Uniting Clinicians, Lived Experience, and AI Systems In Type 1 Diabetes.

CAPSML

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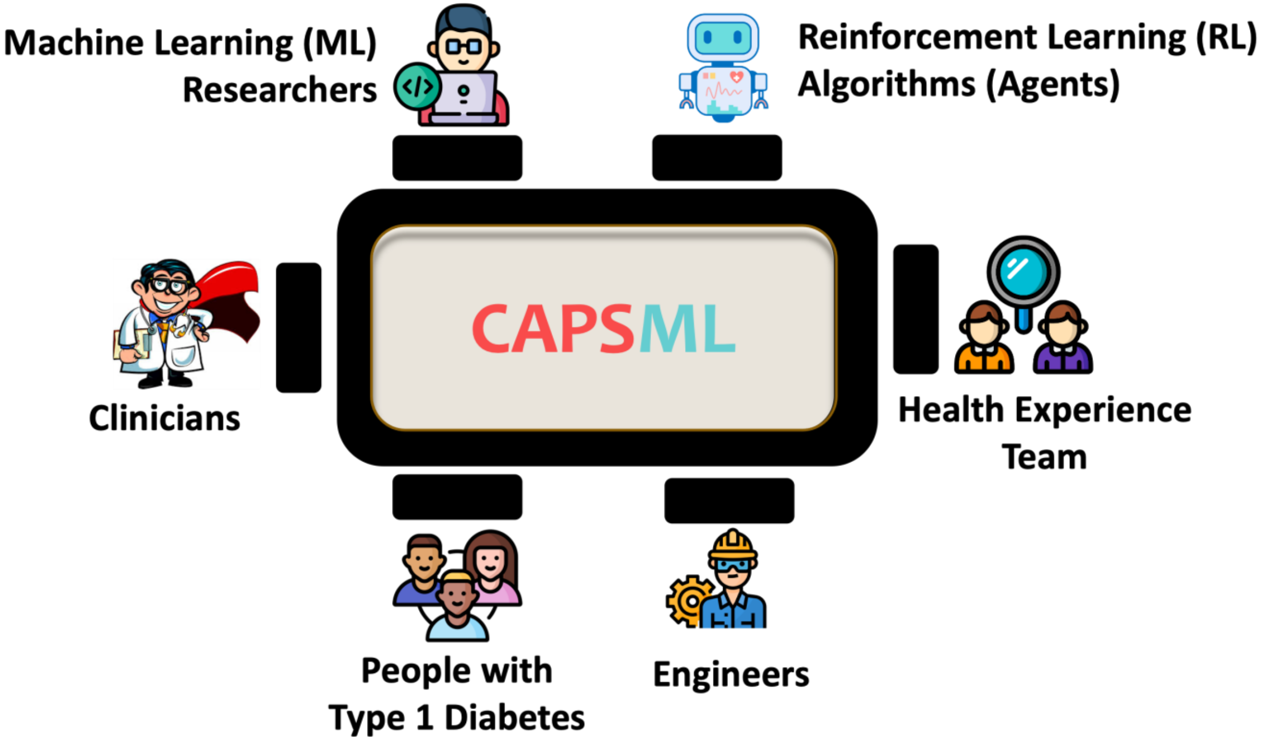
Australian National University

Demonstration Overview



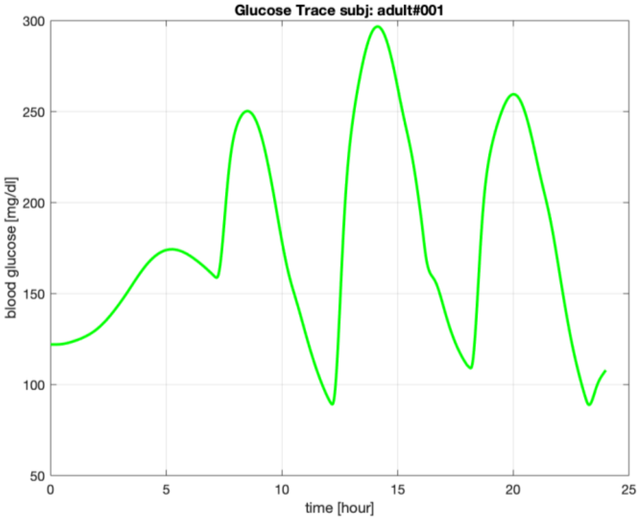
The tool is publicly available as an online tool at "capsml.com"

