

Supporting Information

The Network Simulation Method: a useful tool for locating the kinetic-thermodynamic switching point in complex kinetic schemes

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1. STATIONARY REGIME FOR CONCENTRATIONS [*cis*-2a] AND [*trans*-2a].

In Figure S1 we represent the concentrations [*cis*-2a] (black curves) and [*trans*-2a] (red curves) for long reaction times. As done in the main article, continuous curves correspond to data obtained from our NSM, while dashed ones are plots of eqs. (20) and (21). As can be depicted from the figure, solid curves approximately reach the stationary regime at $t=3.0 \cdot 10^8$, which is near three times greater than that for dashed ones (see main article).

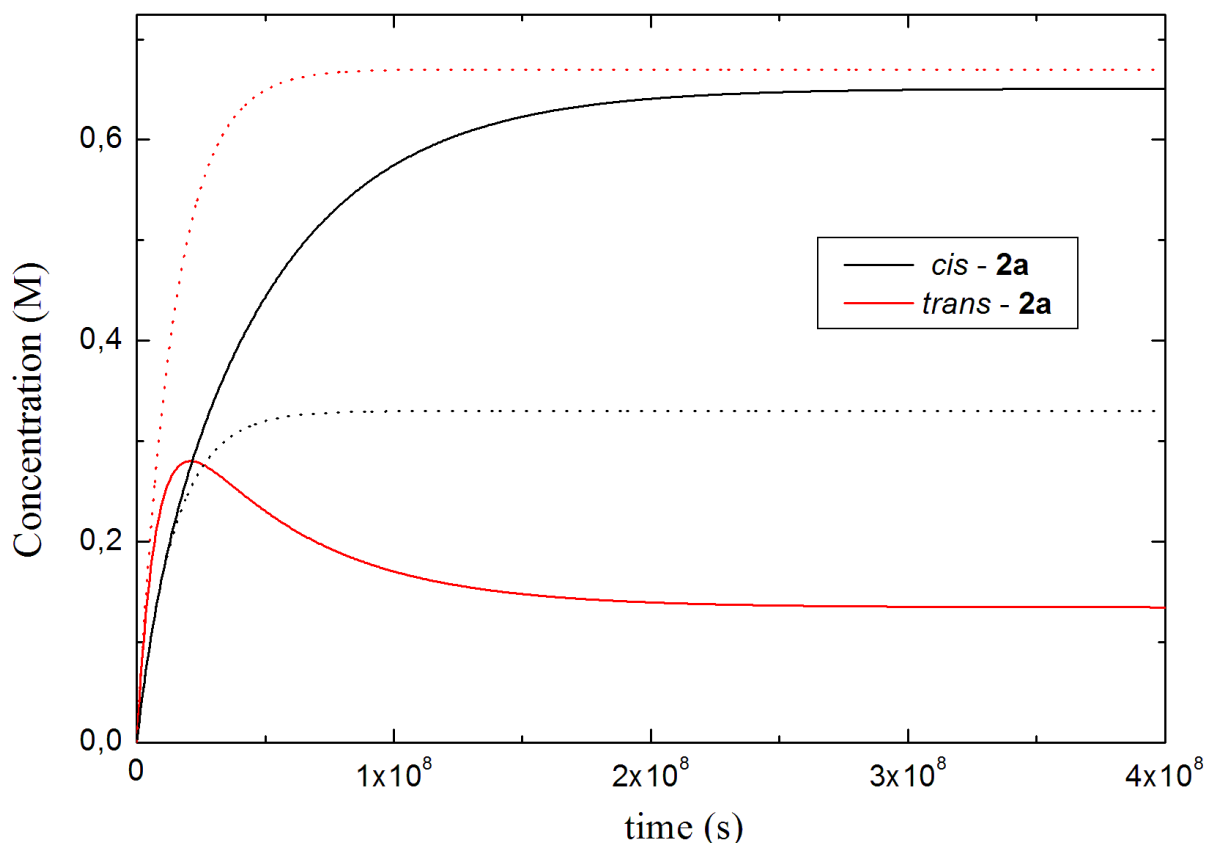


Figure S1. Long time dependence of concentrations [*cis*-2a] (M) (black curves) and [*trans*-2a] (M) (red curves) on the reaction time (s), for $T=410$ K. Solid lines correspond to results calculated from the NSM, while dashed ones are those obtained from eqs. (20) and (21).

