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Recent numerical calculations on combustion and cell metabolism models suggest that ratios of sensitivities may show certain regularities. Here we give exact sufficient, necessary, and sufficient and necessary conditions for these regularities (local similarity, scaling relation, and global similarity) to hold. We also investigate the question, what happens if the conditions are only approximately fulfilled.

Numerical calculations have recently shown that in some circumstances

there exist interesting relations between sensitivities, and

these relations might have deep meaning and consequences on the given chemical or biological phenomena.

Different opinions exist on the chemical and biological sources of these relations. We try to find out the mathematical sources, conditions in the form of restrictions on the right hand sides for the individual relations to hold.

Let $N, P \in \mathbb{N}$, $\mathbf{f} \in \mathcal{C}^2(\mathbb{R}^N \times \mathbb{R}^P, \mathbb{R}^N)$, and consider

$$\dot{\mathbf{c}}(t, \mathbf{p}) = \mathbf{f}(\mathbf{c}(t, \mathbf{p}), \mathbf{p}) \quad \mathbf{c}(0, \mathbf{p}) = \mathbf{c}_0 \tag{1}$$

with $\mathbf{c}_0 \in \mathbb{R}^N$ arbitrary. Let the derivative of the ith coordinate function of this function with respect to the kth parameter be denoted by

$$s_{ik} \quad (i \in \{1, 2, \ldots, N\}; k \in \{1, 2, \ldots, P\}).$$

These functions (the **sensitivities**) obey

$$\begin{aligned} \dot{s}_{ik}(t, \mathbf{p}) &= \sum_{n=1}^{N} \partial_n f_i(\mathbf{c}(t, \mathbf{p}), \mathbf{p}) s_{nk}(t, \mathbf{p}) \qquad (2) \\ &\quad + \partial_{N+k} f_i(\mathbf{c}(t, \mathbf{p}), \mathbf{p}) \\ s_{ik}(0, \mathbf{p}) &= 0 \quad (i = 1, 2, \ldots, N; k = 1, 2, \ldots, P.) \qquad (3) \end{aligned}$$

Definition 1

1. *If for some* $k, m \in \{1, 2, \ldots, P\}$ *and for some* $i, j \in \{1, 2, \ldots, N\}$ *there exists* $\lambda_{ij} : \mathbb{R} \times \mathbb{R}^P \longrightarrow \mathbb{R}$ *such that for all* $\mathbf{c}_0 \in \mathbb{R}^N$

$$\lambda_{ij} s_{jk} = s_{ik} \text{ and also } \lambda_{ij} s_{jm} = s_{im} \tag{4}$$

holds, then the parameters p_k *and* p_m *are* ***locally similar*** *with respect to the state variables* c_i *and* c_j *with the similarity function* λ_{ij}.

2. *If for some* $i, j \in \{1, 2, \ldots, N\}$ *and for all* $k \in \{1, 2, \ldots, P\}$, $\mathbf{c}_0 \in \mathbb{R}^N$

$$\dot{c}_i s_{jk} = \dot{c}_j s_{ik} \tag{5}$$

*is true, then a **scaling relation** is said to hold with respect to the state variables* c_i *and* c_j.

3. *If for some* $k, m \in \{1, 2, \dots, P\}$ *and* $i \in \{1, 2, \dots, N\}$ *there exists a real number* $\mu_{ikm} \in \mathbb{R}$ *such that for all* $\mathbf{c}_0 \in \mathbb{R}^N$

$$s_{ik}(t, \mathbf{p}) = \mu_{ikm} s_{im}(t, \mathbf{p}) \quad (t \in \mathbb{R}) \tag{6}$$

holds, then the parameters p_k *and* p_m *are **globally similar** with respect to the state variable* c_i *with the similarity number* μ_{ikm}.

4. *If* p_k *and* p_m *are globally similar with respect to all the state variables, and*

$$\mu_{1km} = \mu_{2km} = \cdots = \mu_{Nkm} =: \bar{\mu}_{km}, \tag{7}$$

then the parameters p_k *and* p_m *are* ***uniformly globally similar with the similarity number*** $\bar{\mu}_{km}$.

Exact conditions General strategy: use the conditions and the governing equations, and try to eliminate sensitivities to get relations between the coordinate functions of the right hand side of (1).

Scaling relation

Theorem 1 *The scaling relation* (5) *with respect to the state variables* c_i *and* c_j *holds if and only if there exists a function* $\alpha : \mathbb{R}^N \longrightarrow \mathbb{R}$ *such that*

$$\alpha(\mathbf{x}) f_i(\mathbf{x}, \mathbf{p}) = \beta(\mathbf{x}) f_j(\mathbf{x}, \mathbf{p}) \quad (\mathbf{x} \in \mathbb{R}^N) \qquad (8)$$

is true.

Global similarity

Theorem 2 *The parameters* p_k *and* p_m *are uniformly globally similar with the similarity parameter* $\bar{\mu}_{km}$ *if and only if for all* $\mathbf{x} \in \mathbb{R}^N$

$$\partial_{N+k}\mathbf{f}(\mathbf{x}, \mathbf{p}) = \bar{\mu}_{km}\partial_{N+m}\mathbf{f}(\mathbf{x}, \mathbf{p}) \tag{9}$$

holds.

How do the conditions restrict the form of the right hand sides?

Scaling relation In this case we obtained a result of this type in the single step above.