Agenda

1.1 Background: Glucose Regulation

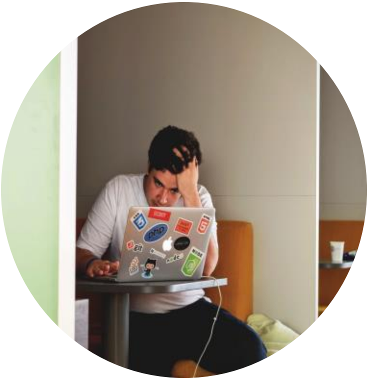
Sleep

Meals



Exercise

Stress

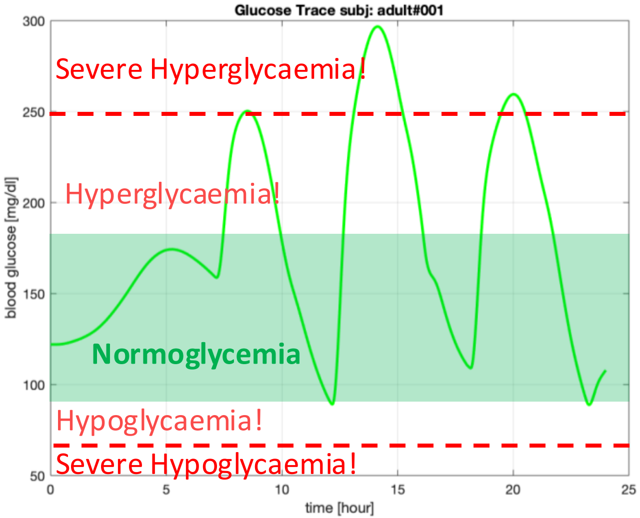


The fluctuation of blood glucose levels.