2. CONCENTRATIONS OF THE INTERMEDIATES

In figure S2 we represent the concentrations of the intermediates, $[Z,Z\text{-INTa}]$, $[E,Z\text{-INTa}]$, $[Z,E\text{-INTa}]$, and $[E,E\text{-INTa}]$ (M), as a function of the reaction time (s), until $t=1.0\cdot 10^9$. Variations of the concentration values are very small over the entire time range, so they can be considered as approximately constant and close to zero with respect to the other species.

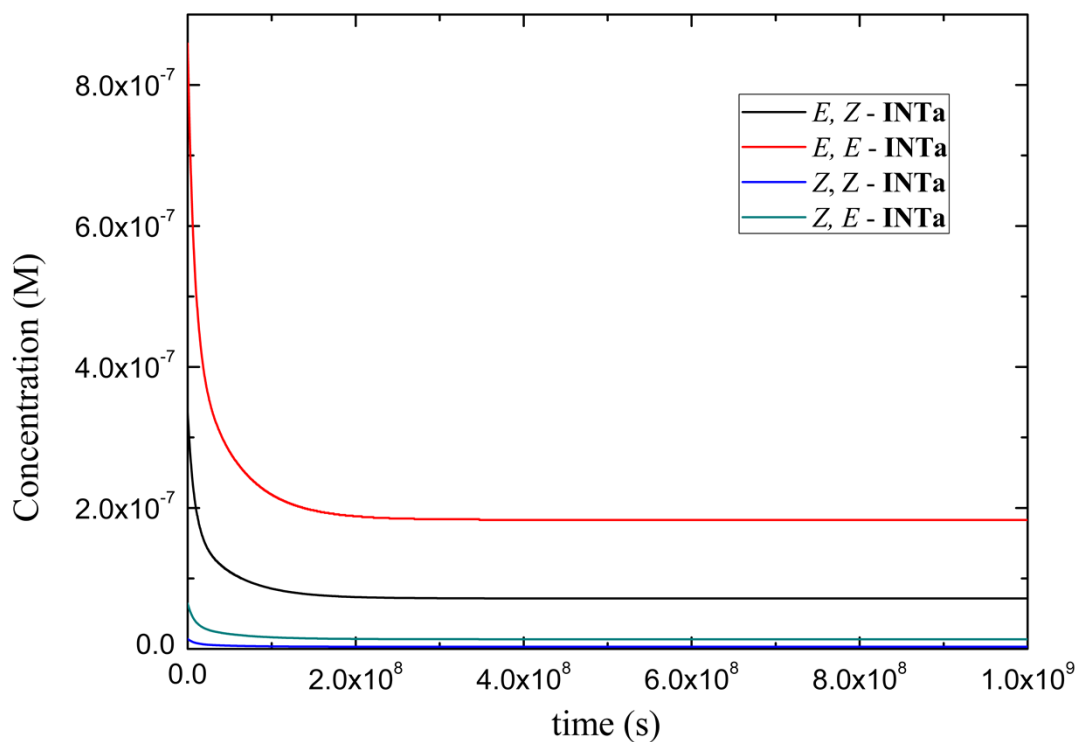


Figure S2. Concentrations (M) of the intermediate species $[E,Z\text{-INTa}]$ (black), $[E,E\text{-INTa}]$ (red), $[Z,Z\text{-INTa}]$ (blue), and $[Z,E\text{-INTa}]$ (dark cyan) as a function of the reaction time (s), for $T=410$ K.

3. ASYMPTOTIC BEHAVIOR OF THE RATIO $[cis-2a] / [trans-2a]$

In Figure S3 we plot the ratio $[cis-2a] / [trans-2a]$ extended until $t=1.0 \cdot 10^9$ s, in order to determine its asymptotic behavior. From the plot we can infer that the ratio tends to a constant value of 4,84. This figure and that showed in the main article (Figure 9) have direct implications in the selectivity of products *cis-2a* and *trans-2a*, concluding that the ratio can be increased until its asymptotic value by only controlling the reaction time.

