## Supporting Information

# Variable Time Normalization Analysis: General Graphical Elucidation of Reaction Orders from Concentration Profiles

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Supporting Information

S-1

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## 1. General Procedures

All figures have been generated by simulating catalytic reactions with a deterministic method LSODA using COPASI and introducing a random error with a normal distribution with Microsoft Excel. The conditions used for the simulation of each catalytic cycle of the manuscript (including the catalytic cycle, the initial concentrations of substances, and the kinetic constants), together with the value of the standard deviation for the normal distribution of the random error, are detailed below. The resulting exact numerical values used to plot the figures are provided in section "6. Numerical Data" at the end of this supporting information.

## 2. Mathematical derivation of the normalization of the abscissa axis

The overlay of reaction profiles that differ in the concentration of one component occurs when the correct order in that component is used in the normalization of one of the plot axis. When rate plots are used, the normalization is applied to the rate axis (ordinate), but when concentration plots are used the normalization needs to be performed in the time axis (abscissa).

In order to find the adequate normalization factor, a change in variable has been used (Figure S1). The new abscissa axis should be such as to make the original concentration reaction profiles become independent of the parameter we are analyzing, in this case **B**. Consequently, the rate equation for the normalized plot should also be independent of the analyzed parameter (equation 2). A simple mathematical derivation reveals that the normalized axis should be an integral of a function that a priori is unknown, but that can be approximated by using the trapezoid rule (equation 4).
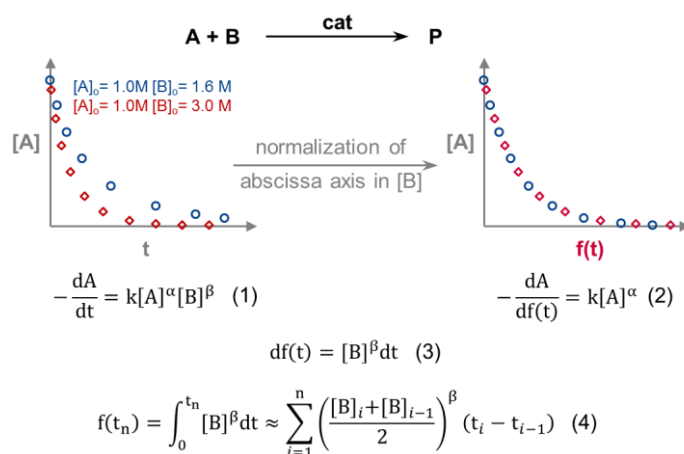


$$-\frac{dA}{dt} = k[A]^\alpha [B]^\beta \quad (1)$$

$$-\frac{dA}{df(t)} = k[A]^\alpha \quad (2)$$

$$df(t) = [B]^\beta dt \quad (3)$$

$$f(t_n) = \int_0^{t_n} [B]^\beta dt \approx \sum_{i=1}^{n} \left( \frac{[B]_i + [B]_{i-1}}{2} \right)^\beta (t_i - t_{i-1}) \quad (4)$$

