Smart Medical Information Technology for Healthcare

# Use Case ASIC
# Report AG 2

Düsseldorf, 5. Februar 2020

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MEDIZIN INFORMATIK INITIATIVE

# Agenda

- Heterogenous Patient Population Discrimination
- Diagnostic Expert Advisor: Framework Demonstration
- Virtual Patient: Warwick Model Demonstration
- Bayer: Current Status / Modelling Approach



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# Heterogenous patient population discrimination

## Approach:

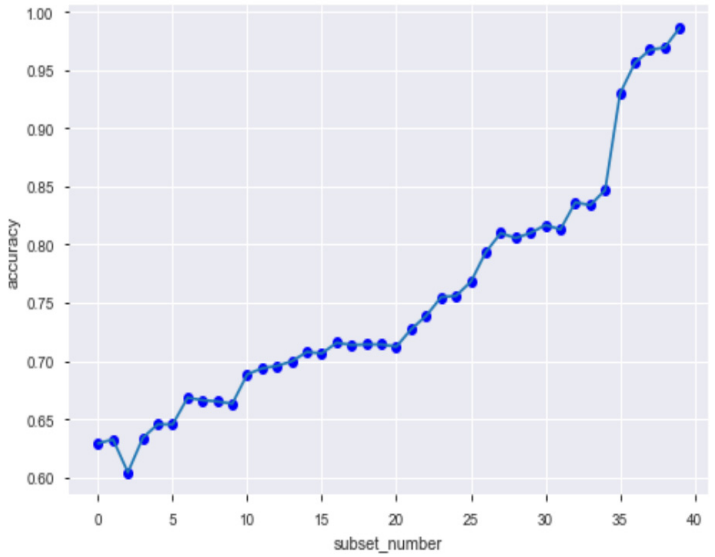
- Multi-hospital ICU patient population data (physiological measurements)
- Find common data variables and perform feature engineering
- Machine learning classifier : For a randomly drawn patient from the populations, predict the hospital from discriminative* feature subset
- Non-discriminative** feature subsets :: used in data merging
- Workflow and software tool developed -> ready to use

* important for class prediction, accuracy > 80%
** accuracy ~ 50%

# Multivariate classification

| | feature_names | feat_importance |
|---|---|---|
| 30 | SaO2_max | 0.212480 |
| 31 | SaO2_mean | 0.173673 |
| 34 | SaO2_std | 0.149747 |
| 33 | SaO2_min | 0.093184 |
| 32 | SaO2_median | 0.050383 |
| 12 | FiO2_median | 0.048584 |
| 36 | SpO2_mean | 0.041322 |
| 13 | FiO2_min | 0.036739 |
| 39 | SpO2_std | 0.026270 |
| 38 | SpO2_min | 0.023798 |
| 37 | SpO2_median | 0.017258 |
| 35 | SpO2_max | 0.013084 |
| 23 | MAP_min | 0.011350 |
| 11 | FiO2_mean | 0.009375 |
| 5 | DAP_max | 0.008738 |
| 14 | FiO2_std | 0.008521 |
| 20 | MAP_max | 0.008348 |
| 28 | SAP_min | 0.006904 |
| 25 | SAP_max | 0.006603 |
| 1 | AF_mean | 0.006585 |
| 2 | AF_median | 0.004754 |
| 26 | SAP_mean | 0.003616 |
| 9 | DAP_std | 0.003609 |
| 27 | SAP_median | 0.003220 |
| 29 | SAP_std | 0.003011 |
| 8 | DAP_min | 0.002502 |
| 21 | MAP_mean | 0.002420 |
| 18 | HF_min | 0.002397 |
| 19 | HF_std | 0.002386 |

classification accuracy increases by
adding more discriminitive features




Data: 17907 patients, 8 variables, univariate features
Classifier: Emsemble classifier*(RandomForest-based)
Train-Test split: 70:30
Accuracy: 99.32%

* weighted combination of multiple different classifiers

# Multivariate classification

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*remove top discriminitive features and retrain*

Data: 17907 patients, univariate statistics
Classifier: Emsemble classifier*(RandomForest-based)
Train-Test split: 70:30
Accuracy: reduces to 79%

* weighted combination of multiple different classifiers

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*remove features and retrain*

Data: 17907 patients, univariate statistics
Classifier: Emsemble classifier*(RandomForest-based)
Train-Test split: 70:30
**Accuracy: reduces to 54%**

* weighted combination of multiple different classifiers

# Multivariate classification :: Data-pooling

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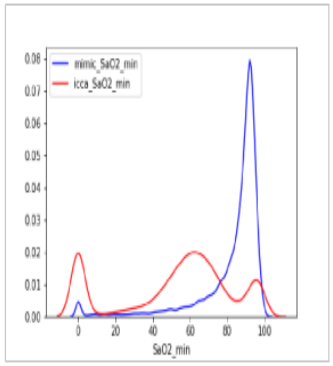
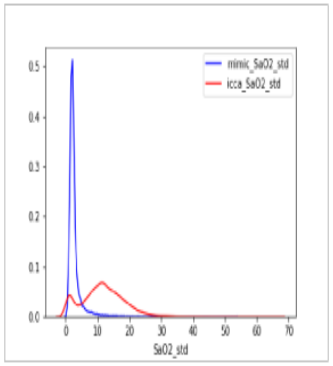
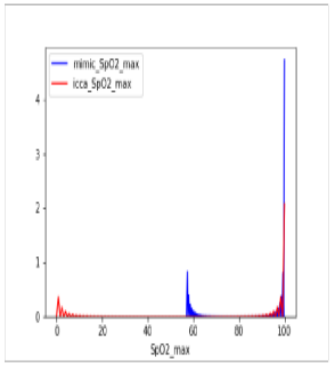
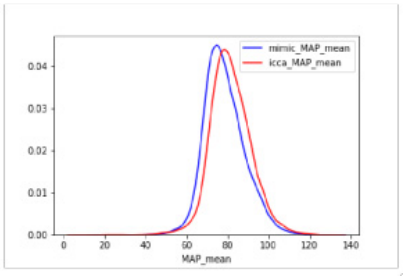
cannot be pooled (accuracy > 80%)

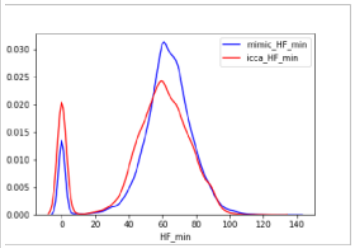


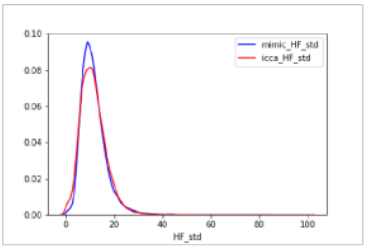




can be pooled (accuracy ~ 50%)