1.1 Background: Glucose Regulation

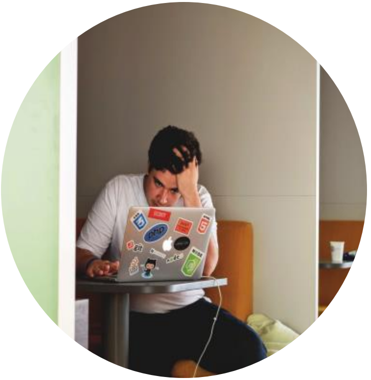
Sleep

Meals



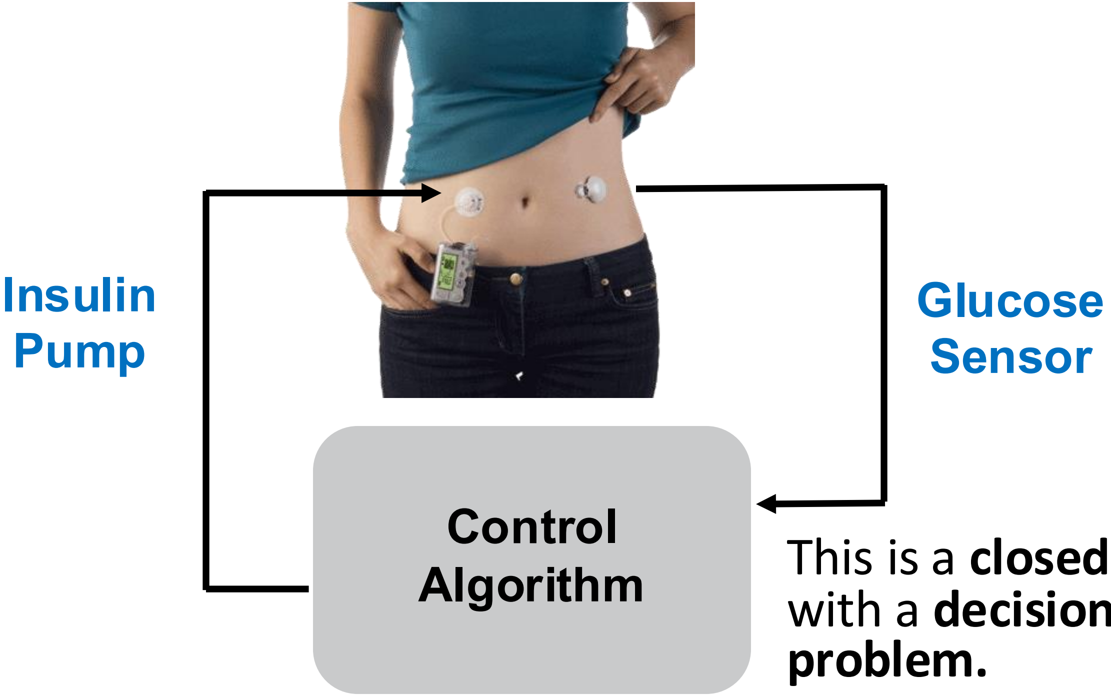
Exercise

Stress



Maintaining glucose homeostasis is vital!

