How to Use the Model Builder

A gentle, practical guide with the exact kinetic equations — now with extra context

Bob van Sluijs

October 16, 2025

Contents

1 What is this and who is it for?

This guide takes you from *lab intuition* to a *simulation-ready ODE model* for an in-vitro flow reactor. It has two goals:

- Be a *cookbook* you can follow the first time you use the tool.
- Be a *reference* you can return to for the actual equations and options.

If you are a wet-lab scientist, a new coder, or just in a hurry, you're in the right place. You'll describe each reaction in a tiny seven-field row, optionally list which species are fed by syringes, choose (or let the tool choose) a kinetic family, pick a reactor variant, and simulate or fit the model to your data.

2 Orientation: how the pieces fit together

1) **Your input** is a list of rows:

$$[E,\ \text{rev},\ K,\ \mathbf{R},\ \mathbf{P},\ \mathbf{A},\ \mathbf{I}]$$

(enzyme or `False`, reversible?, kinetic key or `False`, reactants, products, activators, inhibitors).

2) **The builder** turns each row into a *flux* v_r according to the kinetic family (`K`). If `K=False`, it attaches *all* families for that step so you can compare.

3) **The reactor** adds inflow/outflow terms based on your syringe map. You pick a reactor variant by name when assembling the final model.

4) **The ODEs** are built automatically:

$$\dot{X} = \sum_r \nu_{r\to X}\, v_r + \Phi_X^{\text{reactor}}.$$

5) **You simulate or fit** the returned model using your favorite solver/optimizer.

Tip: You can start with just two reactions and no syringes (batch-like). Once it works, add syringes, regulation, and additional reactions.

3 Quick Start (copy–paste)

1) Describe your network

Each row has seven fields:

$$[\,E,\ \text{rev},\ K,\ \mathbf{R},\ \mathbf{P},\ \mathbf{A},\ \mathbf{I}\,].$$

- E: enzyme string (`'HEX1'`, `'PGI'`, ...) or `False` for non-enzymatic.
- **rev**: `True` if reversible (auto-adds a reverse row), else `False`.
- K: kinetic family (`'MM'`, `'GH'`, `'EO'`, `'PP'`, `'RER'`), or `False` to try *all*.
- **R**, **P**: lists of reactants/products (strings).
- **A**, **I**: optional activators/inhibitors.

Example:

```
network = [
  ['HEX1', False, 'GH', ['Glucose_D','ATP'], ['ADP','G6P'], [], []],
  ['PGI',  True,  'MM', ['G6P'],             ['F6P'],       [], []],
]
```

2) (Optional) Syringe feeds / controlled species

```
syringe_load = {0: ['HEX1'], 1: ['ATP'], 2: ['Glucose_D']}
```

3) Build & assemble

```
reactions = categorize_reactions(network)
reactor_kinetics, reaction_kinetics = construct_model_fluxterms(
    reactions, reactormix=syringe_load
)
basemodel = construct_kinetic_combinations(
    reactor_kinetics, reaction_kinetics,
    name='MyModel',
    reactor_type='reactor_predefined_control_single_reactor'
)
model = basemodel.return_model()
```

The `model` now contains:

- per-species ODEs,
- the kinetic & reactor variants you picked,
- a parameter list (names/initial values) to set or fit.

4 Mapping biology to the input rows (with examples)

4.1 Common patterns

- **Uni–uni enzyme** (*e.g.* isomerase): $[E,\ \_,\ 'MM',\ [S],\ [P],\ A, I]$.
- **Kinase/transferase** (two substrates → two products): $[E,\ \_,\ 'GH',\ [S_1, S_2],\ [P_1, P_2],\ A, I]$.
- **Non-enzymatic** (spontaneous hydrolysis): [`False`, _, _, $[S]$, $[P]$, [], []] — mass action.
- **Regulated** (inhibitor I, activator A): put species in the A or I list; the math handles the rest.

4.2 Naming conventions that save time

- Use `UPPER_Camel_With_Underscores` or `snake_case` and keep it consistent.
- Avoid spaces and symbols in species names (*e.g.* use `Glucose_D`, not "glucose d").
- If two names differ in case, they are different species.

Heads up: Auto-reverse does *not* copy activators/inhibitors. If the reverse is regulated, add an explicit reverse row.

5 Choosing a kinetic family (decision help)

`MM` One substrate → one product. Fast, simple, works well for isomerases and simple conversions.

`GH` Two substrates → two products (bi–bi) with a flexible denominator. Good default for multi-substrate steps.

`EO` Binding occurs in a fixed order (ordered bi–bi). Use if mechanism is known to be ordered.

`PP` Ping–pong (double-displacement). Use if enzyme alternates between forms and substrates don't bind simultaneously.

`RER` Random binding under rapid equilibrium. Use if either substrate can bind first and binding is fast.