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# Diagnostic Expert Advisor

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- Until Now: Analyzing data and finding strategies
- Now: Framework for executing those strategies
  - Prototype for final DEA (Architecture, Interfaces, …)
  - Automated performance evaluation and validation
  - Case-by-Case exploration and analysis
- Next Step: Optimization of Machine Learning Machinery
  - Fine-tune and adapt pattern recognition strategies
  - Optimize parameters
  - Calibrate ensemble for individual hospitals



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# Diagnostic Expert Advisor: Architecture

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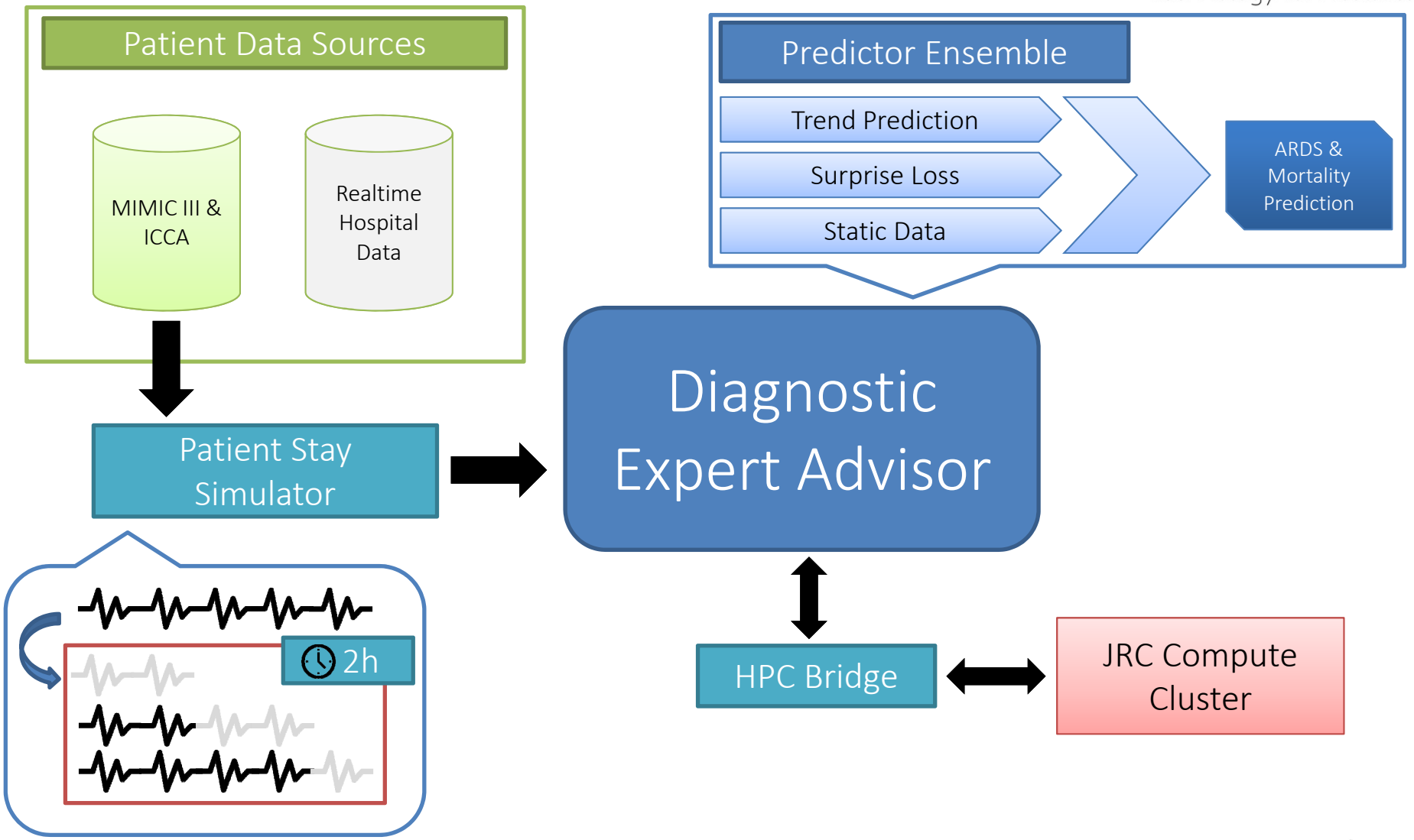





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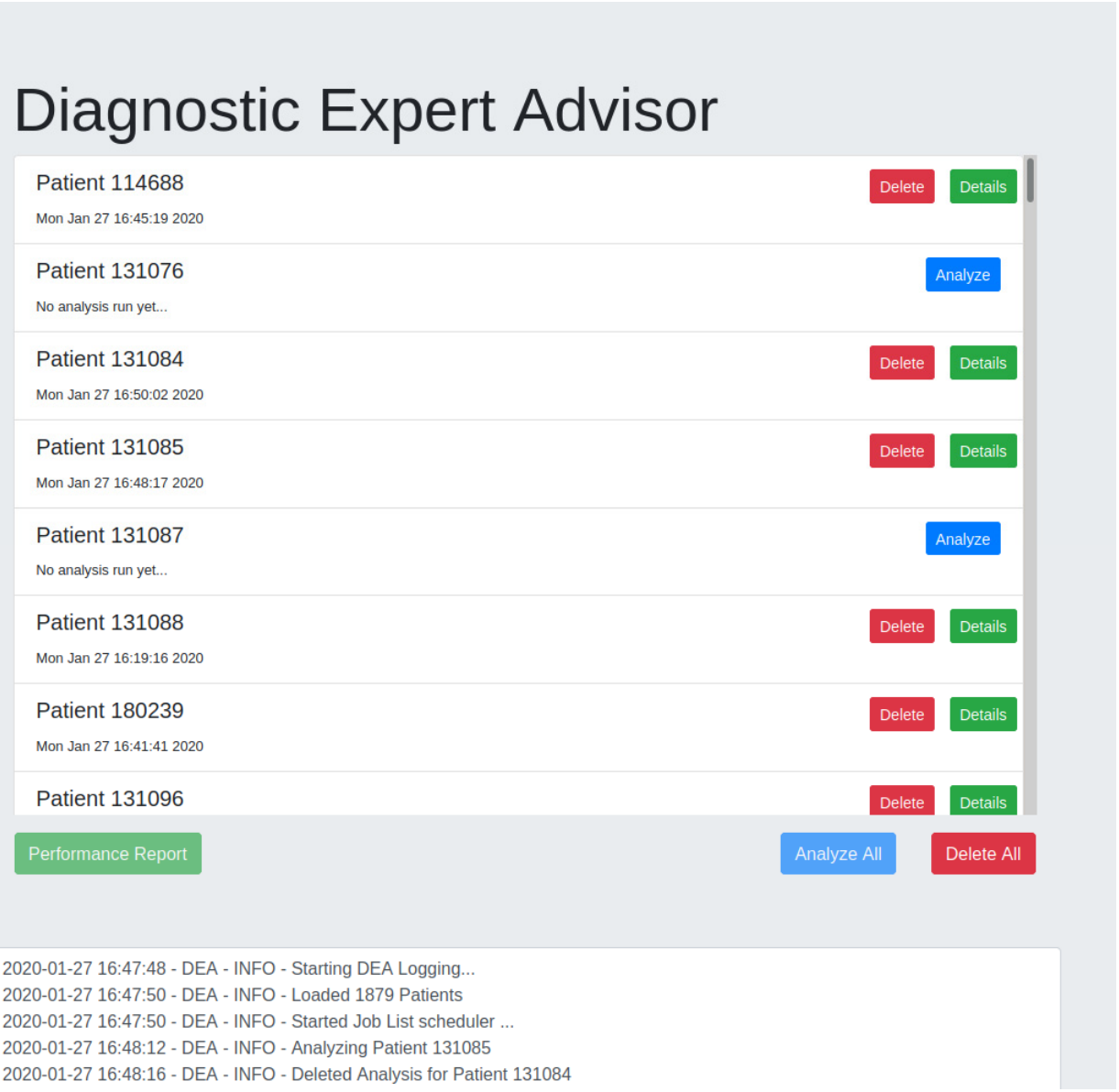