**Figure S1.** Mathematical demonstration of the change of variable performed in order to remove the effect in **[B]**.

The variable time normalization can be applied to as many components as required. Each time we normalize the concentration plot with respect to one component, the effect of this component is removed. When the effect of all components has been removed by normalizing the abscissa axis in each component, the result is the overlay of all the reaction curves in a straight line.
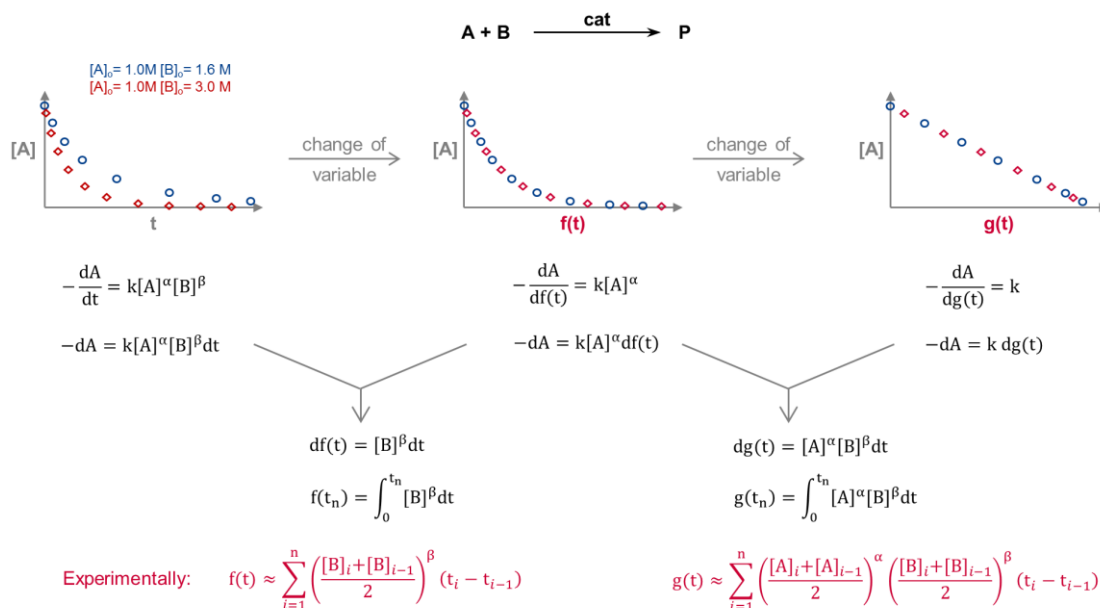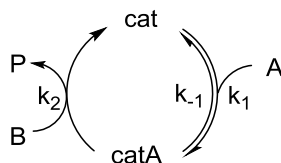
$$A + B \xrightarrow{\text{cat}} P$$

$[A]_o = 1.0\text{M} \; [B]_o = 1.6 \text{ M}$
$[A]_o = 1.0\text{M} \; [B]_o = 3.0 \text{ M}$

$$-\frac{dA}{dt} = k[A]^\alpha[B]^\beta$$

$$-dA = k[A]^\alpha[B]^\beta dt$$

$$-\frac{dA}{df(t)} = k[A]^\alpha$$

$$-dA = k[A]^\alpha df(t)$$

$$-\frac{dA}{dg(t)} = k$$

$$-dA = k\, dg(t)$$

$$df(t) = [B]^\beta dt$$

$$f(t_n) = \int_0^{t_n} [B]^\beta dt$$

$$dg(t) = [A]^\alpha[B]^\beta dt$$

$$g(t_n) = \int_0^{t_n} [A]^\alpha[B]^\beta dt$$

Experimentally:

$$f(t) \approx \sum_{i=1}^{n} \left(\frac{[B]_i + [B]_{i-1}}{2}\right)^\beta (t_i - t_{i-1})$$

$$g(t) \approx \sum_{i=1}^{n} \left(\frac{[A]_i + [A]_{i-1}}{2}\right)^\alpha \left(\frac{[B]_i + [B]_{i-1}}{2}\right)^\beta (t_i - t_{i-1})$$

**Figure S2.** Example of the variable time normalization applied to a two-component reaction where only the two reactants have a variable effect on the reaction rate. The normalization both in A and in B produces two straight lines that overlay.

## 3. Figure 2

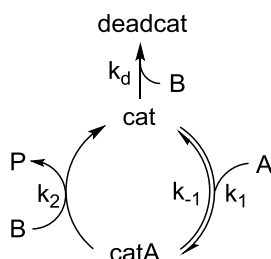The values of concentration and kinetic constants used to simulate figure 2 are shown below.



- $\circ$  $[A]_o = 1.0$ M, $[B]_o = 0.6$ M, $[cat]_T = 0.01$ M
- $\triangle$  **$[A]_o = 0.6$ M**, $[B]_o = 0.6$ M, $[cat]_T = 0.01$ M
- $\square$  $[A]_o = 1.0$ M, **$[B]_o = 0.8$ M**, $[cat]_T = 0.01$ M
- $\diamond$  $[A]_o = 1.0$ M, $[B]_o = 0.6$ M, **$[cat]_T = 0.03$ M**
  
  $k_1 = 1$ M$^{-1}$s$^{-1}$; $k_{-1} = 100$ s$^{-1}$; $k_2 = 1$ M$^{-1}$s$^{-1}$

The concentration results were obtained after applying an error with a normal distribution with a standard deviation of 0.001 to the COPASI simulation, and are listed in section 6.1 of this supporting information.