1.2 Background: Artificial Pancreas Systems (APS)

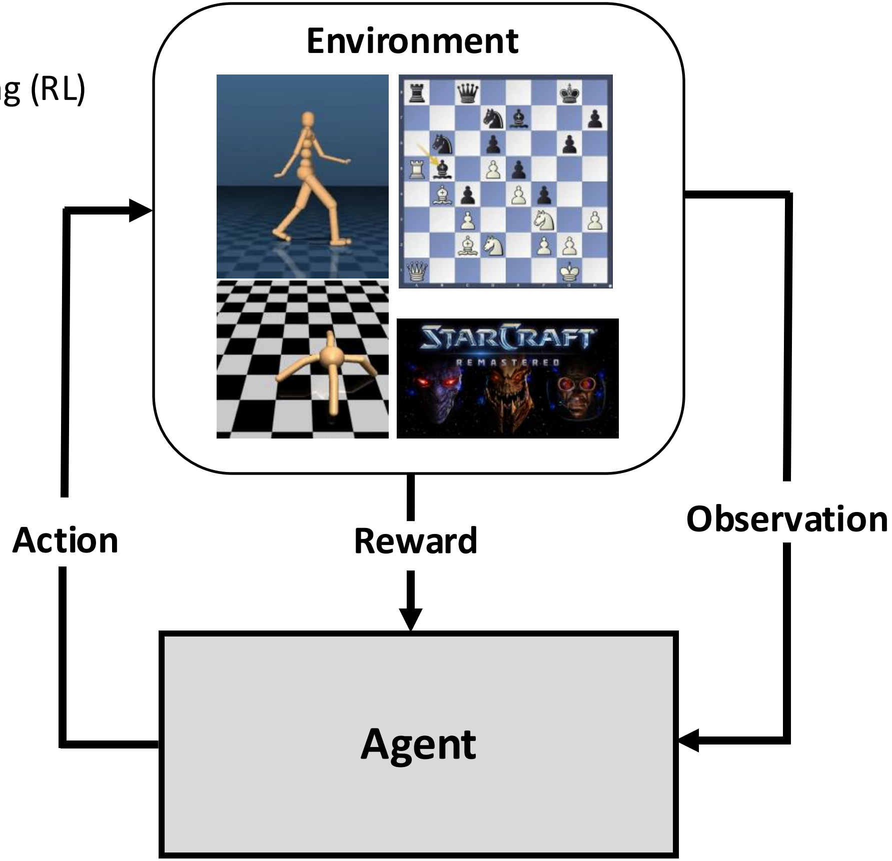


This is a **closed-loop system**, with a **decision-making problem.**

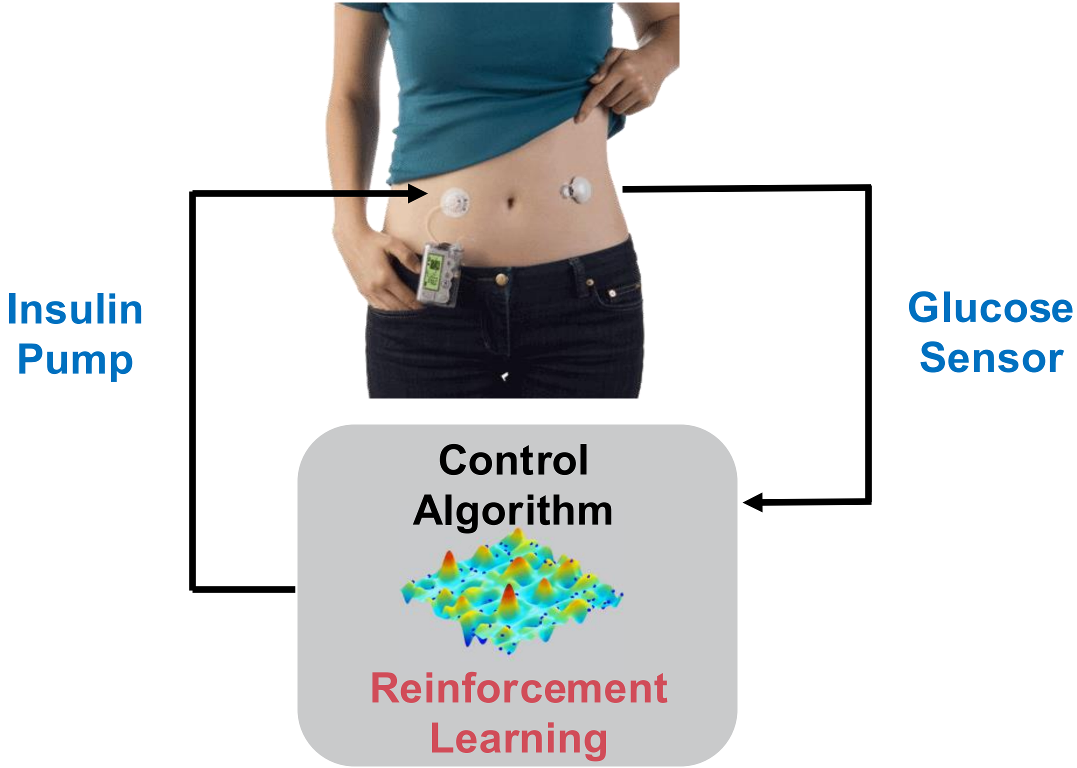
Note: Existing APS are **hybrid-closed loop systems**, which still require manual inputs (meal announcement & carbohydrate estimation). First commercial systems introduced in 2016 the USA and in 2019 in Australia.

