Finding and breaking Lie symmetries: implications for structural identifiability and observability of dynamic models

Gemma Massonis and Alejandro F. Villaverde

afvillaverde@iim.csic.es

CONSEJO SUPERIOR DE INVESTIGACIONES CIENTÍFICAS

BIRS Workshop "Model Theory of Differential Equations, Algebraic Geometry, and their Applications to Modeling"
1–5 June, 2020

Overview

Bibliography

Lie symmetries:

- Bluman, G.; Anco, S. Symmetry and integration methods for differential equations; Vol. 154, Springer Science & Business Media, 2008.
- Arrigo, D.J. Symmetry analysis of differential equations: an introduction; John Wiley & Sons, 2015.

SIO:

- Villaverde, A.F. "Observability and Structural Identifiability of Nonlinear Biological Systems". *Complexity* Vol. 2019, Article ID 8497093, https://doi.org/10.1155/2019/8497093.

MOTIVATION AND BACKGROUND

Observability and Structural Identifiability: the concepts

We consider the following type of dynamic models of ODEs:

$$M_{NL} := \begin{cases} \dot{x}(t) & = f(x(t), \theta, u(t), w(t)) \ , \\ y(t) & = g(x(t), \theta, u(t), w(t)) \ , \\ x(t_0) & = x^0(\theta) \end{cases}$$

with states $x(t) \in \mathbb{R}^m$, parameters $\theta \in \mathbb{R}^q$, outputs $y(t) \in \mathbb{R}^n$, known inputs $u(t) \in \mathbb{R}^{m_u}$, unknown inputs $w(t) \in \mathbb{R}^{m_w}$, f and g vectors of analytical functions.

Observability and Structural Identifiability: the concepts

We consider the following type of dynamic models of ODEs:

$$M_{NL} := \begin{cases} \dot{x}(t) & = f(x(t), \theta, u(t), w(t)) \ , \\ y(t) & = g(x(t), \theta, u(t), w(t)) \ , \\ x(t_0) & = x^0(\theta) \end{cases}$$

with states $x(t) \in \mathbb{R}^m$, parameters $\theta \in \mathbb{R}^q$, outputs $y(t) \in \mathbb{R}^n$, known inputs $u(t) \in \mathbb{R}^{m_u}$, unknown inputs $w(t) \in \mathbb{R}^{m_w}$, f and g vectors of analytical functions.

Observability

A model is observable if it is theoretically possible to infer its states, x(t), by observing its outputs, y(t)

Observability and Structural Identifiability: the concepts

We consider the following type of dynamic models of ODEs:

$$M_{NL} := \begin{cases} \dot{x}(t) & = f(x(t), \theta, u(t), w(t)) \ , \\ y(t) & = g(x(t), \theta, u(t), w(t)) \ , \\ x(t_0) & = x^0(\theta) \end{cases}$$

with states $x(t) \in \mathbb{R}^m$, parameters $\theta \in \mathbb{R}^q$, outputs $y(t) \in \mathbb{R}^n$, known inputs $u(t) \in \mathbb{R}^{m_u}$, unknown inputs $w(t) \in \mathbb{R}^{m_w}$, f and g vectors of analytical functions.

Observability

A model is observable if it is theoretically possible to infer its states, x(t), by observing its outputs, y(t)

Structural Identifiability

A model is structurally identifiable if it is theoretically possible to infer its parameters, θ, by observing its outputs, y(t)

Structural Identifiability and Observability (SIO)

Structural Local Identifiability as Observability

Extend the state vector as:

$$\widetilde{x}(t) = \begin{bmatrix} x(t) \\ \theta \end{bmatrix}, \dot{\widetilde{x}}(t) = \begin{bmatrix} f(\widetilde{x}(t), u(t)) \\ 0 \end{bmatrix} \Rightarrow M_{NL} := \begin{cases} \dot{\widetilde{x}} = \widetilde{f}(\widetilde{x}, u) \\ y = g(\widetilde{x}, u) \end{cases}$$

Structural Identifiability and Observability (SIO)