## 4. Figure 3

The values of concentration and kinetic constants used to simulate figure 3 are shown below.
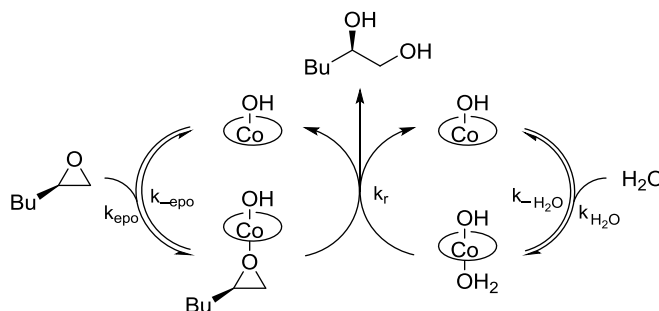


$$[A]_o = 1.0\ M,\ [B]_o = 0.6\ M$$
$$[cat]_T = \circ 0.01\ M \diamond 0.03\ M$$
$$k_1 = 1\ M^{-1}s^{-1};\ k_{-1} = 100\ s^{-1};\ k_2 = 1\ M^{-1}s^{-1};\ k_d = 3 \cdot 10^{-5}\ M^{-1}s^{-1}$$

The concentration results were obtained after applying an error with a normal distribution with a standard deviation of 0.0005 to the COPASI simulation and are listed in section 6.2 of this supporting information.

## 5. Figure 4

The values of concentrations and kinetic constants used to simulate figure 4 are shown below.



- $\circ$  $[epoxide]_o = 6.19\ M,\ [H_2O]_o = 3.63\ M$
- $\triangle$  **$[epoxide]_o = 4.00\ M$**, $[H_2O]_o = 3.63\ M$
- $\square$  $[epoxide]_o = 6.19\ M,$ **$[H_2O]_o = 2.63\ M$**

$$[cat]_T = 0.0308\ M$$
$$k_{epo} = 10^6\ M^{-1}s^{-1};\ k_{-epo} = 8.4890 \cdot 10^6\ s^{-1};\ k_{H2O} = 10^6\ M^{-1}s^{-1};\ k_{-H2O} = 5.5556 \cdot 10^6\ s^{-1};\ k_r = 17.88\ M^{-1}s^{-1}$$

The simulated concentration results against time for the different experiments with different starting concentrations are in section 6.3 of this supporting information.

The plots showing the theoretical variation of the order in epoxide and $H_2O$ for each experiment have been constructed using the elasticity coefficient or normalized sensitivity function.

The rate law for the reaction (equation 4) is obtained by applying the quasi-equilibrium assumption to the reversible reactions of both epoxide and water with the catalyst (equations 1 and 2, respectively) and the mass balance of the catalytic species (equation 3):

Quasi-equilibrium assumption epoxide: $K_{epoxide} = \dfrac{k_{epoxide}}{k_{-epoxide}} = \dfrac{[catepoxide]}{[cat][epoxide]}$ (1)

Quasi-equilibrium assumption $H_2O$: $K_{H_2O} = \dfrac{k_{H_2O}}{k_{-H_2O}} = \dfrac{[catH_2O]}{[cat][H_2O]}$ (2)

Mass Balance of catalytic species: $[cat]_T = [cat] + [catepoxide] + [catH_2O]$ (3)

**Rate law:** $\dfrac{d[P]}{dt} = \dfrac{k_r K_{epoxide} K_{H_2O} [epoxide][H_2O][cat]_T{}^2}{\left(1 + K_{H_2O}[H_2O] + K_{epoxide}[epoxide]\right)^2}$ (4)

**Order of the reaction in [epoxide]:**

$\varepsilon^r_{[epoxide]} = \dfrac{dr}{d[epoxide]} \cdot \dfrac{[epoxide]}{r} = \dfrac{1 + K_{H_2O}\cdot[H_2O] - K_{epoxide}\cdot[epoxide]}{1 + K_{H_2O}\cdot[H_2O] + K_{epoxide}\cdot[epoxide]}$ (5)