1.3 Background: Reinforcement Learning (RL)

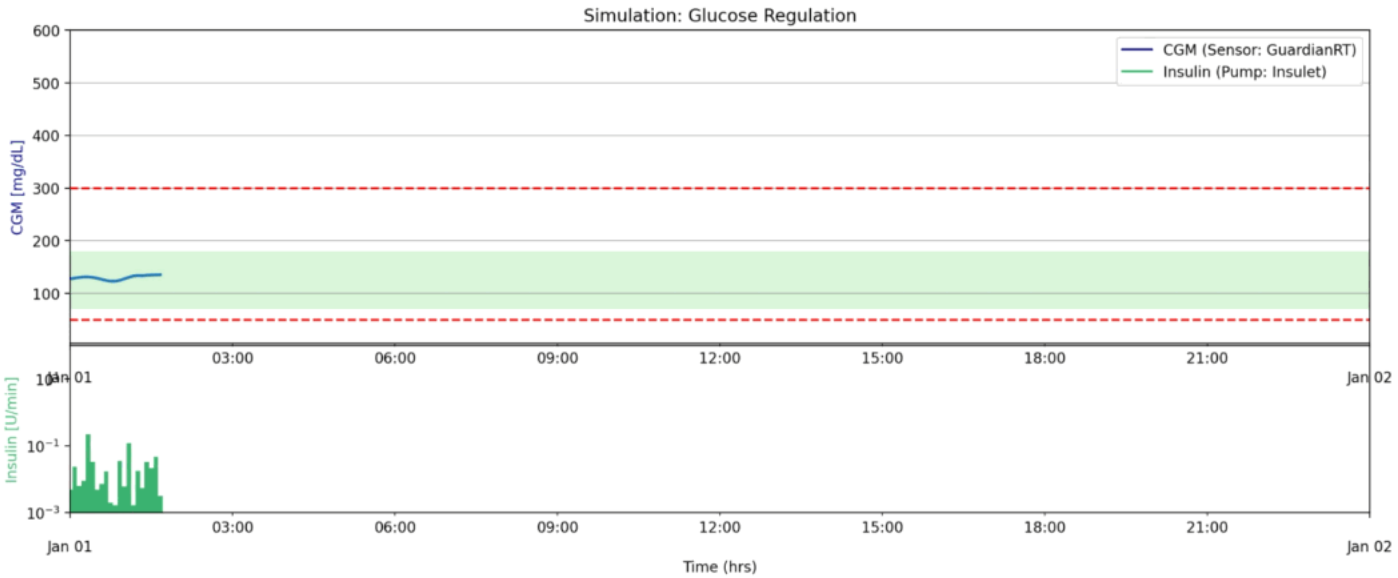
Artificial Intelligence (AI)
↳ Machine Learning (ML)
  ↳ Reinforcement Learning (RL)



1.4 Background: RL-based APS – Towards full automation.



02. Introduction: CAPSML



The treatment strategies learnt by the RL algorithms are complicated and hard to understand.

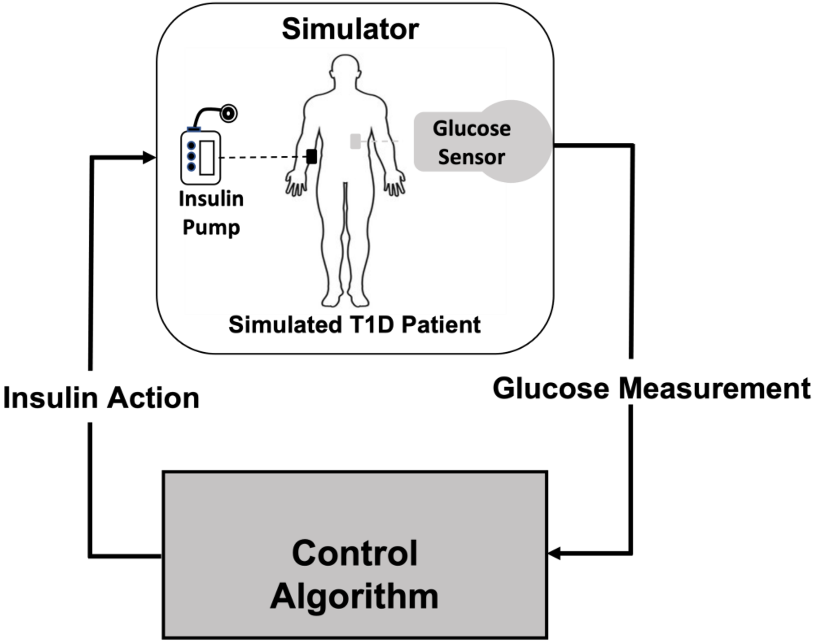
02. Introduction: CAPSML

Table. Clinical performance comparison of RL-based APS and clinical treatment.

