# 3-Henri-Michaelis-Menten

June 13, 2023

[1]:

```
from sympy import *
from DifferentialAlgebra import *
leader,order,rank = var ('leader,order,rank')
derivative = function ('derivative')
init_printing ()
```

[2]:

```
t = var('t')
km1,k1,k2 = var('k_m1,k1,k2')
F1,Fm1,E,S,ES,P = function('F1,F_m1,E,S,ES,P')
params = [km1,k1,k2]
params
```

[2]:

$$[k_{m1},\ k_1,\ k_2]$$

ODE systems arising from chemical reaction systems have the form X' = N . V where 1. X is the vector of the concentrations 2. N is the stoichiometry matrix 3. V is the vector of the reaction rates

[3]:

```
X = Matrix([E(t), S(t), ES(t), P(t)])
```

[4]:

```
V = Matrix([k1*E(t)*S(t), km1*ES(t), k2*ES(t)])
```

[5]:

```
N = Matrix ([[-1, 1, 1], [-1, 1, 0], [1, -1, -1], [0, 0, 1]])
```

The ODE system arising from the chemical reaction system, assuming mass-action law dynamics and no reduction

[6]:

```
initial_system = Derivative (X).doit () - N * V
initial_system
```

[6]:

$$\begin{bmatrix} k_1 E(t) S(t) - k_2 \operatorname{ES}(t) - k_{m1} \operatorname{ES}(t) + \frac{d}{dt} E(t) \\ k_1 E(t) S(t) - k_{m1} \operatorname{ES}(t) + \frac{d}{dt} S(t) \\ -k_1 E(t) S(t) + k_2 \operatorname{ES}(t) + k_{m1} \operatorname{ES}(t) + \frac{d}{dt} \operatorname{ES}(t) \\ -k_2 \operatorname{ES}(t) + \frac{d}{dt} P(t) \end{bmatrix}$$

Lemaire's DAE 1. the contribution of the fast reactions is replaced by a placeholder: F1(t) - Fm1(t) 2. the equilibrium equation is appended

[7]:

```
V = Matrix([F1(t), Fm1(t), k2*ES(t)])
reduced_system = Derivative (X).doit () - N * V
```

```
reduced_system = reduced_system.row_insert (4, Matrix([k1*E(t)*S(t) -␣
 ↪km1*ES(t)]))
reduced_system
```

[7]:

$$\begin{bmatrix} -k_2 \operatorname{ES}(t) + \operatorname{F}_1(t) - \operatorname{F}_{m1}(t) + \frac{d}{dt}E(t) \\ \operatorname{F}_1(t) - \operatorname{F}_{m1}(t) + \frac{d}{dt}S(t) \\ k_2 \operatorname{ES}(t) - \operatorname{F}_1(t) + \operatorname{F}_{m1}(t) + \frac{d}{dt}\operatorname{ES}(t) \\ -k_2 \operatorname{ES}(t) + \frac{d}{dt}P(t) \\ k_1 E(t) S(t) - k_{m1} \operatorname{ES}(t) \end{bmatrix}$$

[8]:

```
R = DifferentialRing (derivations = [t],
                      blocks = [[F1,Fm1], [ES,E,P,S], params],
                      parameters = params)
```

The base field used at elimination stage is Q(k1,km1,k2) to avoid discussing parameter values

[9]:

```
Field_Q_params = BaseFieldExtension (generators = params)
```

[10]:

```
reduced_system = list(reduced_system)
ideal = R.RosenfeldGroebner (reduced_system, basefield = Field_Q_params)
ideal
```

[10]:

```
[regular_differential_chain,
 regular_differential_chain,
 regular_differential_chain]
```

[11]:

```
[ C.equations (solved=True) for C in ideal]
```

[11]:

$$\Bigg[\Bigg[\operatorname{ES}(t) = \frac{k_1 E(t) S(t)}{k_{m1}},\ \frac{d}{dt}S(t) = \frac{-k_1^2 k_2 E(t) S^2(t) - k_1 k_2 k_{m1} E(t) S(t)}{k_1 k_{m1} E(t) + k_1 k_{m1} S(t) + k_{m1}^2},\ \frac{d}{dt}P(t) = \frac{k_1 k_2 E(t) S(t)}{k_{m1}},\ \frac{d}{dt}E(t) = \frac{\quad}{k_1 k_{m1}}$$