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# Diagnostic Expert Advisor

## Detailed Report on Simulated Patient 131254

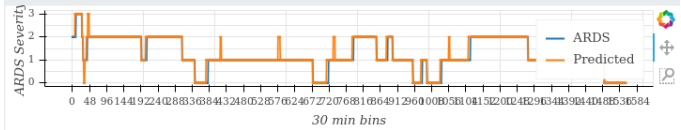
**ARDS**

Correct Alarm: 18 | Correct Severe Alarm: 1 | Longest Correct Future Prediction: 6

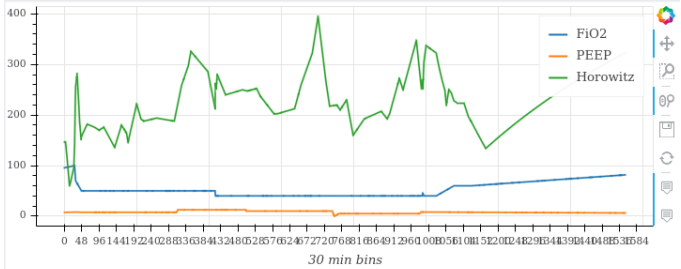
Late Alarm: 4 | Late Severe Alarm: 0 | Longest Delay for Alarm: 0

False Alarms: 0 | Missed ARDS: 0 | Missed Severe ARDS: 0

### Results




### Horowitz

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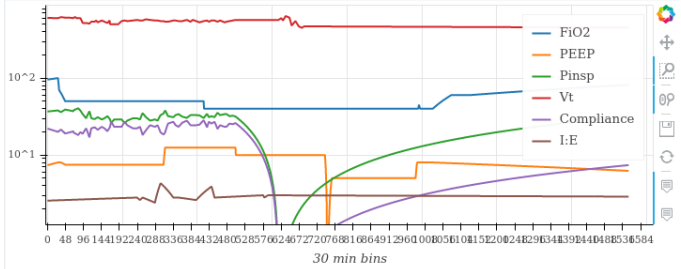


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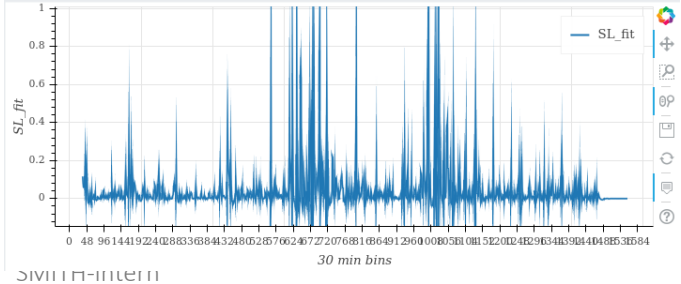


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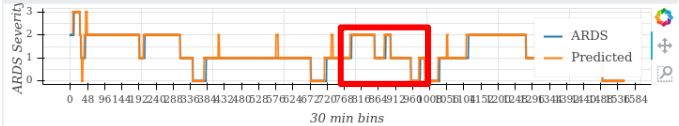


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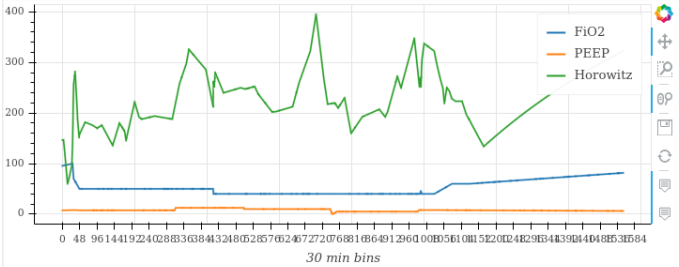


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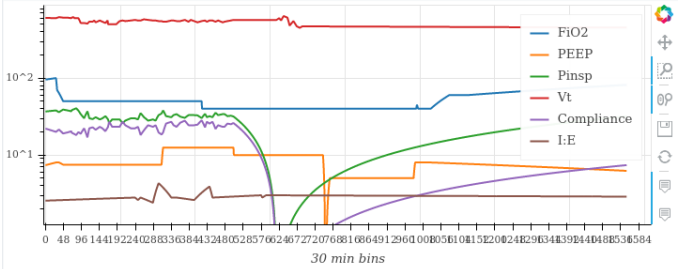


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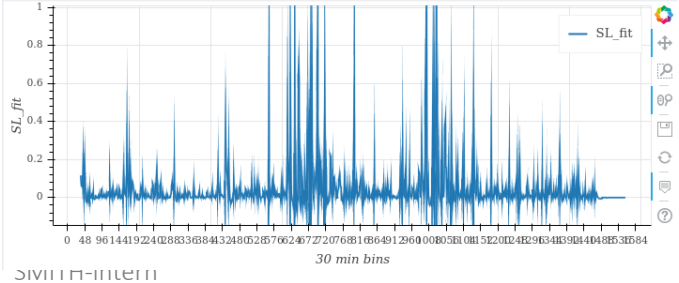


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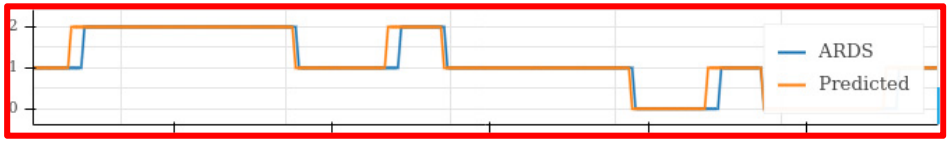




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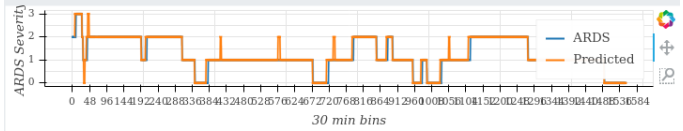


