ARN
Nuclear reactions analysis

RadioPyo Python Module:

Extended Doc

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Reaction Types

"K Reaction" Kinetics

→ Simple reactions like A + 2B -> B + D

With R = [A] x $[B]^2$ x k

k -> Rate constant [$mol.L^{-1}.s^{-1}$]

R -> Reaction Rate [$M.l^{-1}s^{-1}$]

Acid-Base Equilibrium

→ $HA^{\cdot} \underset{k_{a2}}{\overset{k_{a1}}{\rightleftarrows}} H^{+} + A^{\cdot -}$

Radiolytic Reactions

→Production of species due to irradiation

(-> LET dependent)

$[e^{-}_{aq}, OH^{\cdot}, H^{\cdot}, H_2, H_2O_2, R^{\cdot}]$

Enzymatic Reactions

$E + S \overset{k_1/k_{-1}}{\longleftrightarrow} [ES] \overset{k_2}{\rightarrow} E + P$

E -> Enzyme

S -> Substrate

P -> Product

ES -> Enzyme-Substrate complex

Simple Example

Example of input (RON formatted) file

```
bio_param: (
    pH: 7,
),
fixed_concentrations:{ // Unit is [mol]/[l]
    "H2O": 55,
    "catalase": 4,
},
initial_concentrations:{ },// Unit is [mol]/[l] + assumed 0 if not specified

radiolytic: { // Unit is [radical / 100eV / incident particle]
    "e_aq": 2.8,
    "H_r" : 0.62,
    "H2"  : 0.47,
},
acid_base: [
    (
        acid: "H2",
        base: "H_r",
        pKa: 11.9,
    ),
],
k_reactions: [
    (
        reactants: ["e_aq", "H2O"],
        products: ["H_r", "OH_minus"],
        k_value: 10
    ),
    (
        reactants: ["e_aq", "e_aq", "H_r"],
        products: ["H2", "OH_minus", "OH_minus"],
        k_value: 20
    ),
],
// These reactions are implemented via the Michaelis Menten kinetic
enzymatic_reactions: [
    (
        enzyme: "catalase",
        substrate: ["H_r"],
        products: ["H2"],
        k_value: 5, // [1/s]
        k_micha: 1.1, // [mol/l]
    ),
],
)
```

Unrealistic A/B Reaction

$$e_{aq} + H_2O \xrightarrow{k_1} H^{\cdot} + OH^- \quad (k_1 = 10)$$

$$2e_{aq} + H^{\cdot} \xrightarrow{k_2} H_2 + 2OH^- \ (k_2 = 20)$$

$$H^{\cdot} + catalase \xrightarrow{k_3} H_2 \ (k_3 = 5; k_{M3} = 1.1)$$

Building "k-Reactions"matrices

"K Reaction" Kinetics

→ Simple reactions like A + 2B -> B + D

With R = [A] x [B]² x k

k -> Rate constant [mol.L^{-1}.s^{-1}]

R -> Reaction Rate [M.l^{-1}s^{-1}]

Related reaction rates

$$e_{aq} + H_2O \xrightarrow{k_1} H^{\cdot} + OH^- \quad \Rightarrow \quad R_1 = k_1 \,.\, [e_{aq}] \,.\, [H_2O]$$

$$2e_{aq} + H^{\cdot} \xrightarrow{k_2} H_2 + 2OH^- \quad \Rightarrow \quad R_2 = k_2 \,.\, [e_{aq}]^2 \,.\, [H^{\cdot}]$$

Equations to solve

$$\frac{d[e_{aq}]}{dt} = -R_1 - 2R_2$$

$$\frac{d[H^{\cdot}]}{dt} = R_1 - R_2$$

$$\frac{d[H_2]}{dt} = R_2$$

Using matrix calculus

Species concentrations vector ≡ y

$$\frac{d}{dt}\overbrace{\begin{pmatrix}[e_{aq}] & [H^{\cdot}] & [H_2]\end{pmatrix}}^{\text{Species concentrations vector} \equiv y} = \begin{pmatrix}R_1 & R_2\end{pmatrix} \bullet \begin{pmatrix}-1 & 1 & 0\\ -2 & -1 & 1\end{pmatrix}$$

$$\frac{d[OH^-]}{dt} = 0 \quad \Rightarrow \quad \text{Related to pH, assumed cst}$$

$$\frac{d[H_2O]}{dt} = 0 \quad \Rightarrow \quad \text{Declared as } \textit{fixed concentration}$$

