**Biomolecular Networks Are Highly Nonlinear, Extremely Large Scale, and Yet Are Exceptionally Structured**

The concept of layering provides a new way to describe a biological system's structure. Traditional concept of modular decomposition concentrates on a simultaneous partition of the reaction–species sets into interconnected subnetworks. Assumes a partition of the state space of the dynamics. There have instead proposed a new approach, termed layering, that considers the contribution of each subsystem to all species. Subsystem dimensions are defined by matrix ranks.

**Biological Network ODE Model**

\[ \dot{x} = Sv(x) \]

Concentration vector: \( x = [x_1, x_2, x_3]^T \)

Flux vector: \( v(x) = [k_1 x_1, k_2 x_1 x_2, k_3 x_2 x_3]^T \)

Stoichiometric matrix:

\[ S = \begin{bmatrix} 1 & -1 & 0 \\ 0 & 1 & 0 \end{bmatrix} \]

Decompose the stoichiometry:

\[ S = S^f + S^s \]

System dynamics:

\[ \dot{x}(t) = S^f v(x) \]

Layered-dynamics:

\[ \dot{x}(t) = S^f v(x^f + \ldots + x^f) \]

Recompose the layered states:

\[ x = x^f + x^s \]

**Timescale Separation Implies That the Biochemical Network Dynamics Proceed According to Additional Nonlinear Conservation Constraints**

The projection of the slow dynamics given above implies that the approximated dynamics are always orthogonal to the row space of \( M(f) \), which varies with the state.

**Conclusions and Future Work**

- Through layered decomposition we have formulated the QSS approximation of a timescale separated system as a state-dependent projection of the slow dynamics, written in terms of the fast layer's stoichiometric structure and kinetic form.
- We can thus approximate complex dynamics in high dimension into lower-dimensional dynamics, yet remain embedded in the original state space.
- The design of fast dynamics can thus implement tuneable, nonlinear static constraints into a synthetic biomolecular network.
- Conversely, when investigating natural networks, the dynamics on one, fast, timescale define nonlinear static constraints on other, slower timescales, on which dynamics have evolved to perform biological functionalities.
- Consider also layering decomposition without timescale separation, in other dynamical systems. How can the decomposition of dynamics be interpreted as a decomposition into multiple functionalities and constraints on the entire set of original system variables?

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**Layered Synthetic Biomolecular Systems**

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