Towards Developing Safety Assurance Cases for Learning-Enabled Medical Cyber-Physical Systems

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ML-enabled Medical CPS

Machine Learning (ML)

- In the estimation and prediction components
- To make data-driven decisions based on sensor or patient input and guide control actions

Control Algorithm
Safety of ML-enabled Medical CPS

Challenges

- ML component must handle
  - Intricacies of patient physiology
  - Uncertainties in the operational environment
  - Variability in patient profiles

- Mismatch between the training data and the real-world data
  - Erroneous, biased, or incomplete output predictions
Safety of ML-enabled Medical CPS

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Assurance Cases (AC)

Structured arguments, supported by evidence, to justify claims

- Literature on using AC for safety assurance
  - ML lifecycle is not dealt with
  - No concrete learning-enabled use cases
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Our paper presents detailed AC to assure the safety and effectiveness of a general framework of Artificial Pancreas Systems (APS), suitable for all types of APS.
Artificial Pancreas Systems (APS)

Commercially available APS have the same structure and behavior.
Contributions

- Preliminary results on developing a safety assurance case template for ML controllers in MCPS
  - Including patient profiles in its element descriptions.

- Detailed safety assurance case for APS that is supported by a thorough analysis of its ML model

- Defining properties based on the body’s metabolism and checking them against the ML prediction component using formal verification
Safety Assurance Case Template

- Using **assume/guarantee** reasoning

- Instantiating based on **individual patient** profiles or populations
Safety Assurance Case Template

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Assuming that the BG predictions are accurate, the insulin dosage management component is sufficiently safe and effective for treating patients.
Learning-enabled Controller Assurance Case for APS

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The ML glucose prediction component is sufficiently safe and effective.
Safety Assurance Case for the Glucose Prediction Component

C1-1 Description of the ML glucose prediction component

G1-2 The ML glucose prediction component is sufficiently safe and effective

S1-1 Argument over the development and deployment of the component

G2-1 The development of the ML glucose prediction model is sufficiently safe and effective

G2-2 The deployment of the ML glucose prediction component into APS is sufficiently safe and effective

C2-1 ML safety requirements, developed from system safety requirements, allocated to the ML glucose prediction model

S2-1 Argument over the ML safety and effectiveness requirements

G3-1 ML glucose prediction model satisfies the ML requirements

G3-2 ML requirements are a valid development of the APS requirements allocated to the glucose prediction component

C1-2 System safety requirements allocated to ML glucose prediction component
Safety Assurance Case for the Glucose Prediction Component

**C1-1** Description of the ML glucose prediction component

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**S2-2** Argument over the ML safety and effectiveness requirements

**G2-2** The deployment of the ML glucose prediction component into APS is sufficiently safe and effective

**C2-2** System safety requirements allocated to ML glucose prediction component

**G3-1** ML glucose prediction model satisfies the ML requirements

**C3-1** ML requirements are a valid development of the APS requirements allocated to the glucose prediction component
Safety Assurance Case for the Glucose Prediction Component

- **C1-1**: Description of the ML glucose prediction component
  - **G1-2**: The ML glucose prediction component is sufficiently safe and effective
    - **S1-1**: Argument over the development and deployment of the component
      - **G2-1**: The development of the ML glucose prediction model is sufficiently safe and effective
      - **G2-2**: The deployment of the ML glucose prediction model into APS is sufficiently safe and effective
    - **C1-2**: System safety requirements allocated to ML glucose prediction component
      - **C2-1**: ML safety requirements, developed from system safety requirements, allocated to the ML glucose prediction model
      - **S2-1**: Argument over the ML safety and effectiveness requirements
        - **G3-1**: ML glucose prediction model satisfies the ML requirements
        - **G3-2**: ML requirements are a valid development of the APS requirements allocated to the glucose prediction component
Safety Assurance Case for the Glucose Prediction Component