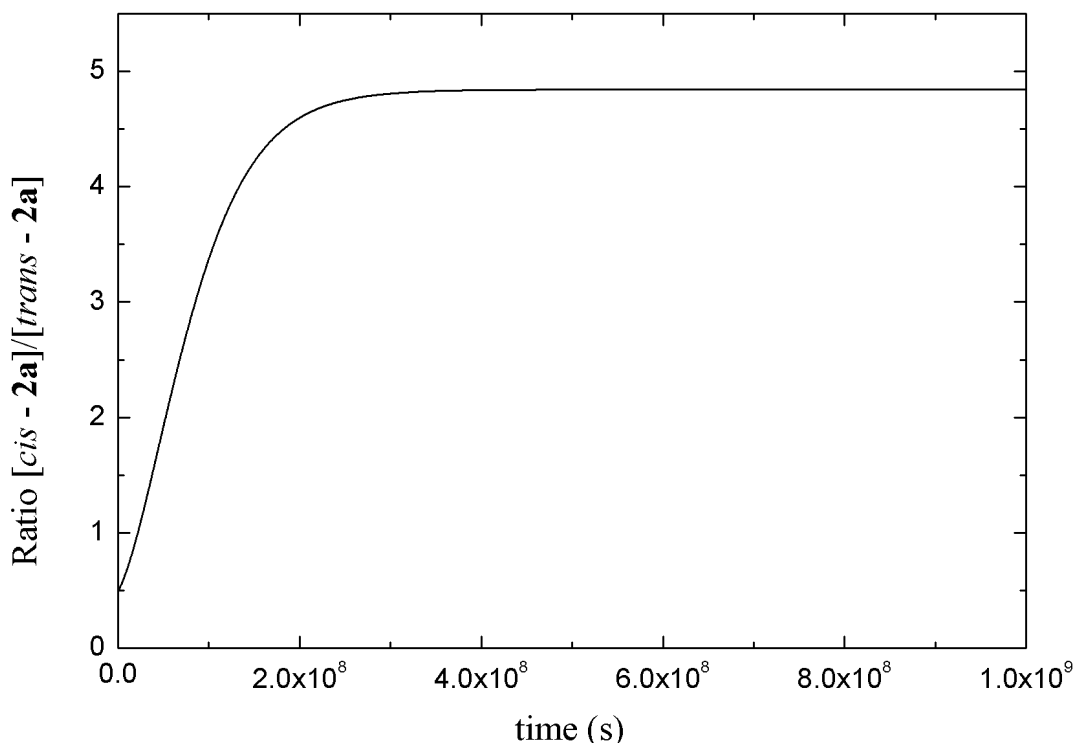


Figure S3. Asymptotic behavior of the ratio $[cis-2a] / [trans-2a]$.

4. CONCENTRATION OF **1a** vs TIME

In figure S4 we plot the concentration [**1a**] extended to a time $t=1.0 \cdot 10^9$ s. The curve tends to an asymptotic value equal to 0.22. Due to this fact, the reaction yield cannot reach its maximum value of 100%, as we reported in the main article.

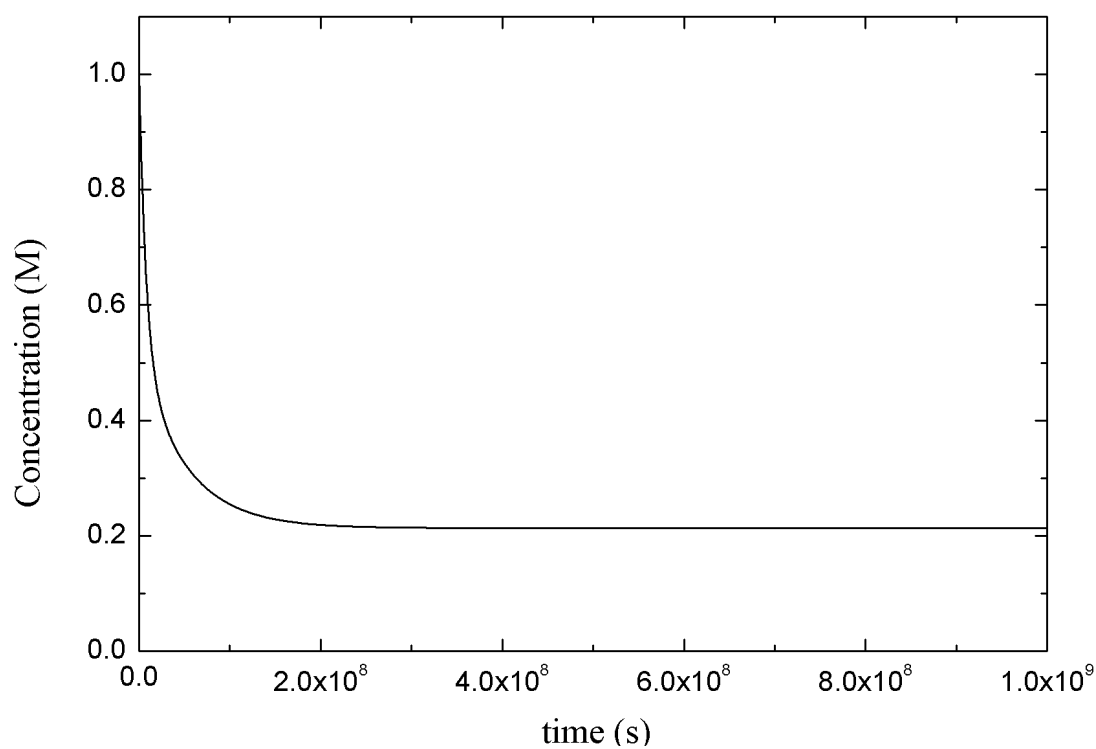


Figure S4. Long time dependence of concentration (M) of species **1a**.

