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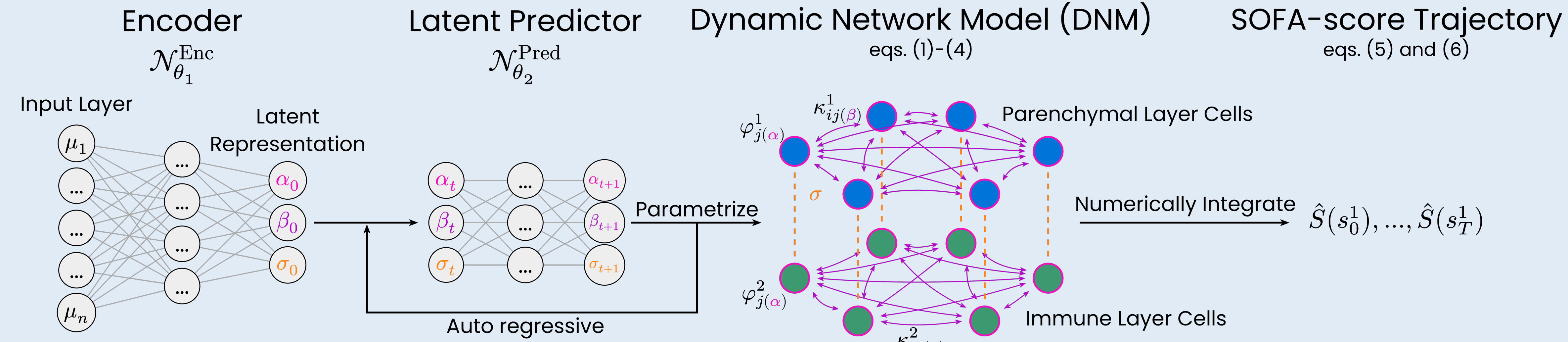
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## Architecture of the End-to-End pipeline



## SOFA-score

**Sequential Organ Failure Assessment [3]**

- Assesses 6 organ systems to measure their failure.
- Higher score (0–24) means greater risk of death.
- Used in hospitals to track patients status, especially in sepsis.

## The Dynamic Network Model

The “Dynamic Network Model” (DNM), introduced in [1] and mathematically defined in Eqs. 1-4, represents the interaction between parenchymal cells (functional organ cells) denoted  $\varphi_i^1$ , and immune cells, denoted  $\varphi_i^2$ , using a two layer partly adaptive oscillator network, with  $i = 1, \dots, N$ , where  $\kappa_{ij}^{1/2}$  are adaptive coupling weights.

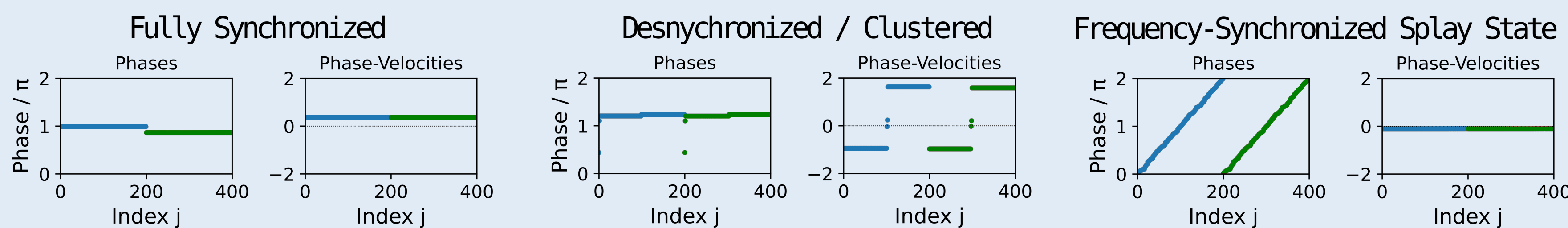
$$\dot{\varphi}_i^1 = \omega^1 - \frac{1}{N} \sum_{j=1}^N ((a_{ij}^1 + \kappa_{ij}^1) \sin(\varphi_i^1 - \varphi_j^1 + \alpha^{11})) - \sigma \sin(\varphi_i^1 - \varphi_i^2 + \alpha^{12}) \quad (1)$$

$$\dot{\kappa}_{ij}^1 = -\varepsilon^1 (\kappa_{ij}^1 + \sin(\varphi_i^1 - \varphi_j^1 - \beta)) \quad (2)$$

$$\dot{\varphi}_i^2 = \omega^2 - \frac{1}{N} \sum_{j=1}^N (\kappa_{ij}^2 \sin(\varphi_i^2 - \varphi_j^2 + \alpha^{22})) - \sigma \sin(\varphi_i^2 - \varphi_i^1 + \alpha^{21}) \quad (3)$$

$$\dot{\kappa}_{ij}^2 = -\varepsilon^2 (\kappa_{ij}^2 + \sin(\varphi_i^2 - \varphi_j^2 - \beta)) \quad (4)$$

Different stable synchronization patterns can occur based on the parameterization:



Snapshots of Parenchymal Cells (blue) and Immune Cells (green)

It is hypothesized that synchronized states in the parenchymal layer represent a healthy patient, whereas desynchronized states most likely capture pathological conditions [2]. The amount of desynchronisation is expressed by the *ensemble average of the standard deviation of the mean phase velocities*, defined by:

$$s^\mu = \frac{1}{M} \sum \sqrt{\frac{1}{N} \sum_j (\langle \dot{\varphi}_j^\mu \rangle - \bar{\omega}^\mu)^2} \quad (5)$$

## Method

Using the MIMIC-III database [4], for each patient’s state snapshot with features  $(\mu_1, \dots, \mu_n)$  at time  $t$ , we want to predict the SOFA-score  $S$  step-wise  $T = 6$  hours into the future. Our approach includes the encoding of patient states into the latent DNM parameter space and track their evolution auto-regressively.

