An LSTM-based Recurrent Neural Network for Neonatal Sepsis Detection

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Sepsis

- Clinical condition which involves a destructive host response to a blood stream infection.
- High mortality and morbidity in all populations (adults, children, newborns)

Prematurity

$<$ 37 weeks of gestation, of all livebirths:

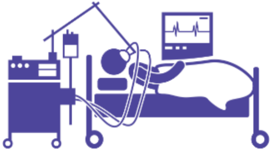
- 8.7% preterm in Europe, 11.1% worldwide [1]
- Almost all pre-term infants are admitted to a Neonatal Intensive Care Unit (NICU)

NICU

- 5-10% of NICU patients get an infection [2]
- 1.5 to 5 fold higher risk neurological disturbances into adulthood [3]

Sepsis detection

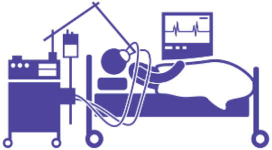
- The analysis of blood samples reveals on-going infections
  - Difficult and **harmful** on preterms
  - Levels are **slow** to rise and lead to delayed treatments.
  - Change in concentration is **unspecific** to sepsis, leads to inadequate antibiotics treatments potentially harmful for pre-terms

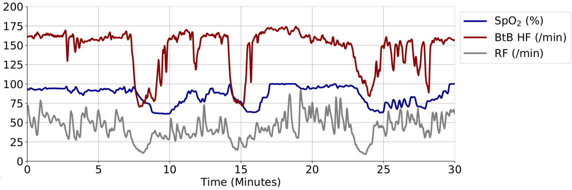


Background

Sepsis detection

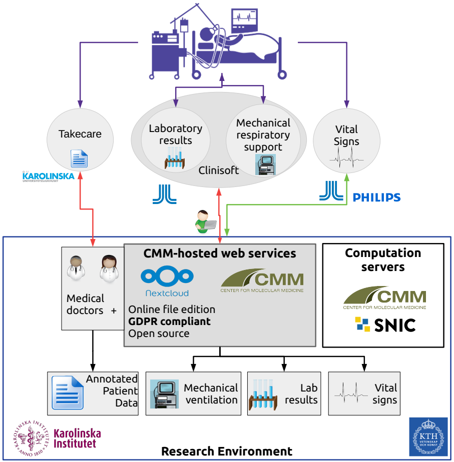
- Certain (unspecific) **patterns** are visible on bed-side monitors, e.g.
  - Drop in oxygen saturation
  - Drop in heart rate
  - Apnea
- Sepsis detection using bed-side monitoring is the way forward, because it can be done **continuously** and **non-invasively**.





Methods

Data collection

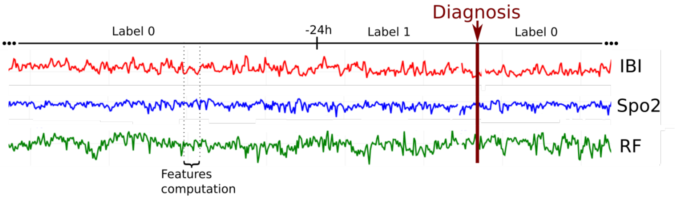


Annotations

- Manual annotation of raw text data
- $\approx$ 250 categorized clinical events

Vital signs

- 3 dimensional time series: SpO_2, IBI, RF.
-



Processing

- **Given** multi-dimensional series $\underline{\boldsymbol{x}}^{(k)} = \left(\boldsymbol{x}_1^{(k)}, \cdots, \boldsymbol{x}_{T_k}^{(k)}\right)$ and binary labels $y_t^{(k)} \in \{0, 1\}$.
- **Segment** the series into overlapping 55 minutes frames.
- **Compute features** developed to quantify known cardio-vascular behaviors, e.g. [4] and [5], sex, birth weight, weight measurement, age.
- **Resulting** in $\underline{\boldsymbol{z}}^{(k)} = \left(\boldsymbol{z}_t^{(k)}\right)_{t=1}^{T_k}$, where $\boldsymbol{z}_t^{(k)} \in \mathbb{R}^{24}$, and binary labels $y_t^{(k)}$.

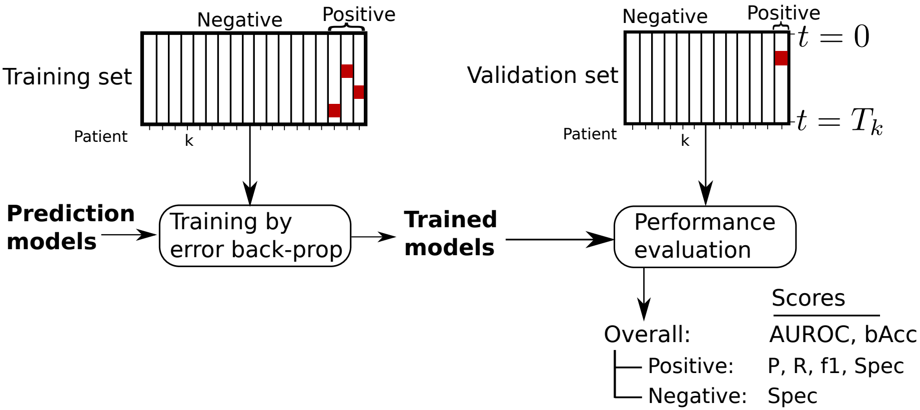
Overall

	# of patients	Average # of samples per patient	# of samples	
Patients			**Total**	**Prevalence**
Positive	10	2 099 (1 280)	20 992	2.86 %
Negative	108	1 053 (952)	113 676	0 %
Overall	118	1 141 (1 027)	134 668	0.48 %