5. ASYMPTOTIC BEHAVIOR OF THE REACTION YIELD (WITH APPROXIMATIONS)

In figure S5 we plot the reaction yield (%) as a function of time (s) when taking into account (a) the steady state approximation and (b) the irreversibility of the reverse processes for the second steps. Data are obtained from the implementation of the NSM in Pspice. The figure clearly shows that the reaction yield tends to an asymptotic value of 100%.

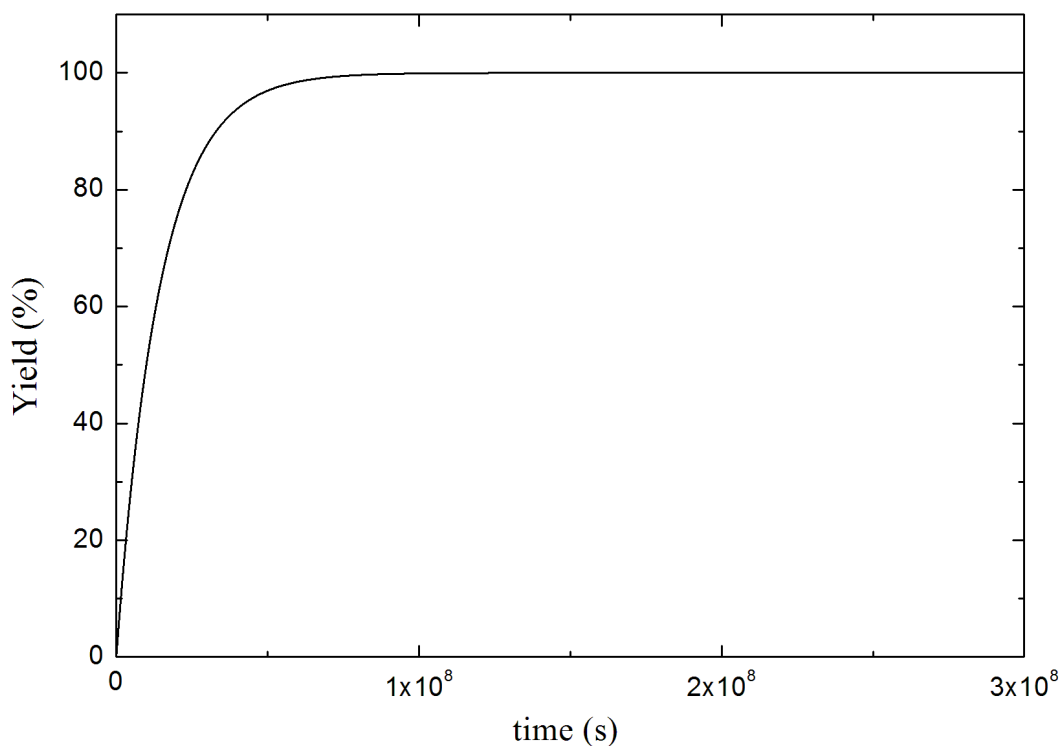


Figure S5. Reaction yield (%) versus time (s) at $T=410$ K obtained from the NSM when taking into account the approximations performed in reference 20 (see main article).

Table S1. Electronic energies^a (in hartrees) and free energies^{a,b} at different temperatures, computed for the stationary points found in the transformations **1a** → *cis-2a* and *trans-2a* calculated at the B3LYP/6-31+G** theoretical method.