Building "k-Reactions" matrices

"K Reaction" Kinetics

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$$e_{aq} + H_2O \xrightarrow{k_1} H^{\cdot} + OH^- \quad \Rightarrow \quad R_1 = k_1 \,.\, [e_{aq}] \,.\, [H_2O]$$

$$2e_{aq} + H^{\cdot} \xrightarrow{k_2} H_2 + 2OH^- \quad \Rightarrow \quad R_2 = k_2 \,.\, [e_{aq}]^2 \,.\, [H^{\cdot}]$$

To achieve this goal several matrices, need to be created as reaction rates cannot be pre-computed as they depends on species concentrations -> time dependent!

$$K_i = \overset{\text{\# Reactions}}{\underset{\longrightarrow}{(k_1 \quad k_2)}}$$

$$R_{iy} = \overset{\text{\# Reactions}}{\underset{\longrightarrow}{\begin{pmatrix} -1 & -2 \\ +1 & -1 \\ 0 & +1 \\ 0 & 0 \\ 0 & 0 \end{pmatrix}}} \quad \overset{\text{\# Species}}{\underset{\downarrow}{\begin{matrix} e_{aq} \\ H^{\cdot} \\ H_2 \\ OH^- \\ H_2O \end{matrix}}}$$

Stoichiometric coefficients

$$R_{ki} = \begin{pmatrix} 1 & 1 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{pmatrix}_{(:,:,\mathbf{0})} \begin{pmatrix} 0 & 1 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 1 & 0 \end{pmatrix}_{(:,:,\mathbf{1})} \begin{pmatrix} nan & 0 \\ nan & 1 \\ nan & 0 \\ nan & 0 \\ nan & 0 \end{pmatrix}_{(:,:,\mathbf{2})}$$

First two dimensions are the same as R_{iy} and the third one is the number of reactants of the one k reaction with the most of it. Here it is R_2 as there 3 reactants: $[e_{aq}]$, $[e_{aq}]$ & $[H^{\cdot}]$

Rem: /!\ Only ONE reactant per column

→ **This matrix will help compute the R_i**

Building "k-Reactions" matrices

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→ Simple reactions like A + 2B -> B + D

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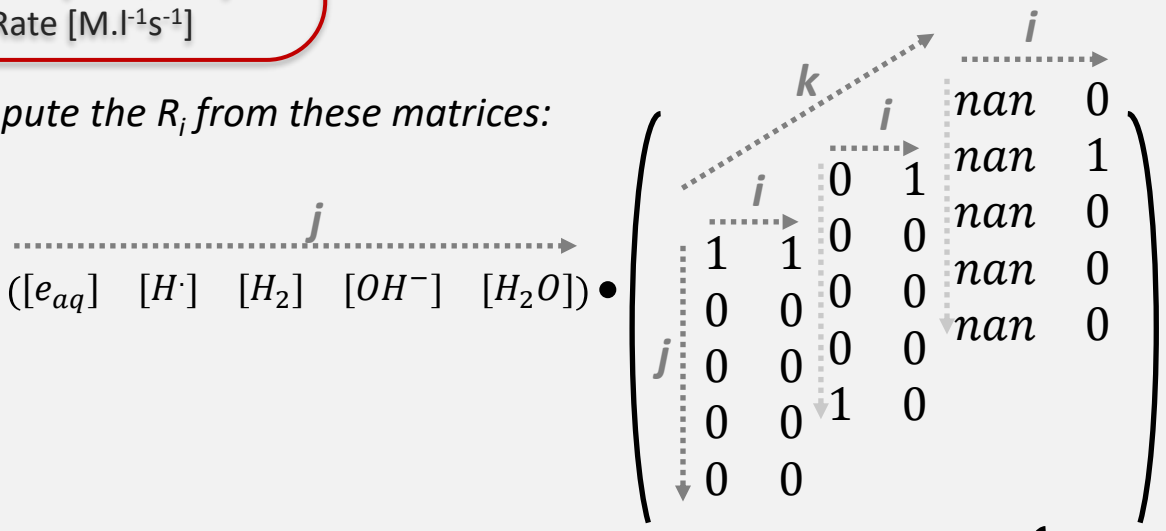
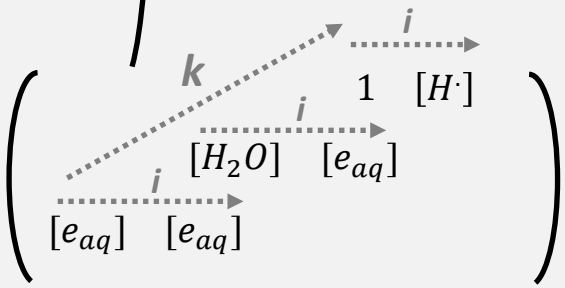
$$e_{aq} + H_2O \xrightarrow{k_1} H^{\cdot} + OH^- \quad \Rightarrow \quad R_1 = k_1 \,.\, [e_{aq}] \,.\, [H_2O]$$