**Order of the reaction in [H₂O]:**

$\varepsilon^r_{[H_2O]} = \dfrac{dr}{d[H_2O]} \cdot \dfrac{[H_2O]}{r} = \dfrac{1 - K_{H_2O}\cdot[H_2O] + K_{epoxide}\cdot[epoxide]}{1 + K_{H_2O}\cdot[H_2O] + K_{epoxide}\cdot[epoxide]}$ (6)

## 6. Numerical data

### 6.1. Figure 2
**Experiment 1: $[A]_o$= 1.0 M, $[B]_o$= 0.6 M, $[cat]_T$= 0.01 M**

| time (h) | [A] (M) | [B] (M) | [P] (M) |
|----------|---------|---------|---------|
| 0 | 0.998 | 0.600 | 0.001 |
| 0.89 | 0.850 | 0.449 | 0.150 |
| 2.03 | 0.726 | 0.326 | 0.273 |
| 3.89 | 0.609 | 0.209 | 0.388 |
| 6.61 | 0.522 | 0.123 | 0.477 |
| 10.00 | 0.468 | 0.067 | 0.534 |
| 14.03 | 0.435 | 0.036 | 0.564 |
| 18.36 | 0.417 | 0.018 | 0.582 |
| 22.97 | 0.409 | 0.009 | 0.592 |
| 27.78 | 0.403 | 0.004 | 0.595 |

**Experiment 2: $[A]_o$= 0.6 M, $[B]_o$= 0.6 M, $[cat]_T$= 0.01 M**

| time (h) | [A] (M) | [B] (M) | [P] (M) |
|----------|---------|---------|---------|
| 0 | 0.602 | 0.601 | 0.000 |
| 0.67 | 0.525 | 0.524 | 0.075 |
| 2.67 | 0.382 | 0.382 | 0.218 |
| 5.67 | 0.272 | 0.272 | 0.329 |
| 12.11 | 0.164 | 0.166 | 0.433 |
| 19.11 | 0.118 | 0.116 | 0.483 |
| 25.22 | 0.093 | 0.093 | 0.508 |
| 46.89 | 0.055 | 0.056 | 0.546 |
| 89.22 | 0.028 | 0.029 | 0.573 |
| 111.11 | 0.021 | 0.025 | 0.578 |

**Experiment 3: $[A]_o$= 1.0 M, $[B]_o$= 0.8 M, $[cat]_T$= 0.01 M**

| time (h) | [A] (M) | [B] (M) | [P] (M) |
|----------|---------|---------|---------|
| 0 | 0.999 | 0.801 | 0.000 |
| 0.33 | 0.915 | 0.715 | 0.086 |
| 1.00 | 0.786 | 0.585 | 0.213 |
| 1.92 | 0.663 | 0.464 | 0.337 |
| 3.08 | 0.560 | 0.359 | 0.441 |
| 4.38 | 0.482 | 0.284 | 0.515 |
| 6.29 | 0.410 | 0.211 | 0.591 |
| 11.54 | 0.310 | 0.108 | 0.691 |
| 22.92 | 0.237 | 0.038 | 0.763 |
| 41.67 | 0.208 | 0.009 | 0.792 |

**Experiment 4: [A]ₒ= 1.0 M, [B]ₒ= 0.6 M, [cat]ₜ= 0.03 M**

| time (h) | [A] (M) | [B] (M) | [P] (M) |
|----------|---------|---------|---------|
| 0 | 1.001 | 0.601 | 0.002 |
| 0.13 | 0.925 | 0.523 | 0.077 |
| 0.47 | 0.787 | 0.387 | 0.214 |
| 0.93 | 0.671 | 0.271 | 0.328 |
| 1.68 | 0.563 | 0.164 | 0.436 |
| 2.85 | 0.485 | 0.087 | 0.512 |
| 3.94 | 0.450 | 0.050 | 0.550 |
| 5.50 | 0.424 | 0.023 | 0.576 |
| 7.00 | 0.406 | 0.011 | 0.589 |
| 8.33 | 0.412 | 0.007 | 0.595 |