[12]:

```
ideal[0].equations (solved=True)
```

[12]:

$$\Bigg[\operatorname{ES}(t) = \frac{k_1 E(t) S(t)}{k_{m1}},\ \frac{d}{dt}S(t) = \frac{-k_1^2 k_2 E(t) S^2(t) - k_1 k_2 k_{m1} E(t) S(t)}{k_1 k_{m1} E(t) + k_1 k_{m1} S(t) + k_{m1}^2},\ \frac{d}{dt}P(t) = \frac{k_1 k_2 E(t) S(t)}{k_{m1}},\ \frac{d}{dt}E(t) = \frac{\quad}{k_1 k_{m1} E}$$

[13]:

```
ideal[0].equations (solved=True, selection=Eq(leader,derivative(S(t))))
```

[13]:

$$\left[\frac{d}{dt}S(t) = \frac{-k_1^2 k_2 E(t) S^2(t) - k_1 k_2 k_{m1} E(t) S(t)}{k_1 k_{m1} E(t) + k_1 k_{m1} S(t) + k_{m1}^2}\right]$$

We have obtained the raw formula. To obtain the Henri-Michaelis-Menten formula, a new base field is defined 1. new parameters are defined (initial concentrations, historical Vmax, K constants) 2. some relations among these parameters are set (mostly renaming equations)

[14]:

```
P0, E0, S0, ES0, K, Vmax = var ('P0, E0, S0, ES0, K, V_max')
relations_among_params = [Eq(P0,0), Eq(ES0,0), Eq(K,km1/k1), Eq(Vmax,k2*E0)]
relations_among_params
```

[14]:

$$\left[ P_0 = 0, \; ES_0 = 0, \; K = \frac{k_{m1}}{k_1}, \; V_{max} = E_0 k_2 \right]$$

[15]:

```
extended_params = params + [ES0, E0, P0, S0, K, Vmax]
R = DifferentialRing (derivations = [t],
                      blocks = [[F1,Fm1], [ES,E,P,S], extended_params],
                      parameters = extended_params)
```

[16]:

```
relations_among_params = RegularDifferentialChain (relations_among_params, R)
relations_among_params
```

[16]: regular_differential_chain

[17]:

```
relations_among_params.equations (solved=True)
```

[17]:

$$\left[ P_0 = 0, \; ES_0 = 0, \; k_2 = \frac{V_{max}}{E_0}, \; k_{m1} = K k_1 \right]$$

[18]:

```
Field_Q_extended_params = BaseFieldExtension (generators = extended_params,
                                              relations =␣
 ↪relations_among_params)
```

In addition, the differential system is enlarged with some linear conservation laws

[19]:

```
conservation_laws = [Eq(E(t) + ES(t), E0 + ES0), Eq(S(t) + ES(t) + P(t), S0 +␣
 ↪ES0 + P0)]
conservation_laws
```

[19]:

$$\left[ E(t) + \mathrm{ES}\,(t) = E_0 + ES_0, \; \mathrm{ES}\,(t) + P(t) + S(t) = ES_0 + P_0 + S_0 \right]$$

[20]:

```
ideal = R.RosenfeldGroebner (reduced_system + conservation_laws,
                             basefield = Field_Q_extended_params)
ideal
```

[20]: [regular_differential_chain]

[21]:

```
ideal[0].equations (solved=True)
```

[21]:

$$\left[ P_0 = 0, \; ES_0 = 0, \; k_2 = \frac{V_{max}}{E_0}, \; k_{m1} = K k_1, \; P(t) = \frac{-E_0 S(t) + K S_0 - K S(t) + S_0 S(t) - S^2(t)}{K + S(t)}, \; E(t) = \frac{E_0 K}{K + S(t}$$

Extract the formula from the regular differential chain

Perform a final simplification (assuming E0*K can be neglected)

[22]:

```
HMM = ideal[0].equations (solved=True, selection=Eq(leader,derivative(S(t))))[0]
HMM
```

[22]:

$$\frac{d}{dt} S(t) = \frac{-K V_{max} S(t) - V_{max} S^2(t)}{E_0 K + K^2 + 2 K S(t) + S^2(t)}$$

[23]:

```
HMM.subs({E0*K:0})
```

[23]:

$$\frac{d}{dt}S(t) = \frac{-KV_{max}S(t) - V_{max}S^2(t)}{K^2 + 2KS(t) + S^2(t)}$$

[24]:

```
simplify (HMM.subs({E0*K:0}))
```

[24]:

$$\frac{d}{dt}S(t) = -\frac{V_{max}S(t)}{K + S(t)}$$

[ ]:

```

```