$$2e_{aq} + H^{\cdot} \xrightarrow{k_2} H_2 + 2OH^- \quad \Rightarrow \quad R_2 = k_2 \,.\, [e_{aq}]^2 \,.\, [H^{\cdot}]$$

Let's compute the R_i from these matrices:



Computing the matrix multiplication along the k axis:
(and converting nan values to 1)



Now simply multiply, elements wise, along k (and multiply by $\mathbf{K_i}$) gives the $\mathbf{R_i}$

Building “k-Reactions” matrices

“K Reaction” Kinetics

→ Simple reactions like A + 2B -> B + D

With R = [A] x $[B]^2$ x k

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$$e_{aq} + H_2O \xrightarrow{k_1} H^{\cdot} + OH^- \quad \Rightarrow \quad R_1 = k_1 \,.\, [e_{aq}] \,.\, [H_2O]$$

$$2e_{aq} + H^{\cdot} \xrightarrow{k_2} H_2 + 2OH^- \quad \Rightarrow \quad R_2 = k_2 \,.\, [e_{aq}]^2 \,.\, [H^{\cdot}]$$

Let’s compute the R_i from these matrices (Python version):

```
# Compute the reaction rate of all k_reactions
    R_i = np.nan_to_num( np.einsum("j, jik -> ik", y, R_ki), nan=1)

# Compute dydt:
    dydt = np.matmul(R_iy, (np.prod(R_i, axis=1) * K_i).T)
```

Building Radiolytic Reactions matrices

Radiolytic Reactions
→Production of species due to irradiation
(-> LET dependent)
$[e^-_{aq}, H^\cdot, H_2]$

 # Species

$$G_i = \begin{pmatrix} G_{e_{aq}} & G_{H^\cdot} & G_{H_2} & 0 & 0 \end{pmatrix} \Longrightarrow \text{Units are [mol/l/Gy]}$$

e_{aq} $H^\cdot$ H_2 OH^- H_2O

Now simply multiply by the dose rate to get [mol/l/s] (which is the unit of dy/dt)

Python code:

```
# Add the Time dependent Radiolytic term
    dydt += Gi * beam.at(t).dose_rate()
```

Building Enzymatic Reactions matrices

Enzymatic Reactions

$$E + S \overset{k_1/k_{-1}}{\longleftrightarrow} [ES] \overset{k_2}{\rightarrow} E + P$$

E -> Enzyme
S -> Substrate
P -> Product
ES -> Enzyme-Substrate complex

Y(t) = $(e_{aq} \quad H^{\cdot} \quad H_2 \quad OH^- \quad H_2O \quad catalase)$

$$H^{\cdot} + catalase \overset{k_3}{\rightarrow} H_2 \; (k_3 = 5; k_{M3} = 1.1)$$

For enzymatic reaction, the Michaelis-Menten kinetics is used to compute the reaction rate of the reactions:

$$ER_i = \frac{k_i \,.\, [E_i] \,.\, [S_i]}{(k_{Mi} + [S_i])}$$

$$\boldsymbol{E_i} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 1 \end{pmatrix}$$ (# Reactions ⟶, # Species ⟶)

Enzyme Selection

$$\boldsymbol{S_i} = \begin{pmatrix} 0 \\ 1 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$ (# Reactions ⟶, # Species ⟶)

Substrate Selection

$$\boldsymbol{K_M} = \begin{pmatrix} k_i & \cdots \\ k_{Mi} & \cdots \end{pmatrix}$$ (# Reactions ⟶)

Constants storage

$$\boldsymbol{E_{iy}} = \begin{pmatrix} 0 \\ -1 \\ 1 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$ (# Reactions ⟶, # Species ⟶)