Tip: Unsure? Set `K=False` to register all families for that step and compare fits or predictive performance.

6 Exact kinetic equations (what is computed)

All enzymatic families share *regulation factors*. Let $\mathcal{A}$ be the activators and $\mathcal{I}$ the inhibitors. For enzyme E:

Allostery (applies to all enzymatic families)

$$A_{\text{act}} = \prod_{A \in \mathcal{A}} \Big(1 + \frac{A}{k_{\text{act}}(E{:}A)}\Big), \tag{1}$$

$$A_{\text{inh}} = \prod_{I \in \mathcal{I}} \Big(1 + \frac{I}{k_{\text{inh}}(E{:}I)}\Big). \tag{2}$$

In every enzymatic rate below, A_{act} multiplies the *numerator* and A_{inh} multiplies the *denominator*.

6.1 MA — Mass Action (non-enzymatic rows only)

If $E =$ `False`:

$$v_{\text{MA}} \;=\; k_{\text{fwd}}(\mathbf{R}) \prod_{S \in \mathbf{R}} S.$$

No activators or inhibitors are applied here.

6.2 MM — Michaelis–Menten (uni–uni as implemented)

Exactly one substrate S and enzyme E:

$$v_{\text{MM}} \;=\; \frac{E\, k_m(E{:}S)\, S\, A_{\text{act}}}{k_m(E{:}S)\, A_{\text{inh}} + S}.$$

Implementation note: k_{cat} may be registered for bookkeeping but does not appear in this flux expression.

6.3 GH — "Generalized Haldane" (bi–bi form)

Two substrates S_1, S_2 (alphabetically sorted) and enzyme E:

$$v_{\mathrm{GH}} \;=\; \frac{E\, k_{\mathrm{cat}}(E{:}S_1{:}S_2)\, S_1\, S_2\, A_{\mathrm{act}}}{A_{\mathrm{inh}}\Big(k_m(E{:}S_1)\, k_m(E{:}S_2) + k_m(E{:}S_2)\, S_1 + k_m(E{:}S_1)\, S_2 + S_1\, S_2\Big)}.$$

6.4 EO — Equilibrium-Ordered (bi–bi)

With ordered binding parameters k_{ai} and k_b (explicit order can be supplied):

$$v_{\mathrm{EO}} \;=\; \frac{E\, k_{\mathrm{cat}}(E{:}S_1{:}S_2)\, S_1\, S_2\, A_{\mathrm{act}}}{A_{\mathrm{inh}}\Big(k_{ai}(E{:}S_1{:}S_2)\, k_b(E{:}S_1) + k_b(E{:}S_1)\, S_1 + S_1\, S_2\Big)}.$$

6.5 PP — Ping–Pong (bi–bi)

With binding parameters $k_a(E{:}S_1)$ and $k_b(E{:}S_2)$:

$$v_{\mathrm{PP}} \;=\; \frac{E\, k_{\mathrm{cat}}(E{:}S_1{:}S_2)\, S_1\, S_2\, A_{\mathrm{act}}}{A_{\mathrm{inh}}\Big(k_b(E{:}S_1)\, S_1 + k_a(E{:}S_2)\, S_2 + S_1\, S_2\Big)}.$$

6.6 RER — Rapid-Equilibrium Random (bi–bi)

With $k_{ai}(E{:}S_1{:}S_2), k_a(E{:}S_1), k_b(E{:}S_2)$:

$$v_{\mathrm{RER}} \;=\; \frac{E\, k_{\mathrm{cat}}(E{:}S_1{:}S_2)\, S_1\, S_2\, A_{\mathrm{act}}}{A_{\mathrm{inh}}\Big(k_{ai}(E{:}S_1{:}S_2)\, k_b(E{:}S_2) + k_b(E{:}S_2)\, S_1 + k_a(E{:}S_1)\, S_2 + S_1\, S_2\Big)}.$$

Parameter sets per family (at a glance)

- MA: $\{k_{\mathrm{fwd}}(\mathbf{R})\}$.
- MM: $\{k_m(E{:}S),\ k_{\mathrm{cat}}(E{:}S)\}$ — only k_m appears in the formula.
- GH: $\{k_m(E{:}S_1),\ k_m(E{:}S_2),\ k_{\mathrm{cat}}(E{:}S_1{:}S_2)\}$.
- EO: $\{k_{ai}(E{:}S_1{:}S_2),\ k_b(E{:}S_1),\ k_{\mathrm{cat}}(E{:}S_1{:}S_2)\}$.
- PP: $\{k_a(E{:}S_1),\ k_b(E{:}S_2),\ k_{\mathrm{cat}}(E{:}S_1{:}S_2)\}$.
- RER: $\{k_{ai}(E{:}S_1{:}S_2),\ k_a(E{:}S_1),\ k_b(E{:}S_2),\ k_{\mathrm{cat}}(E{:}S_1{:}S_2)\}$.