The DNM-System size is  $N = 200$  oscillators per layer. To account for sensitivity to initial conditions, we simulate ensembles of size  $M = 50$  with stochastic initializations of  $\kappa$ ’s and  $\varphi$ ’s.

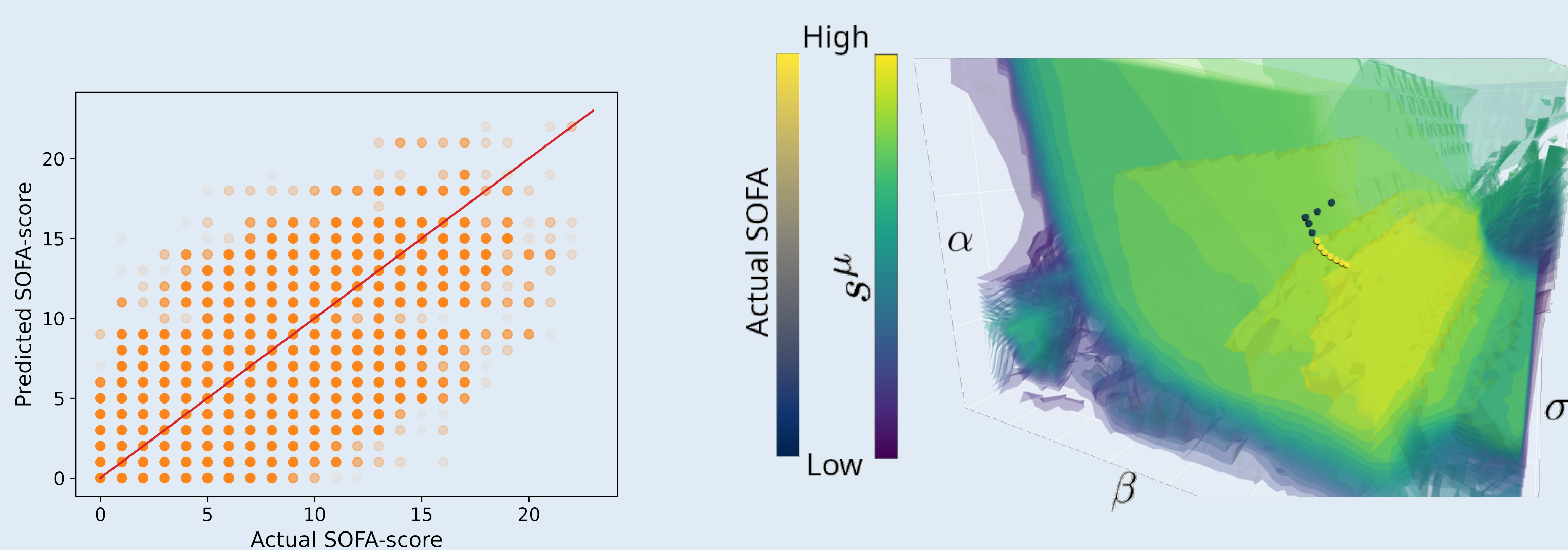
To guide learning, we use a loss function with three additive components:

- Classification**  $BCE(p(l_k), t_k)$ : Binary cross-entropy over  $k = 1 \dots 24$  SOFA levels, with the ground truth SOFA score  $t_k$  and logits  $l_k = \frac{s^1 - \tau_k}{T}$  where the thresholds  $\tau_k$  and temperature  $T$  are learnable.
- Reconstruction**  $MSE(\hat{\mu} - \mu) = \sum_i^n \frac{(\mu_i - \hat{\mu}_i)^2}{n}$ : between the original observations and their reconstruction by a neural decoder ( $\hat{\mu} = \mathcal{N}_{\theta_3}^{\text{Dec}}(\alpha, \beta, \gamma)$ ), encouraging semantic structure in the latent space.
- Correlation Penalty**  $CP(\alpha, \beta, \sigma) = \frac{1}{3}(\rho_{\alpha\beta}^2 + \rho_{\beta\sigma}^2 + \rho_{\alpha\sigma}^2)$ : Where  $\rho_{XY}$  is the correlation between  $X$  and  $Y$ , helping to disentangle the latent representation.

Final SOFA-score prediction:

$$\hat{S}(s_\mu^1) = \max(k | s_\mu^1 > t_k) \quad (6)$$

## Results & Discussion



Prediction on a held-out test dataset

Latent space trajectory of a single patient

- We successfully project real patient data to the latent space of the DNM.
- We are able to capture patient trajectories within the model and make predictions about their development.

### Future Work:

- Include predictions about patient infections.
  - The DNM naturally provides this via its second layer.
  - This would capture the whole Sepsis-3 definition.
- Analyze the semantic latent space structure.
- Rigorous quantitative analysis and comparison with SOTA.

<sup>1</sup> J. Sawicki, R. Berner, T. Löser and E. Schöll “Modeling tumor disease and sepsis by networks of adaptively coupled phase oscillators”, *Frontiers in Network Physiology*, 2674-0109, 2022.

<sup>2</sup> R. Berner, J. Sawicki, M. Thiele, T. Löser and E. Schöll “Critical Parameters in Dynamic Network Modeling of Sepsis”, *Frontiers in Network Physiology*, 2674-0109, 2022.

<sup>3</sup> M. Singer et al. “The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)”, *JAMA*, 2315:801-810, 2016.

<sup>4</sup> A. Johnson et al. “MIMIC-III Clinical Database (version 1.4)”, *PhysioNet*, RRID:SCR 007345, 2016.



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