T (K)	Electronic Energy	Free Energy						
	298.15	298.15	350	380	410	440	470	500
1a	-1263.300853	-1263.353798	-1263.367221	-1263.375501	-1263.384154	-1263.393176	-1263.402563	-1263.412311
Z,Z-TS1a	-1263.256329	-1263.304212	-1263.316555	-1263.324199	-1263.332212	-1263.340592	-1263.349331	-1263.358429
Z,Z-INTa	-1263.281932	-1263.331692	-1263.344489	-1263.352405	-1263.360693	-1263.369352	-1263.378377	-1263.387762
Z,Z-TS2a	-1263.247510	-1263.294558	-1263.306754	-1263.314316	-1263.322245	-1263.330538	-1263.339192	-1263.348201
E,Z-TS1a	-1263.259209	-1263.307186	-1263.319576	-1263.327251	-1263.335294	-1263.343703	-1263.352473	-1263.361600
E,Z-INTa	-1263.285722	-1263.335679	-1263.348529	-1263.356478	-1263.364800	-1263.373492	-1263.382550	-1263.391968
E,Z-TS2a	-1263.246655	-1263.293891	-1263.306087	-1263.313649	-1263.321577	-1263.329870	-1263.338523	-1263.347533
Z,E-TS1a	-1263.253328	-1263.301555	-1263.313957	-1263.321648	-1263.329697	-1263.338116	-1263.346894	-1263.356029
Z,E-INTa	-1263.284076	-1263.333715	-1263.346486	-1263.354389	-1263.362664	-1263.371309	-1263.380319	-1263.389690
Z,E-TS2a	-1263.247557	-1263.295259	-1263.307607	-1263.315257	-1263.323276	-1263.331659	-1263.340408	-1263.349506
E,E-TS1a	-1263.255161	-1263.302828	-1263.315150	-1263.322785	-1263.330788	-1263.339156	-1263.347884	-1263.356970
E,E-INTa	-1263.287696	-1263.337122	-1263.349869	-1263.357757	-1263.366019	-1263.374650	-1263.383647	-1263.393005
E,E-TS2a	-1263.245500	-1263.293076	-1263.305367	-1263.312985	-1263.320971	-1263.329321	-1263.338032	-1263.347099
<i>cis-12a</i>	-1263.313135	-1263.358717	-1263.370543	-1263.377889	-1263.385603	-1263.393682	-1263.402124	-1263.410923
<i>trans-12a</i>	-1263.310862	-1263.356607	-1263.368461	-1263.375824	-1263.383555	-1263.391651	-1263.400110	-1263.408926

^a Including the zero point vibrational correction. ^b Sum of electronic and thermal free energies.

Table S2. Relative free energies^{a,b} (*G*, in kcal·mol⁻¹) computed at different temperatures for the stationary points found in the transformation **1a** → *cis*-**2a** and *trans*-**2a** calculated at the B3LYP/6-31+G** theoretical method.

T (K)	Relative Free Energy, <i>G</i>						
	298.15	350	380	410	440	470	500
1a	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Z,Z-TS1a	31.116	31.79	32.19	32.589	33.00	33.40	33.81
Z,Z-INTa	13.872	14.26	14.49	14.720	14.95	15.18	15.40
Z,Z-TS2a	37.174	37.94	38.39	38.842	39.31	39.77	40.23
E,Z-TS1a	29.249	29.90	30.28	30.655	31.04	31.43	31.82
E,Z-INTa	11.370	11.73	11.94	12.143	12.35	12.56	12.77
E,Z-TS2a	37.592	38.36	38.81	39.261	39.73	40.19	40.65
Z,E-TS1a	32.783	33.42	33.79	34.167	34.55	34.93	35.32
Z,E-INTa	12.602	13.01	13.25	13.483	13.72	13.96	14.19
Z,E-TS2a	36.734	37.41	37.80	38.195	38.60	39.00	39.41
E,E-TS1a	31.984	32.68	33.08	33.482	33.90	34.31	34.73
E,E-INTa	10.464	10.89	11.13	11.378	11.63	11.87	12.11
E,E-TS2a	38.104	38.81	39.23	39.642	40.07	40.49	40.92
<i>cis</i>-12a	-3.087	-2.08	-1.50	-0.909	-0.32	0.28	0.87
<i>trans</i>-12a	-1.763	-0.78	-0.20	-0.376	0.96	1.54	2.12

^a Including the zero point vibrational correction. ^b Sum of electronic and thermal free energies.

Table S3. Free energy barriers^{a,b} (ΔG_i , in kcal·mol⁻¹) calculated at different temperatures (T in Kelvin) for the individual steps involved in the transformation of **1a** into *cis*-**2a** and *trans*-**2a** computed at the B3LYP/6-31+G** theoretical level.