- **G1-2**: The ML glucose prediction component is sufficiently safe and effective
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# System Safety Requirements for ML Glucose Prediction Component

| Performance                                      |
|--------------------------------------------------|
| ML-RQ1                                           |
| Accurately predict the BG values $T$ minutes in the future |
| ML-RQ1.1                                         |
| BG’s rate of change has to be bound by established physiological norms |
| ML-RQ1.2                                         |
| Meal intake has a direct effect on the BG value   |
| ML-RQ1.3                                         |
| Exercise has an inverse effect on the BG value    |
| ML-RQ1.4                                         |
| Within $t$ minutes of a bolus, there should be an accompanying change in BG of more than $\alpha$ |
| ML-RQ1.5                                         |
| The glucose level starts to rise at a specific time after a meal’s onset |
| ML-RQ1.6                                         |
| There is a delay between the injection of insulin and the disposal of glucose |
| ML-RQ1.7                                         |
| The blood concentration of insulin reaches its maximum after a particular time |
| ML-RQ1.8                                         |
| Insulin has an inverse effect on the BG value     |

| Robustness                                       |
|--------------------------------------------------|
| ML-RQ2                                           |
| Perform as required for different patients of different ages/sexes |
| ML-RQ3                                           |
| Perform as required in the presence of external factors such as meals and exercises. |
Argument to Ensure the Sufficiency of the ML Model

C3-1
ML glucose prediction model
ML learning argument

G3-1
ML glucose prediction model satisfies the ML requirements

S3-1
Argument over satisfaction of ML safety requirements

G4-1
ML performance requirements are satisfied.
G4-2
ML Robustness requirements are satisfied.

C3-2
ML clinical / synthetic data
ML data argument
Argument to Ensure the Sufficiency of the ML Model

G3-1
ML glucose prediction model satisfies the ML requirements

C3-1
ML glucose prediction model
ML learning argument

P

S3-1
Argument over satisfaction of ML safety requirements

C3-2
ML clinical / synthetic data
ML data argument

P

G4-1
ML performance requirements are satisfied.

G4-2
ML Robustness requirements are satisfied.
Argument to Ensure the Sufficiency of the ML Data

G4-3
The ML clinical/synthetic data is sufficient.

S4-1
Argument over satisfaction of ML safety requirements

G5-1
ML data requirements are sufficient to ensure it is possible to develop a glucose prediction model that satisfies the ML requirements.

G5-2
ML data satisfies the ML data requirements.

C4-1
Development/verification/test dataset

C4-2
ML data requirements over the clinical/synthetic datasets
## Data Requirements in the ML Lifecycle of APS

### Relevance

| DR.R1 | Each data sample shall assume sensor positioning which is representative of that used on the patients |
|-------|-----------------------------------------------------------------------------------------------------------------|
| DR.R2 | The format of each data sample shall be representative of that captured using sensors deployed on the body       |
| DR.R3 | The type of each data sample (insulin) shall be representative of that used                                      |
| DR.R4 | Each data sample shall represent the diabetes type for which the system is developed                              |
| DR.R5 | Each data sample shall represent the sex, age, and ethnicity of the persons for which the system is developed       |

### Completeness

| DR.C1    | The data samples shall include examples with a sufficient range of meal carbs, different intraday meal intakes, and exercise |
|----------|---------------------------------------------------------------------------------------------------------------------------|
| DR.C2    | The data samples shall include examples with different sensor positioning                                                |
| DR.C3    | The data samples shall include examples with different ages and weights within the allowed ranges                           |
| DR.C4    | The data samples shall include patients with frequent hypoglycemic, hyperglycemic, and ketoacidosis problems               |
| DR.C5    | The data samples shall include the profile of patients during the day and night and illness                                 |
# Data Requirements in the ML Lifecycle of APS

## Accuracy

| Requirement | Description |
|-------------|-------------|
| DR.A1       | Each data sample shall assume sensor positioning which is representative of that used on the patients |
| DR.A2       | CGM sensor readings and pump infusions must be correctly recorded |
| DR.A3       | The total insulin delivered must be within the limit in each data sample |

## Balance

| Requirement | Description |
|-------------|-------------|
| DR.B1       | The datasets shall have a comparable number of samples for features |
ML Safety Requirements

