What is Sepsis and Septic Shock?

- **Sepsis** is a systemic inflammatory response to infection
- 11th leading cause of death in 2010
- Estimated $14.6 billion spent on sepsis in 2008
- **Septic shock** (sepsis-induced hypotension) has a mortality rate of 45.7%
IN-HOSPITAL DETECTION

Demographic Information
Vital Signs
Labs
Clinical Notes
Patient Representation
Predictive Model
MISSING DATA PROBLEM

• Clinical studies must deal with large amounts of missing data

• Measurements are noisy and irregularly sampled

• Highly accurate measurements require invasive techniques (may not be medically necessary)
**Typical Approach**

- Ignore subjects with missing observations
- Ignore features without complete data
- Result: Highly curated datasets with limited features and small samples
OUR SEPTIC SHOCK MODEL

Problem: Given a patient has sepsis, can we predict complications at least one hour prior to onset of septic shock?

- Generalization to patients with partially missing observations
- Simple and accessible approaches
- Focus on commonly observed, non-invasive measurements
CLINICAL FEATURES

• Summary statistics (last measurement, min, mean, and max) in 8 hour window
  • Cardiac: non-invasive blood pressure, heart rate, pulse pressure
  • Other: respiratory rate, SpO$_2$, temperature
• Last measurement only (less observations)
  • White blood cell count
  • Index scores: SOFA, SAPS-I, Shock index
IMPUTATION APPROACHES

- Mean / median imputation
- Matrix factorization techniques
  - Singular value based imputation (SVD)
  - Probabilistic principal component analysis (PPCA)
- K-nearest neighbors (KNN)
Matrix factorization and neighborhood techniques have parameter to control resolution or locality of imputation.

Evaluation metric typically involves randomly removing observations and comparing fit using root mean square error (RMSE) or mean absolute error (MAE).

RMSE / MAE may not necessarily translate to improved predictive performance.
PERFORMANCE-ORIENTED IMPUTATION (POI)

Data

Random splits → Impute → Build & Evaluate

Imputation parameter selection

Data → Impute → Construct Prediction Model

Optimal k
MIMIC-II DATABASE

• Extensive, publicly available ICU data resource

• Data between 2001 and 2007 from Boston’s Beth Israel Deaconess Medical Center ICUs

• Over 40,000 ICU stays from 30,000+ patients

• Clinical records with physiological measures, medication records, laboratory tests, free-form text notes, etc.
**IMPORTANCE OF IMPUTATION**

Less than 22% of the 1,353 patients have complete data.

<table>
<thead>
<tr>
<th>Feature</th>
<th>30 mins</th>
<th>60 mins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory rate</td>
<td>0.67%</td>
<td>0.68%</td>
</tr>
<tr>
<td>Temperature</td>
<td>1.70%</td>
<td>2.05%</td>
</tr>
<tr>
<td>White blood cells</td>
<td>15.30%</td>
<td>14.69%</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>23.28%</td>
<td>23.44%</td>
</tr>
</tbody>
</table>

Non-invasive BP is not always available.
## Differences in Population

<table>
<thead>
<tr>
<th>Time</th>
<th>Missing patients</th>
<th>Complete only</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Sepsis (only)</td>
<td>Shock</td>
</tr>
<tr>
<td>30 mins</td>
<td>749</td>
<td>79</td>
<td>199</td>
</tr>
<tr>
<td>60 mins</td>
<td>723</td>
<td>79</td>
<td>196</td>
</tr>
<tr>
<td>90 mins</td>
<td>705</td>
<td>79</td>
<td>196</td>
</tr>
<tr>
<td>120 mins</td>
<td>685</td>
<td>74</td>
<td>193</td>
</tr>
</tbody>
</table>

Statistically significantly higher ratio of shock patients if you ignore patients with missing data.
# Predictive Power of Mean Imputed Model

<table>
<thead>
<tr>
<th>Train Data</th>
<th>Test Data</th>
<th>30 minutes before (AUC)</th>
<th>60 minutes before (AUC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete</td>
<td>Complete</td>
<td>0.796±0.065</td>
<td>0.777±0.050</td>
</tr>
<tr>
<td>Complete</td>
<td>Imputed</td>
<td>0.815±0.033</td>
<td>0.800±0.053</td>
</tr>
<tr>
<td>Imputed</td>
<td>Imputed</td>
<td>0.834±0.025</td>
<td>0.829±0.030</td>
</tr>
<tr>
<td>Imputed</td>
<td>Complete</td>
<td>0.839±0.044</td>
<td>0.828±0.047</td>
</tr>
</tbody>
</table>

Model generalizes to broader population with slightly better predictive performance
COMPARISON OF SELECTION CRITERIA (SVM)

POI is generally better for AUC + F-measure
Comparing Imputation Approaches (SVD + LogR)

POI outperforms RMSE, but mean and MAE are generally the best
Comparing Imputation Approaches (SVD + LogR)

RMSE favors the simplest model (k=1), MAE favors most complex (k=25), POI lies in between the two.
### Comparing Imputation Approaches (Feature Rank)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Mean</th>
<th>AUC</th>
<th>F1</th>
<th>RMSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP</td>
<td>1.50</td>
<td>1.70</td>
<td>1.70</td>
<td>2.40</td>
</tr>
<tr>
<td>SpO2</td>
<td>2.22</td>
<td>3.00</td>
<td>3.22</td>
<td>2.56</td>
</tr>
<tr>
<td>Shock Index</td>
<td>4.40</td>
<td>4.40</td>
<td>4.60</td>
<td>3.30</td>
</tr>
<tr>
<td>Temp</td>
<td>5.00</td>
<td>5.00</td>
<td>7.50</td>
<td></td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>11.00</td>
<td>8.00</td>
<td>8.25</td>
<td>5.00</td>
</tr>
</tbody>
</table>

Selection criteria influences feature ranking within the same imputation method.
CONCLUSION

• Generalizes to all ICU patients

• Focuses on commonly observed, non-invasive clinical measurements

• Uses simple and accessible approaches for missing data problem