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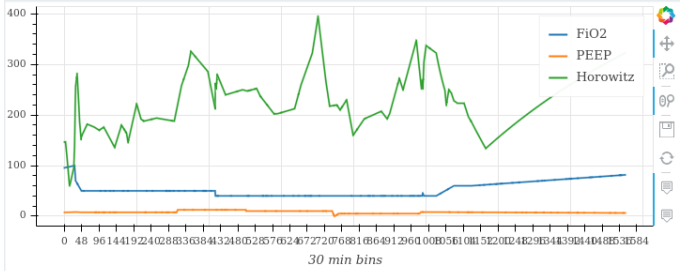


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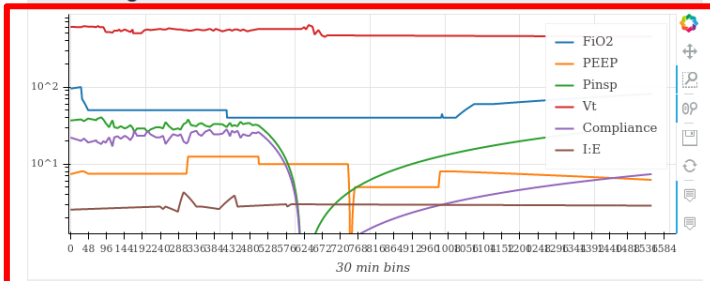


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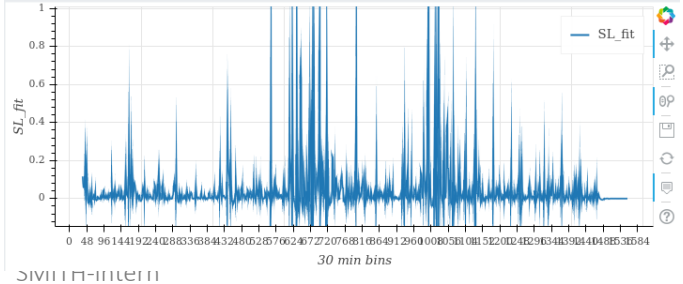


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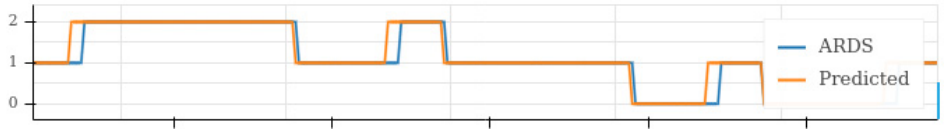


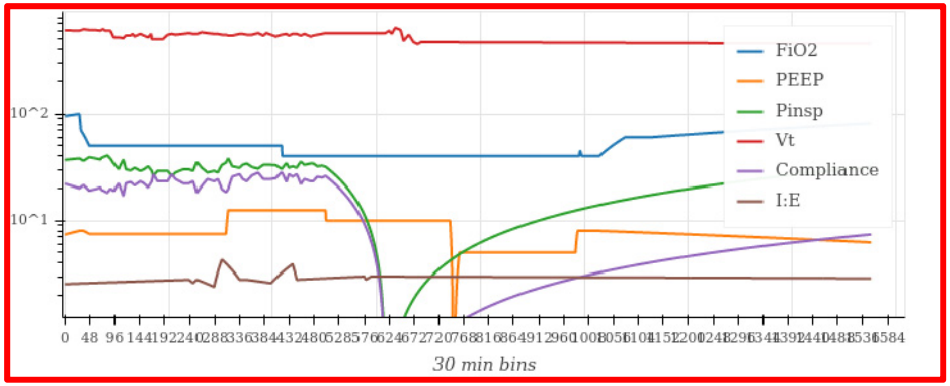




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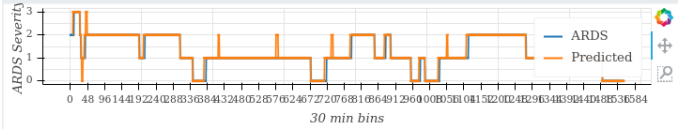


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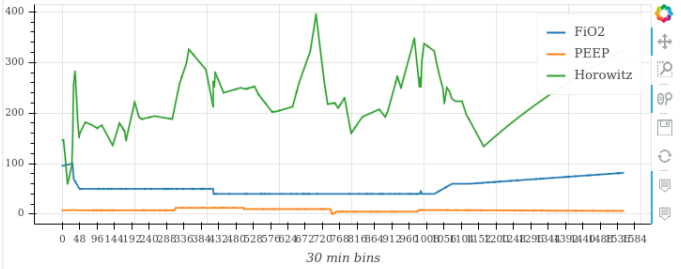


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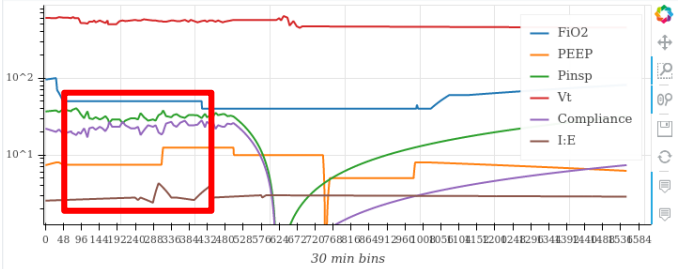


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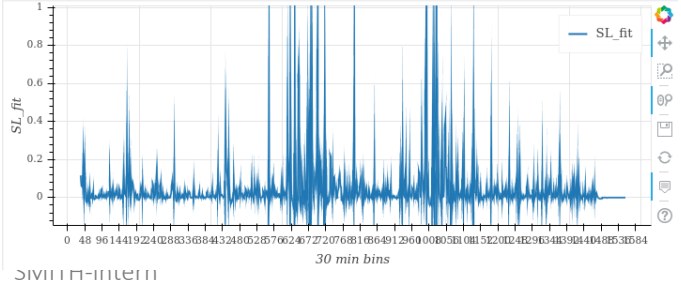


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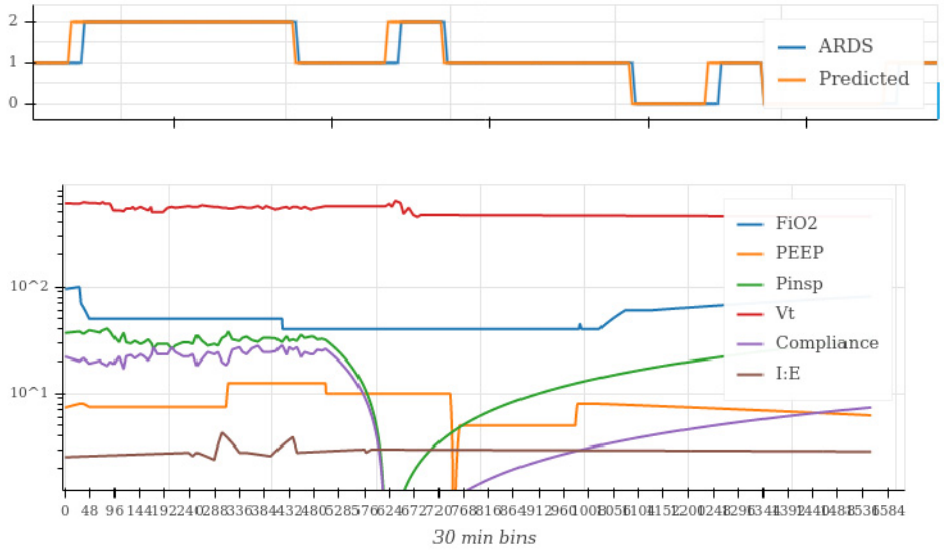