- Feed Forward Neural Network for the BG prediction
- Defining requirements as the **constraints over the inputs and outputs** of the network

| ML-RQ1.1 | $\bigwedge_{i=0}^{T-2} |BG_{i+1}^{I} - BG_{i}^{I}| \leq \Delta \Rightarrow \bigwedge_{i=0}^{T-2} |BG_{j+1}^{O} - BG_{j}^{O}| \leq \Delta$ |
|-----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ML-RQ1.2 | $\bigvee_{i=0}^{T-1} M_{i}^{I} \geq \beta_{1} \Rightarrow \bigvee_{j=0}^{T-1} BG_{j}^{O} \geq \rho_{1}$ |
| ML-RQ1.3 | No available data |
| ML-RQ1.4 | $In_{0}^{I} \geq \beta_{2} \Rightarrow \bigvee_{i=1}^{T-1} |BG_{j}^{O} - BG_{0}^{O}| \geq \alpha$ |
| ML-RQ1.5 | $\bigvee_{i=0}^{T-1} M_{i}^{I} \geq \beta_{3} \Rightarrow \bigvee_{j=1}^{T-1} |BG_{j}^{O} - BG_{0}^{O}| > 0$ |
| ML-RQ1.6 | $In_{0}^{I} \geq \beta_{4} \Rightarrow 70 \leq BG_{T-1}^{O} \leq 180 \land \bigwedge_{j=0}^{T-2} (BG_{j}^{O} \leq 70 \lor BG_{j}^{O} \geq 180)$ |
| ML-RQ1.7 | $In_{0}^{I} \geq \beta_{4} \Rightarrow 70 \leq BG_{T-1}^{O} \leq 180 \land \bigwedge_{j=0}^{T-2} (BG_{j}^{O} \leq 70 \lor BG_{j}^{O} \geq 180)$ |
| ML-RQ1.8 | $\bigvee_{i=0}^{T-1} In_{i}^{I} \geq \beta_{5} \Rightarrow \bigvee_{j=0}^{T-1} BG_{j}^{O} \leq \rho_{2}$ |
ML Safety Requirements

- Checking the properties using DNNV framework and Nnenum ML verifier

| Property                  | Constraints                                                                 | Constraints Reached | Status          |
|---------------------------|------------------------------------------------------------------------------|---------------------|-----------------|
| ML-RQ1.1                  | $BG_i^T \in [130, 180], \text{In}_i^T \in \beta, M_i^T \in \beta, \Delta = 20$ | $(8,8,6)$           | Satisfied       |
| ML-RQ1.1                  | $BG_i^T \in [109, 180], \text{In}_i^T \in \beta, M_i^T \in \beta, \Delta = 20$ | $(128, 64, 8)$      | Satisfied       |
| ML-RQ1.8 ($in_i^{12} = 5 \Rightarrow BG_6^O \leq 230$) | $BG_i^T \in [212, 230], \text{In}_{i \neq 1} = \alpha, M_i^T = 0$ |                    | Violated        |
| ML-RQ1.8 ($in_i^{12} = 5 \Rightarrow BG_6^O \leq 230$) | $BG_i^T \in [211, 220], \text{In}_{i \neq 12} = \alpha, M_i^T = 0$ |                    | Satisfied       |
| ML-RQ1.8 ($in_i^{12} = 5 \Rightarrow BG_6^O \leq 230$) | $BG_i^T \in [212, 222], \text{In}_{i \neq 12} = \alpha, M_i^T = 0$ |                    | Satisfied       |
| ML-RQ1.2 ($m_{12} = 20 \Rightarrow BG_6^O > 210$) | $BG_i^T \in [180, 180], \text{In}_i = \alpha, M_i^{1 \neq 12} = 0$ |                    | Violated        |
| ML-RQ1.2 ($m_{12} = 20 \Rightarrow BG_6^O > 200$) | $BG_i^T \in [180, 180], \text{In}_i = \alpha, M_i^{1 \neq 12} = 0$ |                    | Satisfied       |
| ML-RQ1.2 ($m_{12} = 20 \Rightarrow BG_6^O > 200$) | $BG_i^T \in [180, 183], \text{In}_i = \alpha, M_i^{1 \neq 12} = 0$ |                    | Violated        |
Open Research Problems

- How can we trace the violation of a property back to its origin?
- How can we enforce the ML model to satisfy the properties while it develops over the data?
- How to develop adaptive safety AC for online learning models?
- How to develop quantitative measures to evaluate the confidence in a dynamic assurance case?
- How to build automated tool support for the development and review of safety AC for ML-enabled MCPS?
Thank you!
Dataset

Simglucose is a Python implementation of the FDA-approved UVA-Padova Simulator that employs a glucose-insulin meal model to simulate:

• 30 virtual patients (ten adolescents, ten adults, and ten children)

• All patients for 40 days and nights, where the BG and insulin values are provided every 5 minutes
• Each patient’s data includes 11,521 entries
First timestep 60 min $BG_1^I$

Second timestep 55 min $BG_2^I$

...  