Structural Local Identifiability as Observability

Extend the state vector as:

$$\widetilde{x}(t) = \begin{bmatrix} x(t) \\ \theta \end{bmatrix}, \dot{\widetilde{x}}(t) = \begin{bmatrix} f(\widetilde{x}(t), u(t)) \\ 0 \end{bmatrix} \Rightarrow M_{NL} := \begin{cases} \dot{\widetilde{x}} = \widetilde{f}(\widetilde{x}, u) \\ y = g(\widetilde{x}, u) \end{cases}$$

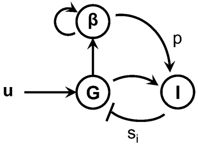
Structurally locally Identifiable or Observable (SIO)

A variable (state or parameter) $\widetilde{x}_i$ is structurally locally identifiable or observable (SIO) if there is a neighbourhood $V(\widetilde{x}_i^*)$ s.t.

$$\hat{\widetilde{x}}_i \in V(\widetilde{x}_i^*) \text{ and } y(\hat{\widetilde{x}}_i) = y(\widetilde{x}_i^*) \Rightarrow \hat{\widetilde{x}}_i = \widetilde{x}_i^*$$

Otherwise it is Structurally Unidentifiable or Unobservable (SU).

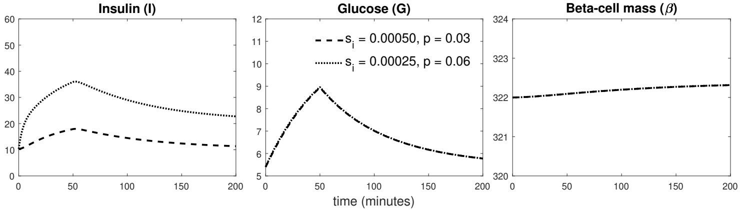
Why it matters: SU models provide wrong insights



$$\dot{G} = \mathrm{u}(0) + \mathrm{u} - (\mathrm{c} + s_i \cdot I) \cdot G$$

$$\dot{\beta} = \beta \cdot \left(\frac{1.4583 \cdot 10^{-5}}{1 + \left(\frac{8.4}{G}\right)^{1.7}} - \frac{1.7361 \cdot 10^{-5}}{1 + \left(\frac{G}{8.4}\right)^{8.5}} \right)$$

$$\dot{I} = \mathrm{p} \cdot \beta \cdot \frac{G^2}{\alpha^2 + G^2} - \gamma \cdot I$$



Model of the glucose-insulin system

If $y(t) = [\beta, G] \Rightarrow [p, s_i]$ are SU and I is unobservable.

c, α, γ, and the product $p \cdot s_i$ are SLI.

LIE SYMMETRIES

Assessing SIO with Lie Symmetries

- Existence of **Lie symmetries** $\Rightarrow$
  existence of similarity transformations[1] $\Rightarrow$
  existence of transformations of $\widetilde{x}$ that leave y unchanged: **non-observability (SU)**.
- Similarity transformations are one-parameter Lie group morphisms that map solutions of a differential equation onto themselves.
- Algorithm for finding Lie symmetries using *Ansatz* polynomials [2] + some modifications [3].

[1] Yates, J.W.; Evans, N.D.; Chappell, M.J. Structural identifiability analysis via symmetries of differential equations. *Automatica* 2009, 45, 25852591.

[2] Merkt, B., Timmer, J., and Kaschek, D. "Higher-order Lie symmetries in identifiability and predictability analysis of dynamic models". *Phys Rev E* 92.1, 2015.

[3] Massonis, G., and Villaverde, A.F. "Finding and Breaking Lie Symmetries: Implications for Structural Identifiability and Observability in Biological Modelling". *Symmetry* 12(3):469, 2020.

One-parameter Lie group of transformations:

$$x^* = X(x;\varepsilon)\ ,$$

We say that:

- $\eta(x) = \frac{\partial X(x;\varepsilon)}{\partial \varepsilon}|_{\varepsilon=0}$ is an infinitesimal
- X is the infinitesimal generator, $X = X(x) = \sum_{i=1}^{n} \eta_i(x)\frac{\partial}{\partial x_i}$
- $x + \varepsilon\eta(x)$ is the infinitesimal transformation of the Lie group of transformations.