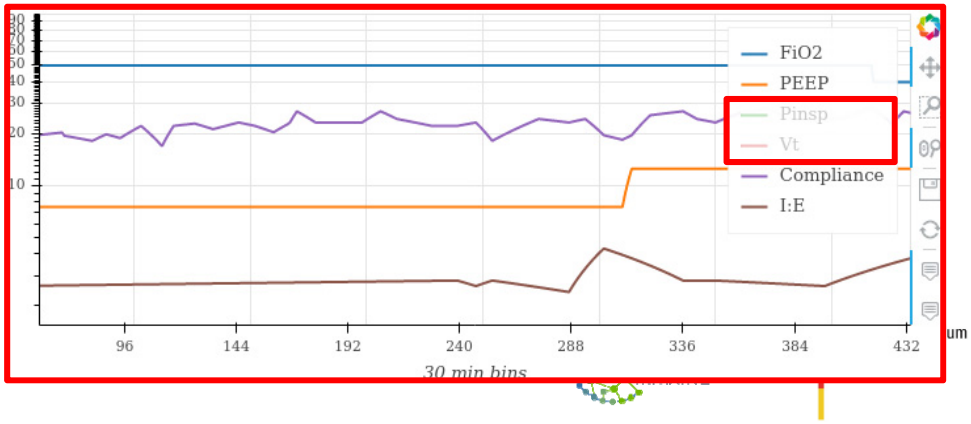

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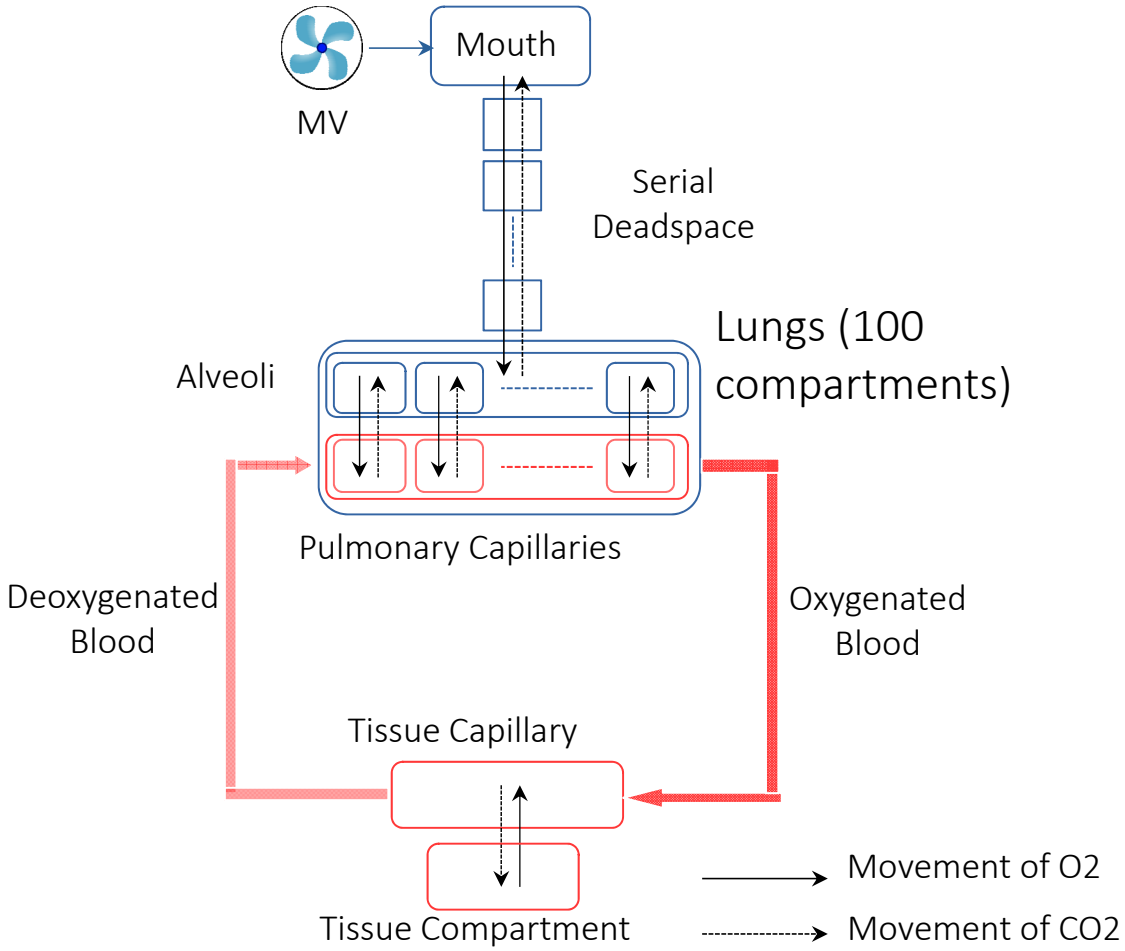
# Warwick Model: Structure




## Components:

1) Ventilator – gradient between lungs and the ventilator
2) Series Deadspace – movement of gases from mouth to the alveolar units and back
3) Alveolar Capillary Interface – equilibration
4) Arterial and Venous Blood – calculation of the transfer of gases
5) Tissue and Tissue Capillary Interface

## Simulation Flow:

1) Inhalation/Exhalation
2) Equilibration between alveoli and capillary compartments
   (partial pressures differ by less than 1%)
3) Arterial blood gas pressures calculation
4) Equilibration in single tissue compartment
   (peripheral tissue equilibration)
5) Venous blood gas pressures calculation

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# Warwick Model: Input Variables