T (K)	298.15	350	380	410	440	470	500
ΔG_{a1}	31.12	31.79	32.19	32.59	33.00	33.40	33.81
ΔG_{b1}	23.30	23.68	23.90	24.13	24.36	24.59	24.82
ΔG_{c1}	17.24	17.53	17.70	17.87	18.05	18.23	18.41
ΔG_{d1}	40.26	40.03	39.89	39.76	39.62	39.49	39.36
ΔG_{a2}	29.25	29.90	30.28	30.66	31.04	31.43	31.82
ΔG_{b2}	26.22	26.63	26.88	27.12	27.37	27.63	27.88
ΔG_{c2}	17.88	18.17	18.34	18.52	18.69	18.87	19.06
ΔG_{d2}	39.35	39.14	39.02	38.89	38.77	38.65	38.52
ΔG_{a3}	32.78	33.42	33.79	34.17	34.55	34.93	35.32
ΔG_{b3}	24.13	24.40	24.56	24.72	24.88	25.04	25.22
ΔG_{c3}	20.18	20.41	20.55	20.69	20.83	20.97	21.12
ΔG_{d3}	38.50	38.19	38.01	37.83	37.65	37.46	37.29
ΔG_{a4}	31.98	32.68	33.08	33.49	33.90	34.31	34.73
ΔG_{b4}	27.64	27.93	28.09	28.27	28.44	28.62	28.81
ΔG_{c4}	21.52	21.79	21.95	22.11	22.27	22.44	22.61
ΔG_{d4}	41.19	40.90	40.73	40.56	40.39	40.22	40.05

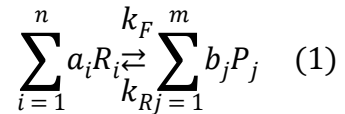
Table S4. Rate constants, k_i , calculated at different temperatures (T in Kelvin) for the individual steps involved in the transformation of **1a** into *cis-2a* and *trans-2a* computed at the B3LYP/6-31+G** theoretical level.

T (K)	298.15	350	380	410	440	470	500
k_{a1}	$9.63913 \cdot 10^{-11}$	$1.02478 \cdot 10^{-7}$	$2.42160 \cdot 10^{-6}$	$3.612032 \cdot 10^{-5}$	$3.74027 \cdot 10^{-4}$	$2.87476 \cdot 10^{-3}$	$1.73433 \cdot 10^{-2}$
k_{b1}	$5.15079 \cdot 10^{-5}$	$1.19491 \cdot 10^{-2}$	$1.42094 \cdot 10^{-1}$	1.178427	7.32379	$3.60838 \cdot 10^1$	$1.46917 \cdot 10^2$
k_{c1}	1.42118	$8.27224 \cdot 10^1$	$5.23934 \cdot 10^2$	$2.54169 \cdot 10^3$	$9.96244 \cdot 10^3$	$3.27888 \cdot 10^4$	$9.38407 \cdot 10^4$
k_{d1}	$1.90790 \cdot 10^{-17}$	$7.39086 \cdot 10^{-13}$	$9.02796 \cdot 10^{-11}$	$5.48608 \cdot 10^{-9}$	$1.91233 \cdot 10^{-7}$	$4.24896 \cdot 10^{-6}$	$6.52397 \cdot 10^{-5}$
k_{a2}	$2.24935 \cdot 10^{-9}$	$1.56436 \cdot 10^{-6}$	$3.05876 \cdot 10^{-5}$	$3.87826 \cdot 10^{-4}$	$3.48770 \cdot 10^{-3}$	$2.37351 \cdot 10^{-2}$	$1.28490 \cdot 10^{-1}$
k_{b2}	$3.72448 \cdot 10^{-7}$	$1.71005 \cdot 10^{-4}$	$2.76659 \cdot 10^{-3}$	$2.97943 \cdot 10^{-2}$	$2.32369 \cdot 10^{-1}$	1.39472	6.76457
k_{c2}	$4.86044 \cdot 10^{-1}$	$3.29877 \cdot 10^1$	$2.24287 \cdot 10^2$	$1.15418 \cdot 10^3$	$4.76044 \cdot 10^3$	$1.64019 \cdot 10^4$	$4.88105 \cdot 10^4$
k_{d2}	$8.79684 \cdot 10^{-17}$	$2.64929 \cdot 10^{-12}$	$2.88481 \cdot 10^{-10}$	$1.58801 \cdot 10^{-8}$	$5.08608 \cdot 10^{-7}$	$1.04890 \cdot 10^{-5}$	$1.51018 \cdot 10^{-4}$
k_{a3}	$5.77878 \cdot 10^{-12}$	$9.83254 \cdot 10^{-9}$	$2.90713 \cdot 10^{-7}$	$5.20619 \cdot 10^{-6}$	$6.32679 \cdot 10^{-5}$	$5.59140 \cdot 10^{-4}$	$3.80947 \cdot 10^{-3}$
k_{b3}	$1.26988 \cdot 10^{-5}$	$4.25682 \cdot 10^{-3}$	$5.97261 \cdot 10^{-2}$	$5.71329 \cdot 10^{-1}$	4.01949	$2.21552 \cdot 10^1$	$9.91282 \cdot 10^1$
k_{c3}	$9.99724 \cdot 10^{-3}$	1.30973	$1.20956 \cdot 10^1$	$8.02822 \cdot 10^1$	$4.13703 \cdot 10^2$	$1.72980 \cdot 10^3$	$6.09979 \cdot 10^3$
k_{d3}	$3.74626 \cdot 10^{-16}$	$1.04401 \cdot 10^{-11}$	$1.09757 \cdot 10^{-9}$	$5.87684 \cdot 10^{-8}$	$1.83645 \cdot 10^{-6}$	$3.72177 \cdot 10^{-5}$	$5.25024 \cdot 10^{-4}$
k_{a4}	$2.22540 \cdot 10^{-11}$	$2.88479 \cdot 10^{-8}$	$7.47825 \cdot 10^{-7}$	$1.20627 \cdot 10^{-5}$	$1.33454 \cdot 10^{-4}$	$1.08740 \cdot 10^{-3}$	$6.90177 \cdot 10^{-3}$
k_{b4}	$3.40722 \cdot 10^{-8}$	$2.66592 \cdot 10^{-5}$	$5.50466 \cdot 10^{-4}$	$7.30628 \cdot 10^{-3}$	$6.82560 \cdot 10^{-2}$	$4.79879 \cdot 10^{-1}$	2.67163
k_{c4}	$1.04293 \cdot 10^{-3}$	$1.81586 \cdot 10^{-1}$	1.89442	$1.40392 \cdot 10^1$	$7.93438 \cdot 10^1$	$3.59586 \cdot 10^2$	$1.36200 \cdot 10^3$
k_{d4}	$3.97051 \cdot 10^{-18}$	$2.11462 \cdot 10^{-13}$	$2.98704 \cdot 10^{-11}$	$2.05649 \cdot 10^{-9}$	$7.98452 \cdot 10^{-8}$	$1.94900 \cdot 10^{-6}$	$3.25280 \cdot 10^{-5}$