Stoichiometric coefficients

Building Enzymatic Reactions matrices

Enzymatic Reactions

$$E + S \overset{k_1/k_{-1}}{\longleftrightarrow} [ES] \overset{k_2}{\rightarrow} E + P$$

E -> Enzyme
S -> Substrate
P -> Product
ES -> Enzyme-Substrate complex

$$H^{\cdot} + catalase \overset{k_3}{\rightarrow} H_2 \; (k_3 = 5; k_{M3} = 1.1)$$

Y(t) = $(e_{aq} \quad H^{\cdot} \quad H_2 \quad OH^- \quad H_2O \quad catalase)$

Python code:

```
# Extract Enzyme cc of each enzymatic reactions.
E = np.matmul(y, Ei)

# Extract substrate cc of each enzymatic reactions.
S = np.matmul(y, Si)

# Compute the reaction rate of all enzymatic reactions.
MM = KM[1, :] * E * S / (KM[0, :] + S)

# Add this term to the total
dydt += np.matmul(Eiy, MM.T)
```

$\boldsymbol{E_i}$ = (# Reactions → 6 × ⋮ ↓ # Species)

Enzyme Selection

$\boldsymbol{S_i}$ = (# Reactions → 6 × ⋮ ↓ # Species)

Substrate Selection

$\boldsymbol{K_M}$ = (# Reactions → 2 × ⋮)

Constants storage

$\boldsymbol{E_{iy}}$ = (# Reactions → 6 × ⋮ ↓ # Species)

Stoichiometric coefficients

Building Acid/Base Reactions matrices

Acid-Base Equilibrium

$$\rightarrow HA^{\cdot} \underset{k_{a2}}{\overset{k_{a1}}{\rightleftarrows}} H^{+} + A^{\cdot -}$$

```
acid: "H2"
base: "H_r"
 pKa: 11.9
```

Unrealistic A/B Reaction

$$Ka = 10^{-pKa}$$

$$C_{tot} = [acid] + [base]$$

$$\frac{d[acid]}{dC_{tot}} = \frac{1}{1 + \frac{Ka}{[H^+]}}$$

$$\frac{d[base]}{dC_{tot}} = \frac{1}{1 + \frac{[H^+]}{Ka}}$$

Y(t) = $(e_{aq} \quad H^{\cdot} \quad H_2 \quad OH^- \quad H_2O \quad catalase)$

$$AB_i = \begin{pmatrix} 0 \\ 1 \\ 1 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

 # A/B Reactions (horizontal) — *# Species* (vertical)

$$AB_y = \begin{pmatrix} 1 \\ 0 \\ 0 \\ 1 \\ 1 \\ 1 \end{pmatrix}$$

 # A/B Reactions (horizontal) — *# Species* (vertical)

$$AB_o = \begin{pmatrix} 0 \\ \frac{d[base]}{dC_{tot}} \\ \frac{d[acid]}{dC_{tot}} \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

 # A/B Reactions (horizontal) — *# Species* (vertical)

Building Acid/Base Reactions matrices

Acid-Base Equilibrium

$$\rightarrow HA^{\cdot} \underset{k_{a2}}{\overset{k_{a1}}{\rightleftarrows}} H^{+} + A^{\cdot -}$$

```
acid: "H2"
base: "H_r"
 pKa: 11.9
```

Unrealistic A/B Reaction

$$Ka = 10^{-pKa}$$

$$C_{tot} = [acid] + [base]$$

$$\frac{d[acid]}{dC_{tot}} = \frac{1}{1 + \frac{Ka}{[H^+]}}$$

$$\frac{d[base]}{dC_{tot}} = \frac{1}{1 + \frac{[H^+]}{Ka}}$$

Y(t) = $(e_{aq} \quad H^{\cdot} \quad H_2 \quad OH^- \quad H_2O \quad catalase)$

Python code:

```
# => Force relationship between the total dydt's for A/B Partners
dydt = AB_y * dydt + np.matmul(AB_o , np.matmul(dydt, AB_i ).T)
```

Reset concentrations of acid and base partners only

Compute C_{tot} matrix
Size: [1 x #A/B Reactions]

Compute new concentrations partition of each [acid]/[base] partners
Size: [#Species x 1]

$([e_{aq}] \quad 0 \quad 0 \quad [OH^-] \quad [H_2O] \quad [catalase])$
Size: [#Species x 1]

➔ This is the last step in computation of dydt