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**Input Variables**

| Label in the model | Full name | Dimension | UOM | In the cMDR ASIC |
|---|---|---|---|---|
| anatShunt | Anatomical Shunt considered, fraction | 1 | 1 | No |
| chPressure | constant pressure mode | 1 | 1 | Yes (always 1) |
| CO | Cardiac Output | 1 | ml | HZV (kontinuierlich) |
| ColVol | Constant collapsing volume | 1 | ml | No, preset constant |
| FatmO2 | Atmospheric concentration of O2 | 1 | 1 | FiO2 |
| Hb | Haemoglobin | 1 | g/ml | Hämoglobin |
| IE | Inhalation:Exhalation ratio | 1 | 1 | I:E |
| Ncomp | Number of alveolar compartments | 1 | 1 | 100 |
| PEEP | Positive End Expiratory Pressure | 1 | cmH2O | PEEP |
| P_ext | External pressure (structural forces of the intact lung that hold alveoli open) | Ncomp | cmH2O | No |
| Rcomp | Flow resistance (Bronchial resistance) | Ncomp | kPa per ml/min | No |
| RQ | Respiratory Quotient | 1 | 1 | No |
| run_RM | to run/not run maneuveres | 1 | 1 | Preset constant |
| run_time | Time of simulation | 1 | min | Preset constant |
| scPressure | Ventilator Pressure | 1 | cmH2O | PEEP+deltaP |
| ST_alv | inherent stiffness of the alveolus (used in the vtoplungs function) | Ncomp | 1 | No |
| Stick_time_rand | how sticky are thhe airways, is used in the cycle to exhale and then in the main sim | Ncomp | ms (?) | No |
| Temperature | Body Temperature | 1 | Degrees Celsius | Körperkerntemperatur |
| TOPcomp | Threshold Opening Pressure of a Compartment | Ncomp | cmH2O | No |
| VDphys | The volume of serial deadspace | 1 | ml | No |
| VentRate | Rate of Ventilator | 1 | 1 | AF |
| VO2 | Metabolic consumption O2 | 1 | ml/min | No |
| VRcomp | Pulmonary Vascular resistance | Ncomp | dynes*s*cm-5*min-1 | PVRI |
| Vtidal | Tidal Volume | 1 | ml | Vt |

Present in the ASIC Catalog of Items

Can be calculated/found in the literature

Cannot be measured/have to be estimated by fit to the data



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# Warwick Model: Output Variables

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## Output Variables

| Label in the model | Full name | Dimension | UOM | In the cMDR ASIC |
|---|---|---|---|---|
| DynComp_Store | Dynamic Compliance | 1 | | Compliance |
| Ptrachea_Store | Tracheal Pressure | 1 | | No |
| Pventilator_Store | Ventilator Pressure | 1 | | PEEP + Driving Pressure |
| SaO2_Store | Saturation of O2 | 1 | | SaO2 |
| Shunt_Store | Anatomical Shunt | 1 | | No |
| Vlungs_Store | Volume of lungs | 1 | | Vt |
| PaO2_Store | Arterial partial pressure of oxygen | 1 | | paO2 (ohne Temp-Korrektur) |
| PaCO2_Store | Arterial partial pressure of CO2 | 1 | | paCO2 (ohne Temp-Korrektur) |
| PvO2_Store | Venous partial pressure of oxygen | 1 | | Not in the CMDR, but can be found in the DB |
| PvCO2_Store | Venous partial pressure of CO2 | 1 | | Not in the CMDR, but can be found in the DB |
| pHa_Store | pH level of arterial blood | 1 | | pH arteriell |
| | | | | |
| Pcompmax_Store | end inspiratory alveolar pressure | Ncomp | | No |
| Pcompmin_Store | end exspiratory alveolar pressure | Ncomp | | No |
| Qcomp_Store | Pulmonary Blood Flow across the comp | Ncomp | | No |
| VQratio_Store | Ventilation/Perfusion ratio | Ncomp | | No |
| Vcomp_Store | Volume of individual alveolar compartments | Ncomp | | No |
| Vcompmax_Store | end inspiratory alveolar volumes | Ncomp | | No |
| Vcompmin_Store | end exspiratory alveolar volumes | Ncomp | | No |
| perfusion_Store | Perfusion per minute (changes every breath) | Ncomp | | No |
| ventilation_Store | Volume change per minute (changes every breath) | Ncomp | | No |

Present in the ASIC Catalog of Items

Can be calculated/found in the literature

Cannot be measured/have to be estimated by fit to the data



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# Warwick Model: Simulation of 2 Patients

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| | IE | CO | FiO2 | RQ | anatShunt | AF | VO2 | VDphys | Hb | Vtidal |
|---|---|---|---|---|---|---|---|---|---|---|
| Healthy | 0.330 | 5000 | 0.21 | 0.8 | 0.02 | 12.000 | 250.00 | 60 | 160 | 400 |
| ARDS | 0.276 | 11100 | 0.80 | 0.6 | 0.01 | 12.253 | 294.25 | 50 | 105 | 420 |

| | | Patient A | |
|---|---|---|---|
| Parameters obtained from data | Hb (g $dl^{-1}$) | 10.5 | |
| | CO (l $min^{-1}$) | 11.1 | |
| | $F_iO_2$ | 0.8 | |
| Parameters obtained through optimization | VR (b $min^{-1}$) | 12.25 | |
| | IE | 0.28 | |
| | RQ | 0.6 | |
| | $VO_2$ (ml $min^{-1}$) | 294.3 | |
| | % of compartments collapsed | 26 | |
| Parameters fixed for RM trials | $P_v$ (cm $H_2O$) | 15 | |
| | PEEP (cm $H_2O$) | 5 | |
| | | Data | Model |
| Results of fitting the model to the data | $PvO_2$ (mmHg) | 47.3 | 49.5 |
| | $PvCO_2$ (mmHg) | 44.4 | 46.2 |
| | Qs/Qt (%) | 28.6 | 31.8 |
| | $PaO_2$ (mmHg) | 153.7 | 149.9 |

Evaluation of lung recruitment maneuvers in acute respiratory distress syndrome using computer simulation Hardman *et.al. Critical Care* volume 19, Article number: 8 (2015)
ARDS patient from Nirmalan M, Willard T, Columb MO, Nightingale P. Effect of changes in arterial-mixed venous oxygen content difference (C(a-v)O2) on indices of pulmonary oxygen transfer in a model ARDS lung. Br J Anaesth. 2001;86:477–85.



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# Warwick Model: Simulation of 2 Patients

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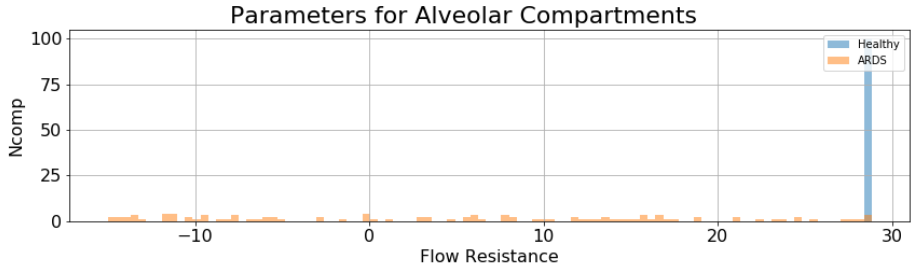