MATHEMATICAL TREATMENT OF THE NSM APPLIED TO CHEMICAL REACTIONS.

The electrical analogy between a set of coupled differential equations and an electric circuit network can be established as follows. It is worth remarking that the NSM is only a formal equivalence, employed to determine the relationship between transport processes. Once the model is completed, we have to simulate the electrical behavior of the network in a suitable software (Pspice is one of the best choices, but also Matlab can be used, for example). For further details, see the book of Horno *et al.* (ref. 10 of the MS).

We start by applying the equivalence to the particular case of a one-step chemical reaction, whose balanced equation can be expressed as follows:



where a_i and b_j are the stoichiometric coefficients belonging to reactant R_i and product P_j , respectively. The rate constant for the forward reaction is denoted by k_F , whereas k_R is that for the reverse step.

Since the number of moles of these species, n_{R_i} and n_{P_j} , are proportional to their stoichiometric coefficients, we can define a quantity $d\xi$ which is, in general, a function of time, but equal in magnitude for all reactants and products:

$$d\xi = d\xi_{R_i} = d\xi_{P_j}, \quad \forall i, j \quad (2)$$

$$d\xi_{R_i} = -\frac{dn_{R_i}}{a_i}, \quad d\xi_{P_j} = \frac{dn_{P_j}}{b_j} \quad (3)$$

The reaction rate R at constant volume can be defined for i -th species as:

$$R = \frac{1}{a_i} \frac{dn_{R_i}}{V dt} = \frac{1}{b_j} \frac{dn_{P_j}}{V dt} = \frac{1}{V} \frac{d\xi}{dt} \quad (4)$$

Where V is the volume of the reaction. We can state from eqs. (2) and (3) that R is independent of the chosen species, but it is a time-varying function.

Now we define J_{R_i} and $J^*_{R_i}$ as the standard and renormalized flow of the reactant R_i , respectively, as follows (equivalent for products, not shown):

$$J_{R_i} = \frac{dn_{R_i}}{dt} \quad (5)$$

$$J^*_{R_i} = \frac{J_{R_i}}{a_i} = \frac{d\xi_{R_i}}{dt} \quad (6)$$

It is more suitable to write eq. (6) and its equivalent for products in terms of the concentration of the species, which defines the currents that establish the analogy between the chemical and electrical systems:

$$J^*_{R_i} = \frac{dn_{R_i}}{a_i dt} = \frac{V d[R_i]}{a_i dt} \quad (7)$$

$$J^*_{P_j} = \frac{dn_{P_j}}{b_j dt} = \frac{V d[P_j]}{b_j dt} \quad (8)$$

In these expressions, $[R_i]$ and $[P_j]$ are the concentrations of the i - and j -th reactant and product, respectively. From expressions (2) and (3) we can derive that:

$$J^* = J^*_{R_i} = J^*_{P_j}, \quad \forall i, j \quad (9)$$

This last relation is the mass local balanced equation corresponding to R_i and P_j , which is a process of creation-annihilation. From eq. (9):

$$J^* - J^*_{R_i} = 0, \quad \forall i \quad (10)$$

which remains valid for products. That is, each species will follow an equation such as (10).