Method	Failure (%)	Severe Hypo.(%) TBR-Level 2	Hypo. (%) TBR-Level 1	Normo. (%) TIR	Hyper. (%) TBR-Level 1	Severe Hyper.(%) TBR-Level 2	RI	LBGI	HBGI
BBI	0.39	$0.00^{\dagger}$ $0.00\text{-}0.00^{*}$ $0.06(0.40)^{\ddagger}$	0.00 0.00-0.00 0.64(2.01)	70.83 61.46-79.17 71.02(11.29)	22.57 17.36-31.94 24.44(10.57)	2.08 0.00-4.86 3.85(5.72)	7.68 6.07-9.38 8.35(4.05)	0.81 0.28-1.68 1.33(1.60)	6.72 4.97-7.94 7.02(2.79)
BBHE	0.35	0.00 0.00-0.00 0.05(0.36)	0.00 0.00-0.00 0.40(1.42)	69.79 60.42-78.47 69.78(11.29)	23.61 18.06-32.29 25.44(10.57)	3.12 0.00-5.21 4.33(5.64)	7.62 5.78-8.69 8.00(3.74)	0.41 0.11-0.93 0.88(1.37)	6.92 5.11-8.11 7.11(2.67)
PPO	2.79	0.00 0.00-0.00 0.32(1.51)	0.00 0.00-1.04 1.19(2.77)	69.44 62.15-76.04 69.12(10.53)	20.83 16.32-25.35 20.93(7.11)	7.99 2.43-12.85 8.44(6.88)	9.56 6.89-12.04 9.79(3.66)	0.89 0.28-2.17 1.64(2.11)	8.05 5.86-10.10 8.14(3.05)
G2P2C	1.62	0.00 0.00-0.00 0.22(1.26)	0.00 0.00-1.04 1.11(2.50)	72.57 66.32-79.86 72.69(9.53)	18.75 15.28-23.26 19.37(6.46)	6.60 0.69-10.76 6.61(5.53)	9.00 6.21-11.04 8.94(3.18)	1.04 0.43-2.14 1.58(1.74)	7.42 5.18-9.35 7.36(2.60)

Statistical performance metrics only provide limited information into the RL-based strategies and doesn't provide any insights towards the operation of the algorithm.