- Birth weight: 927 ± 282g (VLBW)
- Sex: 44% male (52) and 56% female (66)

Methods

Cross-validation



Predictors: RNN

Simple representation of time-dependency

$$\mathbf{h}_t = \mathbf{g}(\mathbf{z}_t, \mathbf{h}_{t-1}) = \tanh(\mathrm{aff}(\mathbf{z}_t) + \mathrm{aff}(\mathbf{h}_{t-1}))$$
$$\hat{y}_t = f(\mathbf{h}_t) = \mathrm{sigmoid}(\mathrm{aff}(\mathbf{h}_t))$$

LSTM

More complex mechanism

$$(\mathbf{h}_t, \mathbf{c}_t) = \mathbf{g}'(\mathbf{z}_t, \mathbf{h}_{t-1}, \mathbf{c}_{t-1})$$
$$\hat{y}_t = f'(\mathbf{h}_t)$$

Differences

- RNN back-propagation through time: vanishing/exploding gradient
- LSTM stabilizes back-propagation through time
- Better at retaining important information with forget gates

Experiments

- The forward pass is done on sub-sequences of feature vectors of length $T = 50$ ($\approx 24h$).
- The RNNs are used in a many-to-one setup.
- Weighted cross-validation loss

Predictors: RNN

Simple representation of time-dependency

$$\mathbf{h}_t = \mathbf{g}(\mathbf{z}_t, \mathbf{h}_{t-1}) = \tanh(\mathrm{aff}(\mathbf{z}_t) + \mathrm{aff}(\mathbf{h}_{t-1}))$$
$$\hat{y}_t = f(\mathbf{h}_t) = \mathrm{sigmoid}(\mathrm{aff}(\mathbf{h}_t))$$

LSTM

Better back-propagation through time:

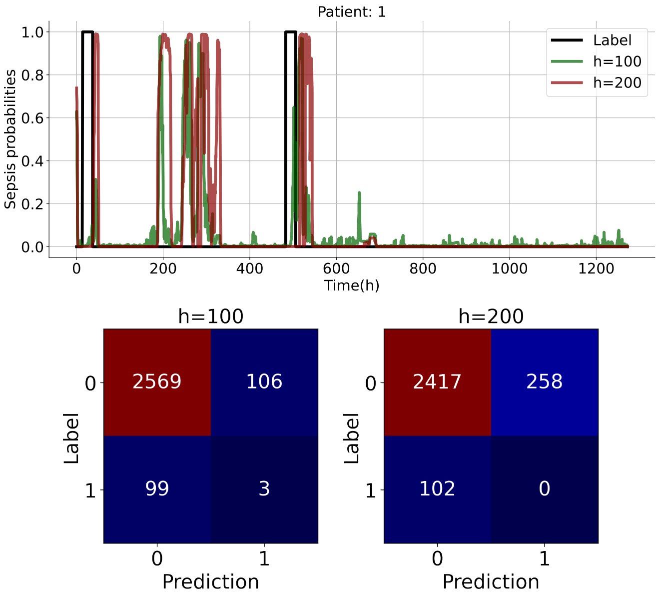
$$(\mathbf{h}_t, \mathbf{c}_t) = \mathbf{g}'(\mathbf{z}_t, \mathbf{h}_{t-1}, \mathbf{c}_{t-1})$$
$$\hat{y}_t = f'(\mathbf{h}_t)$$

Predictions scores

Positive patients		Neg.	Overall	
F1	**Spec.**	**Spec.**	**AUROC**	**bAcc**
Logistic regression				
0.11 (0.07)	0.73 (0.28)	0.77 (0.04)	0.81 (0.15)	0.60 (0.23)
Vanilla RNN				
0.07 (0.07)	0.58 (0.24)	0.70 (0.11)	0.71 (0.18)	0.62 (0.18)
LSTM				
0.18 (0.31)	**0.87** (0.17)	**0.98** (0.03)	0.81 (0.18)	0.66 (0.2)

Results

Example



Conclusions

Future perspectives

Models

+ Using time correlation in LSTM models helps reduce false positive rate:
    - Interpretability can be introduced with attention layers.

Cohort

+ Our scores are obtained in a realistic setting (as opposed to case control)
- Although realistic, the cohort is small, no external test is performed
- Clinical events are grouped, but could be studied separately

Data

+ Features capture useful information
- Raw signals could help further improve performances (so far negative results)

Thank you !

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