

$$\frac{d[A]}{dt} = -k_1[A]$$

$$\frac{d[B]}{dt} = +k_1[A] - k_2[B]$$

$$\frac{d[C]}{dt} = +k_2[B]$$

Same Example in XL

```
import static de.grogra.cells.ChemicalOperators.*;
import static de.grogra.cells.Molecule.*;
import de.grogra.cells.*;
import de.grogra.cells.solver.*;
import java.util.*;

// define new species X1, X2 and X3
const Molecule X1 = new Molecule("X1");
const Molecule X2 = new Molecule("X2");
const Molecule X3 = new Molecule("X3");

public void run ()
{
    // define a new reaction: X1 -> X2
    // rate coefficient is 2
    ChemicalReaction r1 = X1 <=> X2;
    r1.setForwardRateConstant(2);

    ...
}
```


Same Example in XL (2)

...

```
// instantiate a new simulation model
de.grogra.cells.Model model =
    new de.grogra.cells.Model();

// add the chemical reaction to the model
model.addSlope(r1);

// add another chemical reaction to the model
model.add(X2 <=> X3, 1);

// assign integers [0, count) to species
HashMap m = new HashMap();
int count = model.assignIndices(0, m);

// allocate memory for numerical simulation
double[] result = new double[count];
double[] y0 = new double[count];
```

...

Same Example in XL (3)

...

```
// set initial conditions
setValue(m, y0, X1, 10);

// initialise solver
RK4 rk4 = new RK4();
FixedStepSizeSolver fs = new FixedStepSizeSolver(
    rk4, new Chart("concentrations", 10) {
        public void plot(DatasetRef data,
            double t, double[] y)
        {
            data.addRow().set(0, y[0])
                .set(1, y[1]).set(2, y[2]);
        }
    }
);

// calculate solution
fs.init(count);
fs.solve(result, 0, 5, y0, model);
}
```

Screenshot

chemtest - GroIMP

File Edit Objects Panels Net Help

run Run run Stop Reset

jEdit - Model.rgg

File Edit Search Markers Folding View Utilities Macros Plugins Help

Model.rgg (project:/chemtest[1]/)

```
// initialise solver.
RK4 rk4 = new RK4();
//DormandPrice dp = new DormandPrice();
//Plotter plotter = new Plotter(dp, "chemdata.txt");
FixedStepSizeSolver fs = new FixedStepSizeSolver(rk4
//new Chart(data, "concentrations") {.
    new Chart("concentrations", 10) {.
        public void plot(DatasetRef data, double t,
            data.addRow().set(0, y[0]).set(1, y[1]).
        }.
    }.
);
//AdaptiveStepSizeSolver fs = new AdaptiveStepSizeSc
//fs.init(count);
//fs.solve(result, 0, 10, y0, model);

// calculate solution.
fs.init(count);
fs.solve(result, 0, 5, y0, model);
}
```

Messages XL Console concentrations File Explorer

concentrations

77,41-50 67% (xl, XL, US-ASCII) - - - U 48 / 134Mb

File Model.rgg was read.

Second Example

- Irreversible Michaelis Menten:



- Differential equations:

$$\frac{d[S]}{dt} = -k_1[E][S] + k_{-1}[ES]$$

$$\frac{d[E]}{dt} = -k_1[E][S] + k_{-1}[ES] + k_2[ES]$$

$$\frac{d[ES]}{dt} = +k_1[E][S] - k_{-1}[ES] - k_2[ES]$$

$$\frac{d[P]}{dt} = +k_2[ES]$$

Second Example in XL

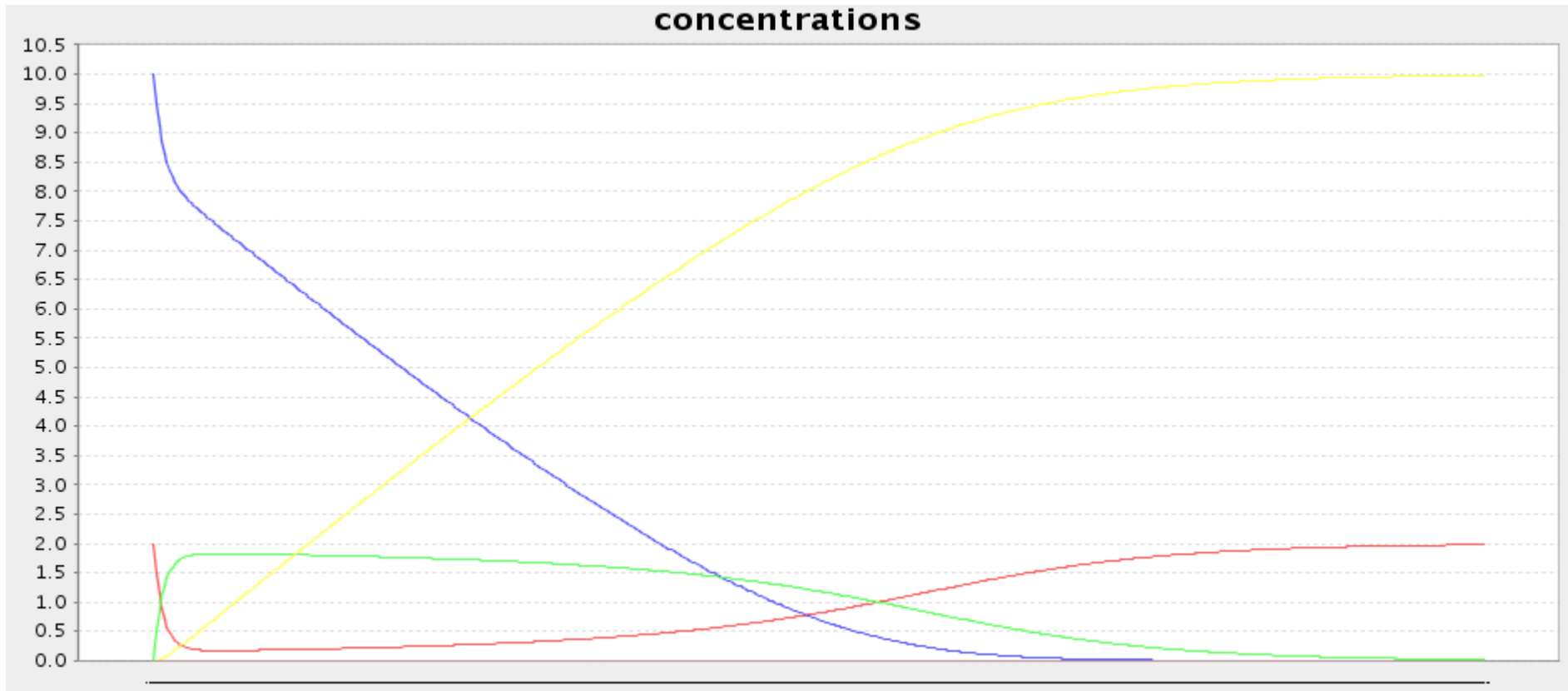
```
const Molecule E = new Molecule("E");
const Molecule S = new Molecule("S");
const Molecule ES = new Molecule("ES");
const Molecule P = new Molecule("P");

...
// define michaelis menten kinetics
de.grogra.cells.Model model =
    new de.grogra.cells.Model();
model.add(E + S <=> ES, 3, 0.1);
model.add(ES <=> E + P, 2);

// set initial conditions
setValue(m, y0, E, 2);
setValue(m, y0, S, 10);

...
// calculate solution
fs.init(count);
fs.solve(result, 0, 5, y0, model);
}
```

Second Example after Simulation



Problems

- Law of mass action only valid for elementary reactions
- But observable reactions mostly are not elementary and intermediate steps are unknown
- Not valid under dimensionally-restricted conditions → fractal kinetics
- But reactions in plant-cells are dimensionally-restricted