If activators/inhibitors are present, the model also includes $\{k_{\mathrm{act}}(E{:}A)\}$ and $\{k_{\mathrm{inh}}(E{:}I)\}$.

7 From rate v to ODEs (assembly and bookkeeping)

For each species X:

$$\dot{X} \;=\; \sum_r \nu_{r\to X}\, v_r(\cdot) \;+\; \Phi_X^{\mathrm{reactor}}, \qquad \nu_{r\to X} = \begin{cases} -1, & X \in \mathbf{R}_r, \\ +1, & X \in \mathbf{P}_r, \\ 0, & \text{otherwise.} \end{cases}$$

The builder creates these $\pm v$ fragments per state and merges them into the final ODEs.

8 Reactor terms (flow/control side) with intuition

A **reactor variant** adds inflow/outflow/control to each species. A commonly used option is:

`reactor_predefined_control_single_reactor`.

Intuition:

1. *Inflow* for species in your `syringe_load` channels (*e.g.* enzyme, ATP, precursors).
2. *Outflow/dilution* for all species proportional to total flow divided by reactor volume.

Typical term for species X:

$$\Phi_X^{\text{reactor}} = \underbrace{\text{inflow}_X}_{\text{from channels}} - \underbrace{\frac{F_{\text{total}}}{V_{\text{reactor}}} X}_{\text{dilution/outflow}} .$$

Tip: To mimic a batch experiment, pick a reactor variant that omits inflow or set all flows to zero.

9 Units, scaling, and initial conditions (practical advice)

- **Concentrations** in µ are typical; keep everything consistent across species and parameters.
- **Rates** like k_{cat} are often in min^{-1}. Flows in µL/min; volumes in µL.
- **Scaling** helps numerical solvers. If states vary by orders of magnitude, consider rescaling inputs or using log-transformed parameters during fitting.
- **Initial conditions**: start close to typical lab pre-mix concentrations (substrates high, enzymes lower). It's fine to begin with zeros for products.

Note: When you add inflow, steady-state levels depend on both kinetics and flow/volume. A quick "sanity sweep" over flow rates is often illuminating.

10 Fitting data: a minimal workflow

1. **Build** the model and set initial guesses for all parameters.
2. **Choose** an objective (*e.g.* sum of squared errors between observables and simulated species).
3. **Simulate** on the same time grid as your data; interpolate as needed.
4. **Optimize** parameters (start with a global search over a few decades, then a local optimizer).
5. **Validate**: hold out a time window or a perturbation and check predictions before/after fitting.

Tip: Use log-parameters for positivity and better conditioning. Start with a subset of parameters (fix flows/volumes first), then free more as needed.

11 Model comparison and sensitivity (when $K = False$)

When you set K=`False` on one or more steps, the builder can assemble a *family* of models (one per combination). To choose among them:

- Compare fit quality (SSE) and complexity (number of parameters).
- Use simple criteria like AIC/BIC if you compute them, or pick the simplest model that fits within a tolerance ("Occam's razor").
- Perform *local sensitivity*: perturb each parameter and see which observables move the most; this guides which constants matter.

12 Parameter names, classes, units, and good defaults

Name pattern	Class	Typical bounds	Unit
`k_m_`	Km	[0.01, 5000]	µ
`k_a_`	Ka	[0.01, 5000]	µ
`k_b_`	Kb	[0.01, 5000]	µ
`k_ai_`	Kai	[0.01, 5000]	µ
`k_inh_`	Kinh	[0.01, 5000]	µ
`k_act_`	Kact	[0.01, 5000]	µ
`k_fwd_`	Kfwd	[0.01, 5000]	min^{-1}
`k_cat_`	Kcat	[0.01, 500]	min^{-1}
`(in)`	Kstock	[0.1, 4000]	µ
`kflow`	Kflow	[6/60, 500/60]	µL/min
`volume`	Kvolume	[190, 191]	µL

Tip: If an optimizer struggles, shrink bounds, tie related parameters (same K_m for isoforms), or fix flows/volumes to measured values.

13 Worked examples (end-to-end snippets)

A) Uni–uni MM with inhibition (forward + auto-reverse)

```
network = [
  ['PGI', True, 'MM', ['G6P'], ['F6P'], [], ['I']],
]
syringe_load = {0:['PGI']}  # optional
```

Rate and ODE fragments:

$$v = \frac{E\, k_m\, S}{k_m \left(1 + \frac{I}{k_{\mathrm{inh}}}\right) + S}, \quad \dot{S} = -v,\ \dot{P} = +v \quad (+\ \Phi^{\mathrm{reactor}}_{\{S,P\}}).$$

Reverse is auto-added. If reverse inhibition exists, add an explicit reverse row.