Global similarity

Theorem 3 *Suppose that* (9) *holds for* $\mathbf{p} \in \Pi \subset \mathbb{R}^P$, *where* Π *is a connected open set, and let us suppose e.g.* $k < m$. *Then the right hand side* $\mathbf{f}$ *is of the following form:*

$$\mathbf{f}(\mathbf{x}, \mathbf{p}) = \mathbf{g}(\mathbf{x}, p_1, p_2, \ldots, p_{k-1}, p_{k+1}, \ldots, p_{m-1}, p_{m+1}, \ldots, p_P, \bar{\mu}_{km} p_k + p_m). \tag{10}$$

Remark 1 *Thus, uniform global similarity implies that the coordinate functions only depend on a (on the same) linear combination of the two parameters concerned.*

Approximate conditions—approximate similarities Now assume that the conditions are fulfilled approximately, and try to estimate the effect of this fact on the error of different similarities. The main reason to investigate approximate fulfilment of the conditions is that the conditions on the right hand sides formulated above such as e.g. (8), (9) are rather stringent, models will usually not fulfil them. Namely, the conditions determine more or less explicitly the forms of the right hand side of (1).

Scaling relation

Theorem 4 *Let* $\Pi \subset \mathbb{R}^P$ *be a connected open subset of parameters, and suppose*

$$\alpha(\mathbf{x}) f_j(\mathbf{x}, \mathbf{p}) + \varepsilon(\mathbf{x}, \mathbf{p}) = f_i(\mathbf{x}, \mathbf{p}) \quad (\mathbf{p} \in \Pi)$$

holds with the differentiable function $\boldsymbol{\varepsilon} : \mathbb{R}^N \times \Pi \longrightarrow \mathbb{R}$ *and with functions* $\varepsilon_k : \mathbb{R}^N \longrightarrow \mathbb{R}^+ \quad (k = 1, 2, \ldots, N)$ *having the property*

$$\sup\{|\varepsilon(\mathbf{x}, \mathbf{p})| + |\partial_{N+k}\varepsilon(\mathbf{x}, \mathbf{p})|; \mathbf{p} \in \Pi\} \leq \varepsilon_k(\mathbf{x}) \quad (11)$$
$$(\mathbf{x} \in \mathbb{R}^N; k = 1, 2, \ldots, N),$$

and let us suppose that there exist $K_{jk} : \mathbb{R}^N \longrightarrow \mathbb{R}^+ \quad (j, k =$

$1, 2, \ldots, N)$ *such that*

$$\sup\{|F_j| + |\partial_{N+k} F_j|; \mathbf{p} \in \Pi\} \leq K_{jk}(\mathbf{x}) \quad (\mathbf{x} \in \mathbb{R}^N), \tag{12}$$

then

$$|\dot{c}_i(t, \mathbf{p}) s_{jk}(t, \mathbf{p}) - \dot{c}_j(t, \mathbf{p}) s_{ik}(t, \mathbf{p})| \leq K_{jk}(\mathbf{c}(t, \mathbf{p})) \varepsilon_k(\mathbf{c}(t, \mathbf{p})). \tag{13}$$

Remark 2 *The theorem is really useful if the functions* K_{jk}, ε_k *are constants.*

Global similarity

Theorem 5 *Let $\Pi \subset \mathbb{R}^P$ be a connected open subset of parameters, and suppose*

$$\mathbf{f}(\mathbf{x},\mathbf{p}) = \mathbf{g}(\mathbf{x}, p_1, p_2, \ldots, p_{k-1}, p_{k+1}, \ldots, p_{m-1}, p_{m+1}, \ldots, p_P, \bar{\mu}$$
$$+ \ \boldsymbol{\varepsilon}(\mathbf{x},\mathbf{p}) \quad (\mathbf{p} \in \Pi)$$

holds with some function g. *Then*

$$\partial_{N+k}\mathbf{f}(\mathbf{x},\mathbf{p}) - \bar{\mu}_{km}\partial_{N+m}\mathbf{f}(\mathbf{x},\mathbf{p}) = \partial_{N+k}\boldsymbol{\varepsilon}(\mathbf{x},\mathbf{p}) - \bar{\mu}_{km}\partial_{N+m}\boldsymbol{\varepsilon}(\mathbf{x},\mathbf{p} \qquad (15)$$

Theorem 6 *Let us suppose that for all* $\mathbf{x} \in \mathbb{R}^N$

$$\partial_{N+k}\mathbf{f}(\mathbf{x},\mathbf{p}) - \bar{\mu}_{km}\partial_{N+m}\mathbf{f}(\mathbf{x},\mathbf{p}) = \boldsymbol{\varepsilon}(\mathbf{x},\mathbf{p}) \qquad (16)$$

holds, and let a Lipschitz constant for $\mathbf{f}$ *be* $L \in \mathbb{R}^+$:

$$\|f(\mathbf{x}, \mathbf{p}) - f(\mathbf{y}, \mathbf{p})\| \leq L\|\mathbf{x} - \mathbf{y}\|,$$

and let

$$\varepsilon(\mathbf{x}) := \sup\{\|\boldsymbol{\varepsilon}(\mathbf{x}, \mathbf{p})\|; \mathbf{p} \in \Pi\}$$

Then

$$\|\bar{\mu}_{km}\mathbf{s}_{\cdot m}(t, \mathbf{p}) - \mathbf{s}_{\cdot k}(t, \mathbf{p})\| \leq \frac{\varepsilon(\mathbf{x})}{L} e^{L|t|}.$$

Problems

1. The explicit meaning of the conditions in case of mass action kinetics, or in case of linear dependence on the parameters.
2. Connections with qualitative properties, with lumpability, with controllability and observability etc.
3. Other models (PDE, stochastic etc.)