From the point of view of the network model, the last equation can be considered as Kirchhoff's current law (KCL), and it is equivalent to the corresponding differential equations of the compounds. Each chemical species presents a flow term $J^*_{R_i}$, whose theoretical expression, eq. (8), resembles the expression of the current intensity I_c at the ends of a condenser: $I_c = C dV/dt$ (C and V are the capacity and voltage at the ends of the device). Because of this similarity, the derivative of first order of the concentration inside each kinetic differential equation is modeled with a condenser, whose voltage V_i is then equivalent to $[R_i]$ (analogous for products). The remaining term of eq. (10), J^* , which was unknown at the beginning, is now easy to determine, since each differential equation has to satisfy KCL, because they are mass local balanced equations. If we take a look to each differential equation, J^* thus represents the remaining addends of the equation. For example, eq. (17) of the MS is:

$$\frac{d[R]}{dt} + (k_a + k_b)[R] - k_{-a}[A] - k_{-b}[B] = 0$$

The first derivative is modeled through a condenser of 1 F. Concentration $[R]$ is always a positive quantity so, if we choose a ground node at one end of the condenser to design the equivalent circuit, the branch current J^*_R is always outgoing from a particular node (see Figure S6). This node is labeled as **R** and its voltage is just the voltage of the condenser (which is equivalent to the

concentration of the reactant, $[R]$). Since the first derivative has units of current, the rest of the addends also have. So, J^* represents all the remaining addends. Each of them has to be placed in the electric circuit as a parallel branch to verify KCL. Due to the fact that all the species concentrations are positive, also all the node voltages are, and the mathematical sign of each addend determines if the branch current is incoming or outgoing. In the particular case of eq. (17) of the MS, the second addend is equivalent to an outgoing current, while third and fourth addends correspond to incoming currents, as shown in Figure 3 of the MS.

In general, the flows J^* and $J_{R_i}^*$ satisfy KCL at a point of the circuit called node i , or equivalent, R_i (see Figure S6).

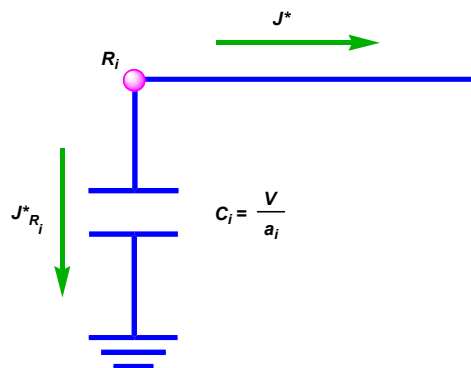


Figure S6. Connection of flows $J_{R_i}^*$ and J^* at the concentration point R_i .

It remains to model, for each differential equation, the addends which represent the flow term J^* (different from the first derivatives), employing appropriate electric devices. In general, these addends are functions of the node voltages, even including the proper node voltage of the circuit, so they can present coupled terms between equations (see, for example, eq. (17) of the MS). The electric device known as voltage-controlled current source is a standard device in circuit analysis, defined as a current source whose value depends on a function of other

voltages somewhere else in the network. The addends which conform the flow term J^* are, in general, functions of the node voltages of the whole network, so they can be easily implemented by the voltage-controlled current sources in Pspice. In summary, each addend of a particular differential equation will be modeled as a parallel current branch containing one of these controlled currents. Besides, to establish the connection between isolated circuits, we define a common ground node (see Figure 3 of the MS), easily implemented in Pspice.

The resistor placed in parallel inside each individual circuit (see Figure 3 of the MS) does not model any term of the differential equations, but it is necessary in order to satisfy criteria of continuity, and it is chosen as very large.

The generalization of the analogy established by the NSM to multi-step chemical reactions is immediate. The key is to employ again voltage-controlled current sources. In these kind of problems we will have one circuit per species, which contains a capacitor (associated to the time derivative) and as many controlled current sources as addends, no matter what kind of dependence have on the voltage nodes of the network (see Figure 5 of the MS).