First, augment the state vector x:

$$x := \begin{cases} \dot{x}_i(t) = f_i(x(t), u(t)), & i = 1, ..., m \\ x_i(t) = \theta, & i = m+1, ..., m+q \\ x_i(t) = w_i(t), & i = m+q+1, ..., n^* = m+q+m_w. \end{cases}$$

Then, consider different types of polynomial *Ansatz* for the infinitesimals (univariate, partially variate, and multivariate).

Univariate:

$$\eta_i(\mathbf{x}) = \sum_{d=0}^{d_{max}} r_{i,d} x_i^d, \quad i = 1, ..., n^* \ .$$

Partially variate:

$$\eta_i(\mathbf{x}) = \sum_{d_i, d_{m+1}, \ldots, d_{m+q}=0}^{|d|=d_{max}} r_{i,d} x_i^{d_i} x_{m+1}^{d_{m+1}} \cdots x_{m+q}^{d_{m+q}}, \quad i = 1, \ldots, m \ ,$$

$$\eta_i(\mathbf{x}) = \sum_{d_{m+1}, \ldots, d_{m+q}=0}^{|d|=d_{max}} r_{i,d} x_{m+1}^{d_{m+1}} \cdots x_{m+q}^{d_{m+q}}, \quad i = m+1, \ldots, m+q \ ,$$

$$\eta_i(\mathbf{x}) = \sum_{d_i, d_{m+1}, \ldots, d_{m+q}=0}^{|d|=d_{max}} r_{i,d} x_i^{d_i} x_{m+1}^{d_{m+1}} \cdots x_{m+q}^{d_{m+q}}, \quad i = m+q+1, \ldots, n^* \ .$$

Multivariate:

$$\eta_i(\mathbf{x}) = \sum_{d_1, \ldots, d_{m+q}=0}^{|d|=d_{max}} r_{i,d} x_1^{d_1} \cdots x_{m+q}^{d_{m+q}}, \quad i = 1, \ldots, m \ ,$$

$$\eta_i(\mathbf{x}) = \sum_{d_{m+1}, \ldots, d_{m+q}=0}^{|d|=d_{max}} r_{i,d} x_{m+1}^{d_{m+1}} \cdots x_{m+q}^{d_{m+q}}, \quad i = m+1, \ldots, m+q \ ,$$

$$\eta_i(\mathbf{x}) = \sum_{d_1, \ldots, d_{n^*}=0}^{|d|=d_{max}} r_{i,d} x_1^{d_1} \cdots x_{n^*}^{d_{n^*}}, \quad i = 1, \ldots, n^* \ .$$

Theorem

The system $M_{NL} := \begin{cases} \dot{x}(t) & = f(x(t), \theta, u(t)) \ , \\ y(t) & = g(x(t), \theta, u(t)) \end{cases}$ *admits a one-parameter Lie group of transformations defined by* $X \iff$ *:*

$$\mathbf{X}' \cdot (\dot{x}_k - f_k(x)) = 0, \quad k = 1, ..., m \ ,$$

$$\mathbf{X} \cdot (y_l - g_l(x)) = 0, \quad l = 1, ..., n \ .$$

where X' is the derivative of infinitesimal generators:

$$X' = \sum_{i=1}^{n^*} \eta_i(x) \frac{\partial}{\partial x_i} + \sum_{i=1}^{n^*} \eta_i'(x) \frac{\partial}{\partial \dot{x}_i} \ , \quad \text{where} \quad \eta_i'(x) = \sum_{j=1}^{n^*} \dot{x}_j \frac{\partial \eta_i}{\partial x_j} \ .$$

The previous theorem leads to:

$$\sum_{j=1}^{n^*} \dot{x}_j \frac{\partial \eta_k}{\partial x_j}(\mathbf{x}) - \sum_{i=1}^{n^*} \eta_i(\mathbf{x}) \frac{\partial f_k}{\partial x_i}(\mathbf{x}) = 0, \quad k = 1, ..., m ,$$
$$\sum_{i=1}^{n^*} \eta_i(\mathbf{x}) \frac{\partial g_l}{\partial x_i}(\mathbf{x}) = 0, \quad l = 1, ..., n .$$