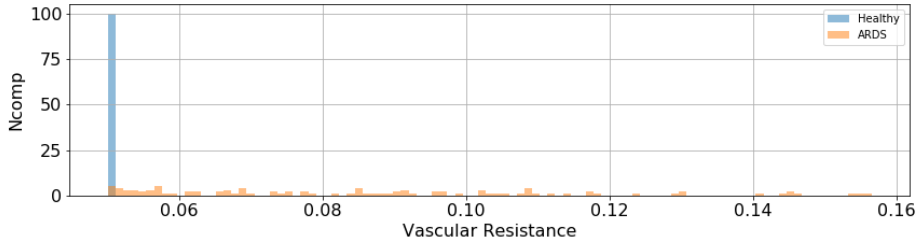


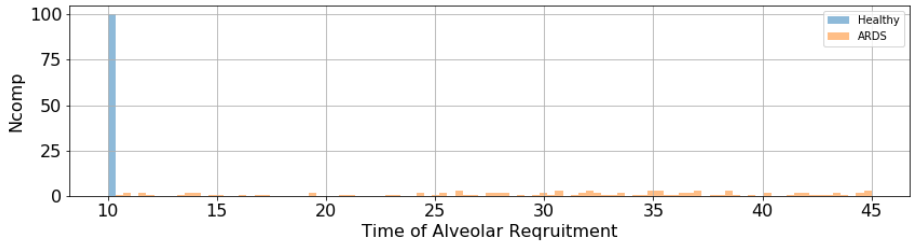


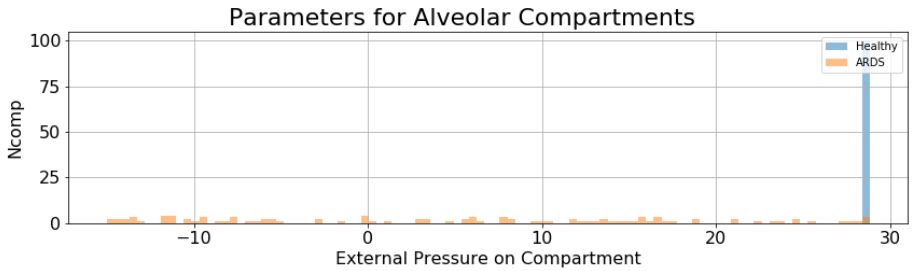


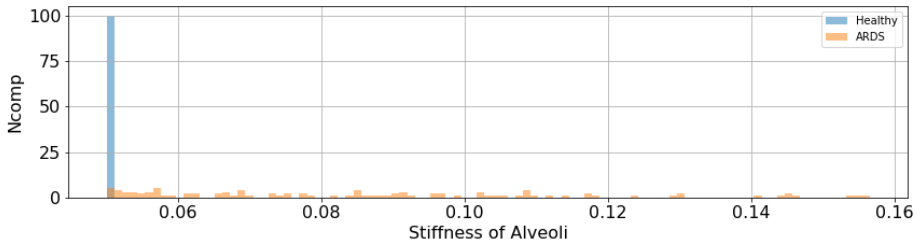


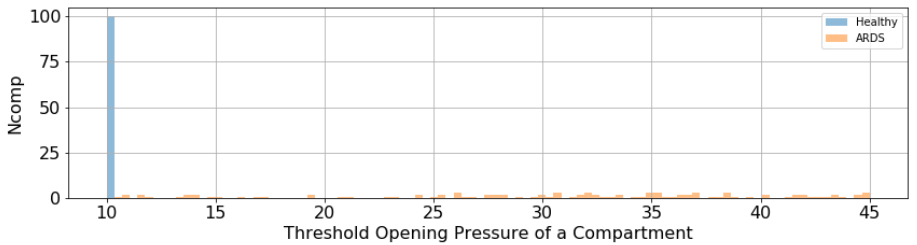


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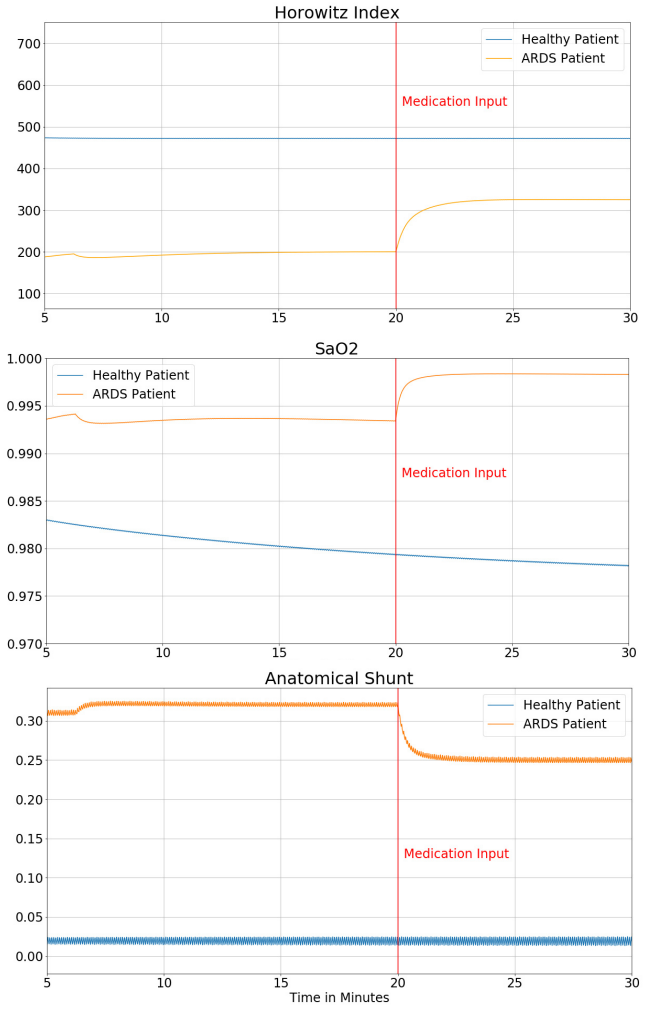
# Warwick Model: Simulation Outputs

- Outputs are produced for individual compartments or for the whole lung, depending on the parameter in question.
- Numerical results can be plotted to visualise changes in the patient's physiological condition.
- In case of input medications (in this case vasodilators) the effect is visible in the output parameters.







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# Agenda

- Heterogenous Patient Population Discrimination
- Diagnostic Expert Advisor: Framework Demonstration
- Virtual Patient: Warwick Model Demonstration
- **Bayer: Current Status / Modelling Approach**



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# Modelling approach

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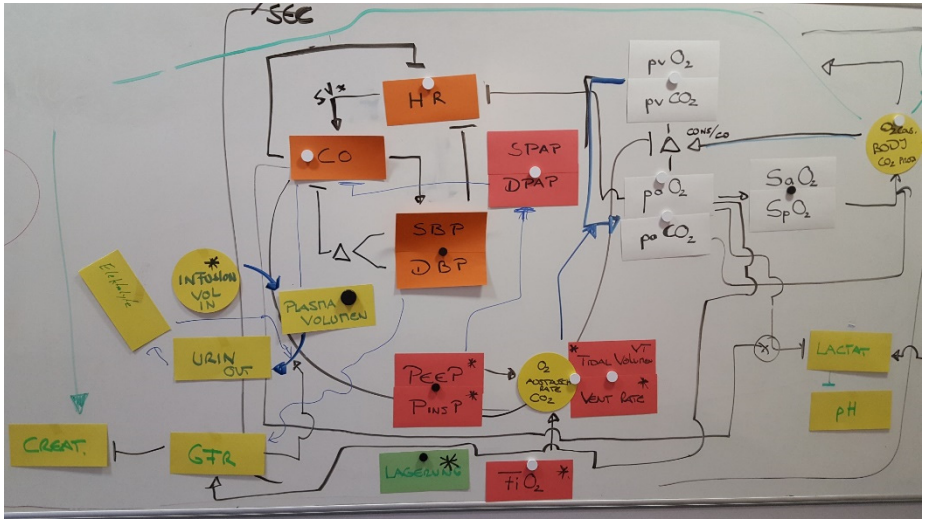
- Establish a basic mechanistic model based on
  - Cardiovacular system
  - Cardio-renal system
  - Pulmonary systems
- Use mass balances to integrate and combine different components of the overall model
- Mass balances
  - Plasma balance
  - Gas exchange
  - Acid-base balance
- Regulation