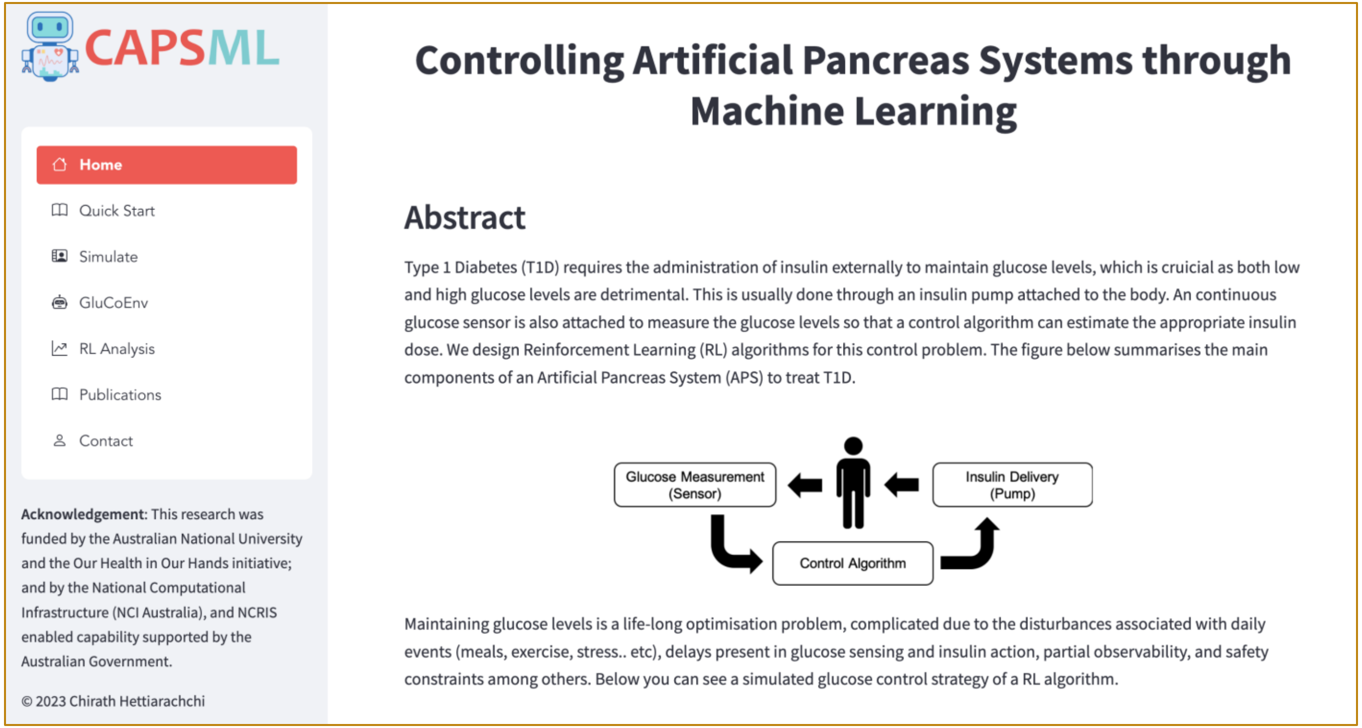
02. Introduction: CAPSML



Existing simulation tools require technical knowledge and inaccessible to the general public.

2.1 Quick Start

The tool is publicly available online at: “capsml.com” under the MIT license.
A demonstration of the system is available at: https://youtu.be/JO5MkPCuqCw.

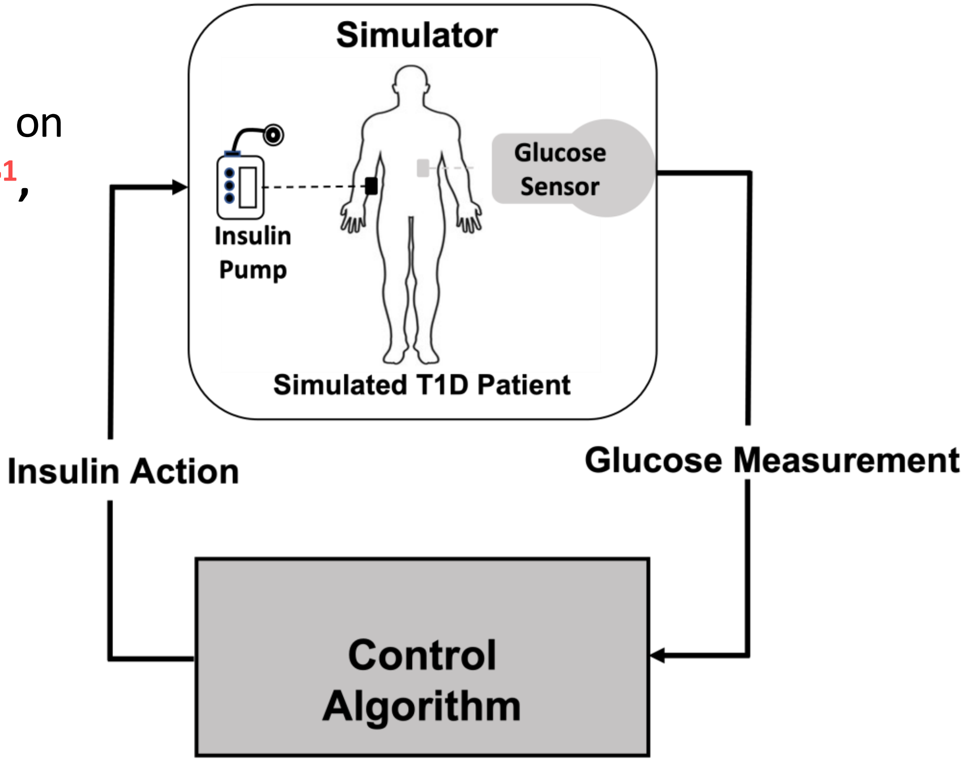


2.1 Quick Start

Step 1. The Simulator

- The simulator used in CAPSML is based on the open-source **Simglucose Simulator**[1], which uses the **FDA-approved UVA/PADOVA 2008**[2] model.