Twelfth timestep 5 min $BG_{12}^I$

Dense layer 8 neurons

Dense layer 8 neurons

Dense layer 6 neurons

$BG_1^O$ 5 min First timestep

$BG_2^O$ 10 min Second timestep

$BG_3^O$ 15 min

$BG_4^O$ 20 min...

$BG_5^O$ 25 min

$BG_6^O$ 30 min Sixth timestep
# Requirements for Learning-enabled APS Controller

| Requirement | Description |
|-------------|-------------|
| RQ.C.1 | Accurately calculate dose of basal and bolus insulin |
| RQ.C.1.1 | Determine the output every T minutes (e.g., T=5 in MiniMed) |
| RQ.C.1.2 | Stop dosing if a maximum amount has been delivered by the pump |
| RQ.C.1.3 | Suspend dosing if the actual or predicted CGM readings fall below a threshold |
| RQ.C.1.4 | Interrupt in a safe way if trustworthy control is not guaranteed |
| RQ.C.1.5 | BG should not remain below 10th-percentile threshold for more than α1 minutes |
| RQ.C.1.6 | BG should not remain above 90th-percentile threshold for more than α2 minutes following a bolus injection |
| RQ.C.1.7 | BG should not remain above 90th-percentile threshold for more than α3 minutes |
| RQ.C.1.8 | The BG value is always greater than 70 and less than 180 |
| RQ.C.1.9 | The controller infuses additional insulin while the blood glucose level is below a target level |
| RQ.C.1.10 | The morning wake up blood glucose level can not exceed β |
The properties checked on the FFNN of the glucose prediction. The third and forth columns indicate whether the property is satisfied over networks with 8,8,6 and 128,64,8 neurons. We use $BG_i$, $In_i$, and $M_i$ to denote BG, insulin, and meal intake, where $i \in [1, 12]$, $\alpha = 0.006525$, and $\beta = [0, 1]$. The superscript $i$ indicates the input and $O$ indicates the output. * denotes that the property was satisfied using another verifier (Marabou) as Nenum raised error, and † shows that the property was satisfied after 16 days (using Marabou). The verification time for other requirements was fast enough.

| Property | Constraints | (8,8,6) | (128,64,8) |
|----------|-------------|---------|------------|
| ML-RQ1.1 | $BG_i^t \in [130, 180], In_i^t \in \beta, M_i^t \in \beta, \Delta = 20$ | Satisfied | Nenum Error* |
| ML-RQ1.1 | $BG_i^t \in [109, 180], In_i^t \in \beta, M_i^t \in \beta, \Delta = 20$ | Satisfied | Nenum Error † |
| ML-RQ1.8 ($In_1^t = 5 \Rightarrow BG_6^O \leq 230$) | $BG_i^t \in [212, 230], In_i^t \neq 1 = \alpha, M_i^t = 0$ | Violated | Satisfied |
| ML-RQ1.8 ($In_1^{12} = 5 \Rightarrow BG_6^O \leq 230$) | $BG_i^t \in [211, 220], In_i^t \neq 12 = \alpha, M_i^t = 0$ | Satisfied | Satisfied |
| ML-RQ1.8 ($In_1^{12} = 5 \Rightarrow BG_6^O \leq 220$) | $BG_i^t \in [212, 222], In_i^t \neq 12 = \alpha, M_i^t = 0$ | Satisfied | Violated |
| ML-RQ1.2 ($M_1^{12} = 20 \Rightarrow BG_6^O > 210$) | $BG_i^t \in [180, 180], In_i^t = \alpha, M_i^t \neq 12 = 0$ | Violated | Satisfied |
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