B) Bi–bi step with unknown mechanism (compare families)

```
network = [
  ['HEX1', False, False, ['Glucose_D','ATP'], ['ADP','G6P'], [], []],
]
```

Here `K=False` registers `GH`, `EO`, `PP`, and `RER` for the step. Build the model set, fit each, and pick the simplest one that explains your data.

C) Reactor feeding a subset of species

```
syringe_load = {
  0: ['HEX1'],       # enzyme channel
  1: ['ATP','PEP'],  # energy channel
  2: ['Glucose_D']   # substrate channel
}
```

Pick `reactor_predefined_control_single_reactor`. Each listed species gets an inflow from its channel; all species get a dilution term.

14 Common pitfalls (and quick fixes)

- **Species spelling**: `Glucose_D` $\neq$ `glucose_d`; a typo creates a second species.
- **Reverse regulation**: auto-reverse doesn't inherit activators/inhibitors — add a dedicated reverse row if needed.
- **Exploding trajectories**: check units, reduce time step, lower k_{cat} and flow rates, verify initial conditions.
- **Too many parameters**: start with `MM`/`GH` and only then try `EO`/`PP`/`RER`. Tie or fix weakly identifiable parameters.
- **Batch vs flow mismatch**: choose a reactor variant that matches your experiment (no inflow for batch).

15 FAQ (new-user edition)

Do I need exact parameter values to start? No. Build first. The model lists what you need. Use literature or ballpark guesses and fit.

Which kinetic family should I try first? `MM` for single-substrate steps; `GH` for two-substrate steps. If you know the mechanism is ordered, try `EO`; if ping–pong is likely, try `PP`. Otherwise, `RER`. If unsure, use K`=False`.

Can I mix enzymatic and non-enzymatic steps? Yes. Use E`=False` for mass action and a string for enzymatic steps.

How do I do a closed (batch) run? Pick a reactor variant with no inflow or set all `kflow` to zero.

How do I export or reuse models? Keep your network list, syringe map, and parameter CSV/YAML together and version them (date + short description). That file set *is* your model.

16 Cheat sheet (one page of essentials)

Input row

$$[\, E,\ \text{rev},\ K,\ \mathbf{R},\ \mathbf{P},\ \mathbf{A},\ \mathbf{I}\,]$$

Kinetics

$$\begin{aligned}
v_{\mathrm{MA}} &= k_{\mathrm{fwd}} \prod_{S\in\mathbf{R}} S,\\
v_{\mathrm{MM}} &= \frac{E\, k_m\, S\, A_{\mathrm{act}}}{k_m\, A_{\mathrm{inh}} + S},\\
v_{\mathrm{GH}} &= \frac{E\, k_{\mathrm{cat}}\, S_1 S_2\, A_{\mathrm{act}}}{A_{\mathrm{inh}}(k_{m1}k_{m2} + k_{m2}S_1 + k_{m1}S_2 + S_1S_2)},\\
v_{\mathrm{EO}} &= \frac{E\, k_{\mathrm{cat}}\, S_1 S_2\, A_{\mathrm{act}}}{A_{\mathrm{inh}}(k_{ai}k_b + k_bS_1 + S_1S_2)},\\
v_{\mathrm{PP}} &= \frac{E\, k_{\mathrm{cat}}\, S_1 S_2\, A_{\mathrm{act}}}{A_{\mathrm{inh}}(k_bS_1 + k_aS_2 + S_1S_2)},\\
v_{\mathrm{RER}} &= \frac{E\, k_{\mathrm{cat}}\, S_1 S_2\, A_{\mathrm{act}}}{A_{\mathrm{inh}}(k_{ai}k_b + k_bS_1 + k_aS_2 + S_1S_2)}.
\end{aligned}$$

ODE assembly

$$\dot{X} = \sum_r \nu_{r\to X} v_r + \Phi_X^{\mathrm{reactor}}, \quad \nu_{r\to X} \in \{-1, 0, +1\}.$$

Reactor (typical)

$$\Phi_X^{\mathrm{reactor}} = \mathrm{inflow}_X - \frac{F_{\mathrm{total}}}{V_{\mathrm{reactor}}}\, X.$$

Parameter patterns

$k_m,\ k_a,\ k_b,\ k_{ai},\ k_{\mathrm{cat}},\ k_{\mathrm{act}},\ k_{\mathrm{inh}},\ k_{\mathrm{fwd}},\ kflow,\ volume,$ (in).

You're ready

Start with two or three reactions, `MM`/`GH` kinetics, and a reactor variant that matches your setup. Simulate a short time window. When the behavior looks sensible, add regulation, explore `EO`/`PP`/`RER`, or set K=`False` to compare mechanisms. Keep your inputs, parameters, and notes together — that's reproducible modeling.