## 6.2. Figure 3

**Experiment 1: [A]ₒ= 1.0 M, [B]ₒ= 0.6 M, [cat]ₜ= 0.01 M**

| time (h) | conversion | [P] (M) | [cat]ₜ (M) |
|----------|------------|---------|------------|
| 0 | 0.00 | 0.000 | 0.0070 |
| 0.42 | 12.71 | 0.076 | 0.0099 |
| 1.25 | 29.94 | 0.179 | 0.0070 |
| 2.50 | 45.47 | 0.273 | 0.0060 |
| 5.00 | 61.78 | 0.371 | 0.0047 |
| 8.33 | 72.47 | 0.435 | 0.0037 |
| 14.17 | 81.47 | 0.489 | 0.0049 |
| 19.58 | 85.81 | 0.514 | 0.0030 |
| 27.08 | 89.34 | 0.536 | 0.0020 |
| 39.58 | 92.54 | 0.555 | 0.0013 |

**Experiment 2: [A]ₒ= 1.0 M, [B]ₒ= 0.6 M, [cat]ₜ= 0.03 M**

| time (h) | conversion | [P] (M) | [cat]ₜ (M) |
|----------|------------|---------|------------|
| 0 | 0.00 | 0.003 | 0.0298 |
| 0.28 | 23.34 | 0.139 | 0.0271 |
| 0.56 | 38.63 | 0.231 | 0.0279 |
| 0.97 | 53.71 | 0.322 | 0.0275 |
| 1.53 | 66.24 | 0.397 | 0.0251 |
| 2.22 | 75.83 | 0.454 | 0.0238 |
| 3.19 | 83.78 | 0.504 | 0.0247 |
| 4.03 | 87.98 | 0.528 | 0.0214 |
| 5.00 | 91.20 | 0.547 | 0.0222 |
| 5.97 | 93.35 | 0.559 | 0.0218 |

## 6.3. Figure 4
**Experiment 1: [epoxide]$_o$= 6.19 M, [H$_2$O]$_o$= 3.63 M, [cat]$_T$= 0.0308 M**

| time (h) | [epoxide] (M) | [H$_2$O] (M) | [P] (M) | Order in epoxide | Order in H$_2$O |
|----------|---------------|--------------|---------|------------------|-----------------|
| 0 | 6.190 | 3.630 | 0.000 | 0.388 | 0.452 |
| 0.08 | 5.771 | 3.213 | 0.409 | 0.398 | 0.488 |
| 0.17 | 5.396 | 2.838 | 0.785 | 0.408 | 0.524 |
| 0.25 | 5.054 | 2.496 | 1.127 | 0.418 | 0.560 |
| 0.33 | 4.745 | 2.187 | 1.436 | 0.428 | 0.597 |
| 0.42 | 4.467 | 1.910 | 1.715 | 0.437 | 0.632 |
| 0.50 | 4.218 | 1.662 | 1.963 | 0.447 | 0.667 |
| 0.58 | 3.997 | 1.441 | 2.184 | 0.456 | 0.700 |
| 0.67 | 3.802 | 1.247 | 2.379 | 0.464 | 0.732 |
| 0.75 | 3.631 | 1.076 | 2.551 | 0.472 | 0.761 |
| 0.83 | 3.481 | 0.926 | 2.701 | 0.480 | 0.789 |
| 0.92 | 3.351 | 0.796 | 2.831 | 0.487 | 0.814 |
| 1.00 | 3.238 | 0.683 | 2.945 | 0.493 | 0.837 |
| 1.08 | 3.140 | 0.585 | 3.043 | 0.499 | 0.857 |
| 1.17 | 3.055 | 0.501 | 3.127 | 0.504 | 0.876 |
| 1.25 | 2.982 | 0.428 | 3.200 | 0.508 | 0.892 |
| 1.33 | 2.920 | 0.366 | 3.263 | 0.512 | 0.907 |
| 1.42 | 2.866 | 0.312 | 3.317 | 0.516 | 0.919 |
| 1.50 | 2.820 | 0.266 | 3.363 | 0.519 | 0.931 |
| 1.58 | 2.781 | 0.227 | 3.402 | 0.521 | 0.940 |
| 1.67 | 2.747 | 0.194 | 3.436 | 0.524 | 0.949 |