The above system of PDEs can be converted to a system of ODEs if we assume **rational** functions...

$$\dot{x}_k = f_k(\mathbf{x}) = \frac{P^k(\mathbf{x})}{Q^k(\mathbf{x})}, \quad k = 1, ..., m ,$$
$$y_l = g_l(\mathbf{x}) = \frac{R^l(\mathbf{x})}{S^l(\mathbf{x})}, \quad l = 1, ..., n .$$

... leading to:

- Univariate + Partially variate:

$$P^k Q^k \frac{\partial \eta_k}{\partial x_k} - \sum_{i=1}^{n^*} \eta_i [P^k_{x_i} Q^k - P^k Q^k_{x_i}] = 0, \quad k = 1, \ldots, m \ ,$$

$$\sum_{i=1}^{n^*} \eta_i [R^l_{x_i} S^l - R^l Q^l_{x_i}] = 0, \quad l = 1, \ldots, n \ .$$

- Multivariate:

$$\sum_{j=1}^{m} P^j Q^k \left(\prod_{b \neq j} Q^b \right) \frac{\partial \eta_k}{\partial x_j} - \sum_{i=1}^{n^*} \eta_i \left(\prod_{b \neq k} Q^b \right) [P^k_{x_i} Q^k - P^k Q^k_{x_i}] = 0,$$

$$\sum_{i=1}^{n^*} \eta_i [R^l_{x_i} S^l - R^l Q^l_{x_i}] = 0.$$

If the model contains specific initial conditions, they should be included in the equations.

$$\mathbf{X} \cdot (x_k - \mathbf{p}_{ini})_{|_{x=\mathbf{p}_{ini}}} = 0, \quad k = 1, ..., m \ . \tag{1}$$

Thus, following the same procedure as before:

$$\sum_{i=1}^{n^*} \eta_i(\mathbf{p}_{ini}) - \sum_{i=1}^{n^*} \eta_i \frac{V_{x_i}^k W^k - V^k W_{x_i}^k}{(W^k)^2}_{|_{x=\mathbf{p}_{ini}}} = 0, \quad k = 1, ..., m \ . \tag{2}$$

1. Consider the vector $\mathbf{r} = (r_{1,0}, r_{1,1}, \ldots, r_{n^*,d_{max}})$,

$$\sum_{i_1,\ldots,i_n} c_{i_1,\ldots,i_n}(\mathbf{r}) x_1^{i_1} \cdots x_n^{i_n} = 0 \Longrightarrow \mathbf{C} \cdot \mathbf{r} = 0 \ .$$

   (Coefficients $c_{i_1,\ldots,i_n}$ are linear in $\mathbf{r}$).

2. To find symmetries, solve the linear system by computing the

$$\text{kernel of } \mathbf{C} = \begin{pmatrix} \cdots & \cdots & \cdots & \cdots \\ \vdots & \ddots & & \vdots \\ \vdots & & \ddots & \vdots \\ \cdots & \cdots & \cdots & \cdots \end{pmatrix} .$$

3. Take the vectors $\mathbf{r}$: $\begin{pmatrix} \vdots \end{pmatrix}, \begin{pmatrix} \vdots \end{pmatrix}, \ldots$ and replace them in η_i to obtain the infinitesimal generators $\mathbf{X} = \sum_{i=1}^{n} \eta_i(\mathbf{x}) \frac{\partial}{\partial x_i}$

- Build the expression of x* with the infinitesimal generators **X**
- When the infinitesimal transformation is given by powers of one variable $\rightarrow$ "elementary" transformation. Examples:

$$x_i^* = x_i + \varepsilon, \ \mathbf{X} = \frac{\partial}{\partial x_i} \ \text{(translation)} \ ,$$

$$x_i^* = \exp(\varepsilon) x_i, \ \mathbf{X} = x_i \frac{\partial}{\partial x_i} \ \text{(scaling)} \ ,$$

$$x_i^* = \frac{x_i}{1 - \varepsilon x_i}, \ \mathbf{X} = x_i^2 \frac{\partial}{\partial x_i} \ \text{(Mobius)} \ ,$$

$$x_i^* = \frac{x_i}{[1 - (p-1)\varepsilon x_i^{p-1}]^{\frac{1}{p-1}}}, \ \mathbf{X} = x_i^p \frac{\partial}{\partial x_i} \ \text{(higher order)} \ .$$

The most common ones are translation and scaling.