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# Modelling approach

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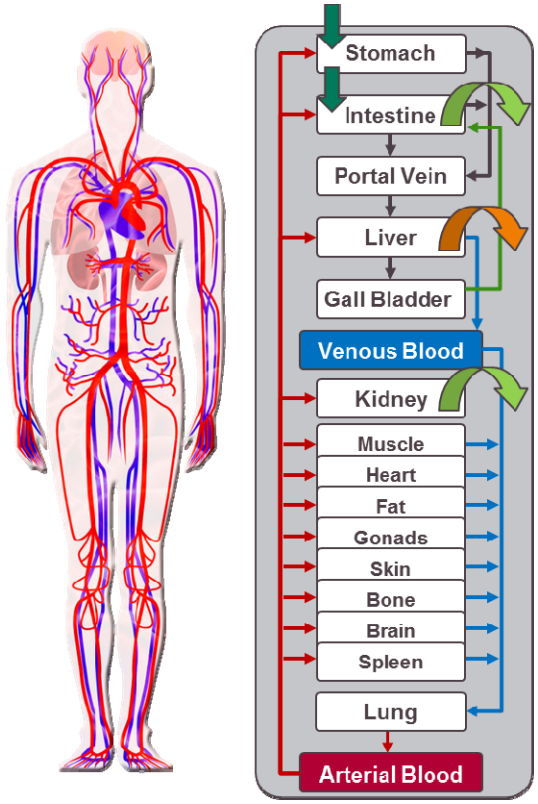
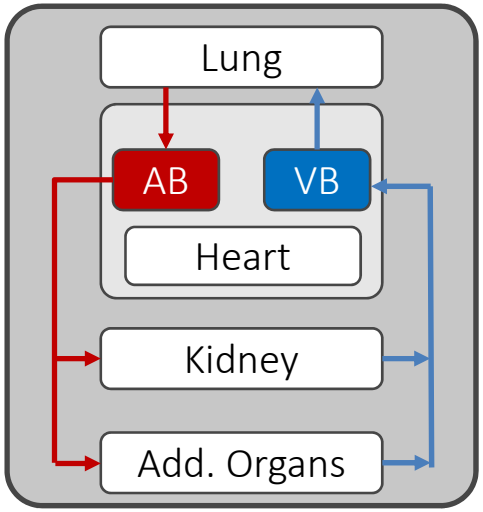
## Physiologically-based pharmacokinetic (PBPK) modelling




## Physiologically-motivated modelling







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# Example: Cardiovcasular system (Francheteau et al., 1993)

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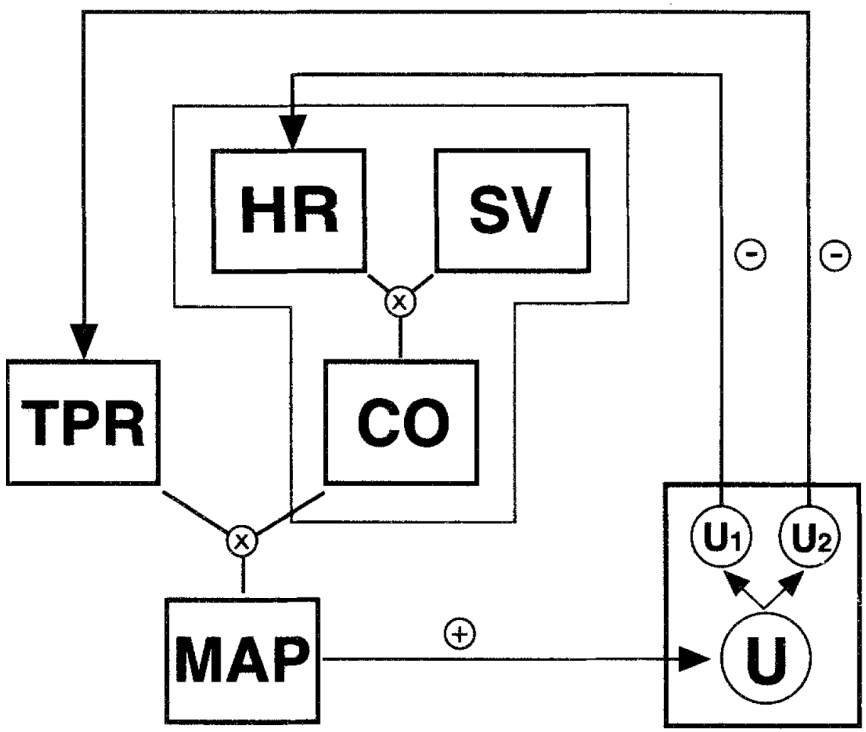





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# Modelling approach

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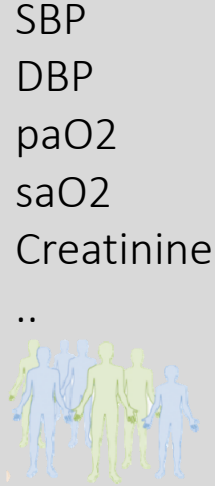
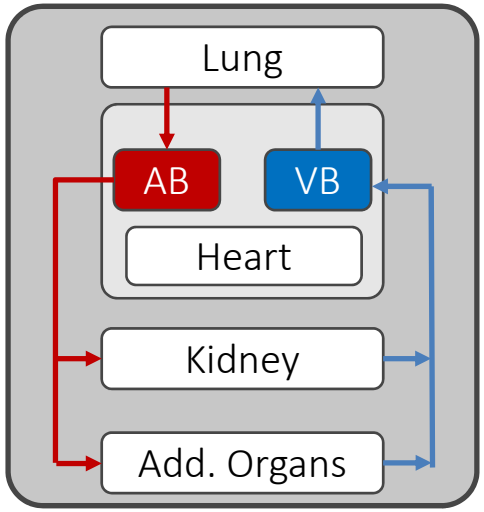
- HR
- SBP
- DBP
- paO2
- saO2
- Creatinine
- ..






- MAP
- Horovitz-Quotient
- …

Model development and training together with UK Aachen and FZ Jülich

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# Vielen Dank für Ihre Aufmerksamkeit!

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