**Experiment 2: [epoxide]$_o$= 4.00 M, [H$_2$O]$_o$= 3.63 M, [cat]$_T$= 0.0308 M**

| time (h) | [epoxide] (M) | [H$_2$O] (M) | [P] (M) | Order in epoxide |
|----------|---------------|--------------|---------|------------------|
| 0 | 4.000 | 3.630 | 0.000 | 0.556 |
| 0.12 | 3.516 | 3.143 | 0.478 | 0.582 |
| 0.25 | 3.098 | 2.726 | 0.896 | 0.607 |
| 0.37 | 2.736 | 2.364 | 1.258 | 0.631 |
| 0.49 | 2.425 | 2.053 | 1.570 | 0.655 |
| 0.61 | 2.158 | 1.787 | 1.837 | 0.677 |
| 0.86 | 1.737 | 1.366 | 2.259 | 0.718 |
| 1.10 | 1.431 | 1.061 | 2.565 | 0.752 |
| 1.35 | 1.207 | 0.837 | 2.789 | 0.780 |
| 1.59 | 1.041 | 0.671 | 2.956 | 0.803 |
| 1.84 | 0.916 | 0.547 | 3.081 | 0.821 |
| 2.08 | 0.820 | 0.451 | 3.177 | 0.836 |
| 2.33 | 0.745 | 0.376 | 3.252 | 0.848 |
| 2.57 | 0.686 | 0.317 | 3.312 | 0.858 |
| 2.82 | 0.638 | 0.269 | 3.360 | 0.866 |
| 3.06 | 0.599 | 0.230 | 3.399 | 0.873 |
| 3.31 | 0.567 | 0.198 | 3.431 | 0.879 |
| 3.55 | 0.540 | 0.171 | 3.458 | 0.884 |
| 3.80 | 0.518 | 0.149 | 3.480 | 0.888 |
| 4.04 | 0.499 | 0.130 | 3.500 | 0.891 |
| 4.29 | 0.483 | 0.114 | 3.516 | 0.894 |

**Experiment 3: [epoxide]$_o$= 6.19 M, [H$_2$O]$_o$= 2.63 M, [cat]$_T$= 0.0308 M**

| time (h) | [epoxide] (M) | [H$_2$O] (M) | [P] (M) | Order in H$_2$O |
|---|---|---|---|---|
| 0 | 6.190 | 2.630 | 0.000 | 0.570 |
| 0.12 | 5.707 | 2.152 | 0.473 | 0.624 |
| 0.23 | 5.302 | 1.747 | 0.878 | 0.676 |
| 0.35 | 4.960 | 1.405 | 1.220 | 0.725 |
| 0.47 | 4.675 | 1.121 | 1.505 | 0.770 |
| 0.58 | 4.441 | 0.888 | 1.739 | 0.810 |
| 0.70 | 4.251 | 0.698 | 1.929 | 0.845 |
| 0.82 | 4.099 | 0.547 | 2.082 | 0.876 |
| 0.94 | 3.978 | 0.426 | 2.203 | 0.901 |
| 1.05 | 3.883 | 0.331 | 2.298 | 0.922 |
| 1.17 | 3.808 | 0.256 | 2.373 | 0.938 |
| 1.29 | 3.749 | 0.198 | 2.432 | 0.952 |
| 1.40 | 3.704 | 0.152 | 2.477 | 0.963 |
| 1.52 | 3.669 | 0.117 | 2.512 | 0.971 |
| 1.64 | 3.641 | 0.090 | 2.539 | 0.978 |
| 1.75 | 3.621 | 0.069 | 2.560 | 0.983 |
| 1.87 | 3.604 | 0.053 | 2.577 | 0.987 |
| 1.99 | 3.592 | 0.041 | 2.589 | 0.990 |
| 2.11 | 3.582 | 0.031 | 2.599 | 0.992 |
| 2.22 | 3.575 | 0.024 | 2.606 | 0.994 |