Summary

1. Choose the type of polynomial *Ansatz* (uni-, partial, multi-) and the maximum degree.
2. Create infinitesimal polynomials, η_i
3. Build the expressions for states, outputs, (& ICs)
4. Cast as $\mathbf{C} \cdot \mathbf{r} = 0$ and find $\mathbf{r}$ by kernel($\mathbf{C}$)
5. Replace $\mathbf{r}$ in η_i to obtain transformations $\mathbf{X}$

Implementations

- MinimalOutputSets (Mathematica)[4]
- SADE (Maple) [5]
- symmetryDetection (Python)[6]
- LieSymmetries (Matlab) [7]
  - Maximizes number of elementary transformations.
  - Computes non-elementary transformations.
  - Choose the states for which initial conditions are considered.

---

[4] Anguelova, M.; Karlsson, J.; Jirstrand, M. "Minimal output sets for identifiability". *Mathe Biosci*, 239:139153, 2012.

[5] Rocha Filho, T.M.; Figueiredo, A. "[SADE] a Maple package for the symmetry analysis of differential equations". *Comput Phys Commun*, 182:467476, 2011.

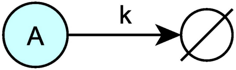
[6] Merkt, B., Timmer, J., and Kaschek, D. "Higher-order Lie symmetries in identifiability and predictability analysis of dynamic models". *Phys Rev E* 92.1, 2015.

[7] Massonis, G., and Villaverde, A.F. "Finding and Breaking Lie Symmetries: Implications for Structural Identifiability and Observability in Biological Modelling". *Symmetry* 12(3):469, 2020.

EXAMPLES

Simple chemical reaction

(1) Model diagram:



(2) Model equations:

$$\dot{A} = -\,2kA^2\ ,$$
$$A^{obs} = s_1 \frac{A}{1 + s_2 A}\ .$$

(3) Two infinitesimal generators:

$$\mathbf{X} = A\frac{\partial}{\partial A} - k\frac{\partial}{\partial k} - s_1\frac{\partial}{\partial s_1} - s_2\frac{\partial}{\partial s_2}\ .$$
$$\mathbf{X} = A^2\frac{\partial}{\partial A} + \frac{\partial}{\partial s_2}\ .$$

(4) New variables (all transformations are elementary):

$$A^* = e^{\varepsilon}A,\ k^* = e^{-\varepsilon}k\ ,$$
$$s_1^* = e^{-\varepsilon}s_1,\ s_2^* = e^{-\varepsilon}s_2\ .$$
$$A^* = \frac{A}{1 - \varepsilon A},\ s_2^* = s_2 + \varepsilon\ .$$

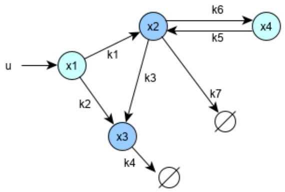
Simple chemical reaction

MATLAB output

```
>> Lie_Symmetry
Ansatz --> OK
Derivatives Ansatz --> OK
Numerator and denominator --> OK
Derivatives numerator and denominator --> OK
States Polynomial --> OK
Observation Polynomial --> OK
System --> OK
Kernel --> OK


 -------------------------
>>> Exist Symmetry
 -------------------------
 -------------------------
>>> Generators
[    x1, -k, -s1, -s2]
[ x1^2,   0,    0,    1]

 -------------------------
>>> New Variables
[       x1*exp(epsilon), k*exp(-epsilon), s1*exp(-epsilon), s2*exp(-epsilon)]
[ -x1/(epsilon*x1 - 1),                k,                s1,      epsilon + s2]

Elapsed time is 5.325316 seconds.
```

Pharmacokinetic model

(1) Model diagram:



(2) Model equations:

$$
\begin{aligned}
\dot{x}_1 &= u - (k_1 + k_2)x_1 \ , \\
\dot{x}_2 &= k_1 x_1 - (k_3 + k_6 + k_7)x_2 + k_5 x_4 \ , \\
\dot{x}_3 &= k_2 x_1 + k_3 x_2 - k_4 x_3 \ , \\
\dot{x}_4 &= k_6 x_2 - k_5 x_4 \ , \\
x_2^{\text{obs}} &= s_2 x_2 \ , \\
x_3^{\text{obs}} &= s_3 x_3 \ .
\end{aligned}
$$

(3) Infinitesimal generator:

$$
\mathbf{X} = k_1 \left(\frac{\partial}{\partial k_1} - \frac{\partial}{\partial k_2} \right) - \frac{k_3(k_1 + k_2)}{k_2} \left(\frac{\partial}{\partial k_3} - \frac{\partial}{\partial k_7} \right) - s_2 \frac{\partial}{\partial s_2} +
$$

$$
+ \frac{k_1 s_3}{k_2} \frac{\partial}{\partial s_3} + x_2 \frac{\partial}{\partial x_2} - \frac{k_1 s_3}{k_2} \frac{\partial}{\partial x_3} + x_4 \frac{\partial}{\partial x_4} \ .
$$

Pharmacokinetic model

(4) New variables (I):

$$x_2^* = x_2 e^{\varepsilon},\ x_4^* = x_4 e^{\varepsilon},\ k_1^* = k_1 e^{\varepsilon},\ s_2^* = s_2 e^{-\varepsilon}$$

$$x_3^* = x_3 - \frac{\varepsilon k_1 x_3}{k_2} - \frac{\varepsilon^2 k_1 x_3}{2k_2} - \frac{\varepsilon^3 k_1 x_3}{6k_2} - \frac{\varepsilon^4 k_1 x_3}{24k_2},$$

$$k_2^* = k_2 - \varepsilon k_1 - \frac{\varepsilon^2 k_1}{2} - \frac{\varepsilon^3 k_1}{6} - \frac{\varepsilon^4 k_1}{24},$$

$$k_3^* = k_3 - \frac{k_3(k_1+k_2)\varepsilon}{k_2} + \frac{\varepsilon^2 k_3(k_1+k_2)}{2k_2} - \frac{\varepsilon^3 k_3(k_1+k_2)}{6k_2} + \frac{\varepsilon^4 k_3(k_1+k_2}{24k_2}$$

$$k_7^* = k_7 + \frac{k_3(k_1+k_2)\varepsilon}{k_2} - \frac{\varepsilon^2 k_3(k_1+k_2)}{2k_2} + \frac{\varepsilon^3 k_3(k_1+k_2)}{6k_2} - \frac{\varepsilon^4 k_3(k_1+k_2}{24k_2}$$

$$s_3^* = s_3 + \frac{\varepsilon k_1 s_3}{k_2} + \frac{\varepsilon^2 k_1 s_3(2k_1+k_2)}{2k_2^2} + \frac{\varepsilon^3 k_1 s_3(6k_1^2+6k_1k_2+k_2^2)}{6k_2^3} +$$

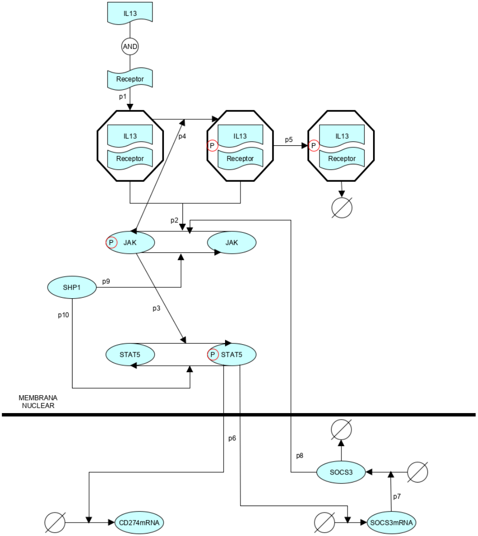
$$+ \frac{\varepsilon^4 k_1 s_3(24k_1^3 + 36k1^2 k_2^2 + 14k_1k_2^2 + k_2^3)}{24k_2^4}.$$

