**Latent space modelling of high dimensional cytokine dynamics**

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**Context**

- Immunotherapies are being developed [1]: engineered T cells, cancer vaccines, etc.
- New experimental and modelling tools are needed to assess and improve them.
- Success of immunotherapy treatments depend on antigen quality (potency) [2].
- Immune cells produce different cytokine response for antigens of different qualities.
- We lack quantitative principles to interpret high dimensional cytokine dynamics [3].

**Data: cytokine time series**

![Figure 1](image1.png)

**Antigen encoding in latent space**

**Goal:** find a low-dimensional representation in which cytokine dynamics can be modelled and classified according to antigen quality.

![Antigen Quantity](image2.png)

**Figure 2:** Using a small neural network, we found that time integrals of the logs of cytokines can be projected to a 2D space in which trajectories are separated according to antigen quality. We term this structure "antigen encoding".

**Modelling latent space dynamics**

We found simple dynamical equations to describe trajectories in latent space.

\[
\mathbf{r}(t) = \begin{cases} 
\mathbf{v}_0 t \\ \frac{\mathbf{v}_0}{k} + \mathbf{v}_1 (1 - e^{-k(t - t_0)}) + \mathbf{v}_2 (t - t_0) + \mathbf{v}_3 t_0 \\
\end{cases} \quad t \leq t_0 \\
\frac{\mathbf{v}_0}{k} + \mathbf{v}_1 (1 - e^{-k(t - t_0)}) + \mathbf{v}_2 (t - t_0) + \mathbf{v}_3 t_0 \\
\end{cases} \quad t > t_0
\]

**Figure 2:** (Left) model parameterization of latent space curves. (Right) parameter values fitted on each curve reflect antigen quality (color of dots).

**References**


**Model-generated cytokine data**

1. Select model parameters
2. Compute curves of latent space model
3. Reconstruct

![Figure 4](image3.png)

**Figure 4:** Combining the latent space model and a non-linear reconstruction method allows us to generate model-derived cytokine time series.

**Application to engineered T cells**

![Figure 5](image4.png)

**Figure 5:** Values of model parameter v0 fitted on cytokine trajectories coming from anti-CD19 chimeric antigen receptor (CAR) T cells reveal sub-optimal activation those T cells by CD-19.

**Conclusions**

- Cytokine time series encode antigen quality in a 2D latent space.
- A simple dynamical model captures this dependency of the latent space on quality and can generate new cytokine time series.
- This model allows us to quantify the response of T cells engineered for therapy.

**Acknowledgements**

This work was also supported by a grant from the Simons Foundation to PF and an NSERC-CREATE Graduate Award in Complex Dynamics to FB. The Immunodynamics group is supported by the intramural research program of the National Cancer Institute.