Pharmacokinetic model

(4) New variables (II):

$$
\begin{aligned}
x_2^* =& x_2 e^{\varepsilon},\ \ x_4^* = x_4 e^{\varepsilon},\ \ k_1^* = k_1 e^{\varepsilon},\ \ s_2^* = s_2 e^{-\varepsilon}\ , \\
k_2^* =& k_1 + k_2 - k_1 e^{\varepsilon}\ , \\
k_3^* =& \frac{k_3 e^{-\varepsilon}(k_1 + k_2 - k_1 e^{\varepsilon})}{k_2}\ , \\
k_7^* =& k_7 + \frac{k_3(k_1 + k_2)}{k_2} - \frac{k_3 e^{-\varepsilon}(k_1 + k_2)}{k_2}\ , \\
x_3^* =& \frac{x_3(k_1 + k_2 - k_1 e^{\varepsilon})}{k_2}\ , \\
s_3^* =& \frac{k_2 s_3}{(k_1 + k_2 - k_1 e^{\varepsilon})}\ .
\end{aligned}
$$

JAK-STAT signaling pathway



JAK-STAT signaling pathway

Infinitesimal generators:

$$\begin{aligned} \mathbf{X} &= t_{13}\frac{\partial}{\partial t_{13}} - t_{17}\frac{\partial}{\partial t_{17}} + t_{22}\frac{\partial}{\partial t_{22}} \ , \\ \mathbf{X} &= -x_{10}\frac{\partial}{\partial x_{10}} - t_{11}\frac{\partial}{\partial t_{11}} - t_{15}\frac{\partial}{\partial t_{15}} + t_{21}\frac{\partial}{\partial t_{21}} \ . \end{aligned} \tag{3}$$

New variables:

$$t_{13}^* = t_{13}e^{\varepsilon}, \quad t_{17}^* = t_{17}e^{-\varepsilon}, \quad t_{22}^* = t_{22}e^{\varepsilon} \ , \tag{4}$$

$$x_{10}^* = x_{10}e^{-\varepsilon}, \quad t_{11}^* = t_{11}e^{-\varepsilon}, \quad t_{15}^* = t_{15}e^{-\varepsilon}, \quad t_{21}^* = t_{21}e^{\varepsilon} \ . \tag{5}$$

DISCUSSION

Conclusions

- Symmetries inform about lack of SIO — and about its source.
- Their study can *replace* or *complement* other SIO tests.
- We have illustrated the use of a symbolic computation tool that finds Lie symmetries and the corresponding transformations automatically.
- Open-source implementation in MATLAB. Integrated in the STRIKE-GOLDD toolbox.
- Other tools in Mathematica, Python, Maple.
- Based on previous results (Merkt et al) + a few additions, incl. automatically calculating symmetry-breaking transformations.
- Symmetry-breaking transformations fix observability... but the mechanistic meaning is generally lost (so are they any good?).

Bonus: other uses of symmetry in biological modelling

The study of symmetries can inform about observability. But there are other possible uses, see e.g. (& recent, open special issues in MDPI Symmetry journal):

- morphological (a)symmetries in development
- homeostasis processes
- ...

PLOS COMPUTATIONAL BIOLOGY

RESEARCH ARTICLE

Conservation laws by virtue of scale symmetries in neural systems

Erik D. Fagerholm[1]*, **W. M. C. Foulkes**[2], **Yasir Gallero-Salas**[3,4], **Fritjof Helmchen**[3,4], **Karl J. Friston**[5], **Rosalyn J. Moran**[1], **Robert Leech**[1]

1 Department of Neuroimaging, King's College London, London, United Kingdom, **2** Department of Physics, Imperial College London, London, United Kingdom, **3** Brain Research Institute, University of Zürich, Zürich, Switzerland, **4** Neuroscience Center Zürich, Zürich, Switzerland, **5** Wellcome Centre for Human Neuroimaging, University College London, London, United Kingdom

Acknowledgements

She did the work

- Gemma Massonis Feixas

They provided the funding

- Spanish Ministry of Science, Innovation and Universities ref. DPI2017-82896-C2-2-R (SYNBIOCONTROL)

And thank you for your attention