- **Used for pre-clinical trials.**



1. Xie, Jinyu. "Simglucose v0. 2.1 (2018)." *URL https://github. com/jxx123/simglucose* (2018).
2. Kovatchev, Boris P., et al. "In silico preclinical trials: a proof of concept in closed-loop control of type 1 diabetes." (2009): 44-55.

2.1 Quick Start

Step 2. Select T1D *in-silico* Subject

Alice **Bob** **Chloe** **David**

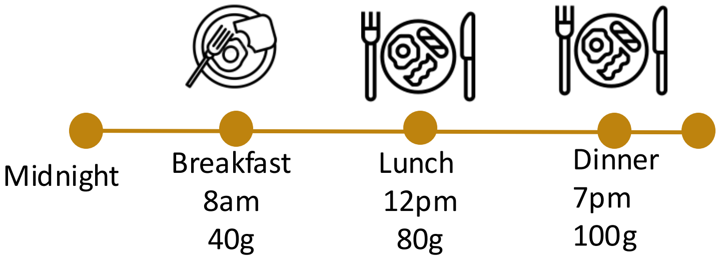
- Select from 10 Adolescents & 10 Adults.
- Subjects have different body Weights, Ages, Insulin to Carbohydrate Ratios (ICR), & Insulin Sensitivity Factors (ISF).

Table. Parameters of *in-silico* subjects.

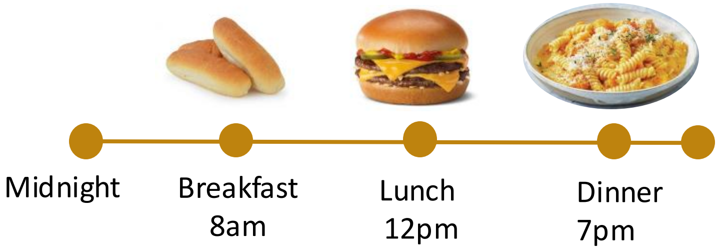
	Subject Name	Body Weight (Kg)	Age	Total Daily Insulin (TDI)	Insulin to Carbohydrate Ratio (ICR)	Insulin Sensitivity Factor (ISF)
0	adolescent0	68.7060	18	36.7339	12	15.0360
1	adolescent1	51.0460	19	62.0310	5	13.1751
2	adolescent2	44.7910	15	24.2428	23	33.5260
3	adolescent3	49.5640	17	35.2529	14	21.8225
4	adolescent4	47.0740	16	34.0047	12	20.9084
5	adolescent5	45.4080	14	49.5813	7	17.6966
6	adolescent6	37.8980	16	43.6381	8	12.4932
7	adolescent7	41.2180	14	63.3867	4	11.9355
8	adolescent8	43.8850	19	24.0782	21	20.0139
9	adolescent9	47.3780	17	33.1735	14	31.8685
10	adult0	102.3200	61	50.4167	10	8.7731
11	adult1	111.1000	65	57.8688	8	9.2128
12	adult2	81.6310	27	56.4297	9	17.9346
13	adult3	63.0000	66	33.8079	16	42.6534
14	adult4	94.0740	52	68.3159	5	8.2313
15	adult5	66.0970	26	61.3888	10	18.2133
16	adult6	91.2290	35	42.0066	22	26.1531
17	adult7	102.7900	48	42.7788	13	12.2506
18	adult8	74.6040	68	67.2115	5	7.6432
19	adult9	73.8590	68	64.4485	5	10.6926

2.1 Quick Start

Step 3. Select Meal Protocol - Set up meals based on the time and carbohydrate content or portion size of different meals/food items.



(A)



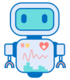
(B)

Note: In-between snacks can also be incorporated[1], currently not implemented on CAPSML.

1. Hettiarachchi, Chirath, et al. "A Reinforcement Learning Based System for Blood Glucose Control without Carbohydrate Estimation in Type 1 Diabetes: In Silico Validation." 2022.

2.1 Quick Start

Step 4. Select Control Algorithm

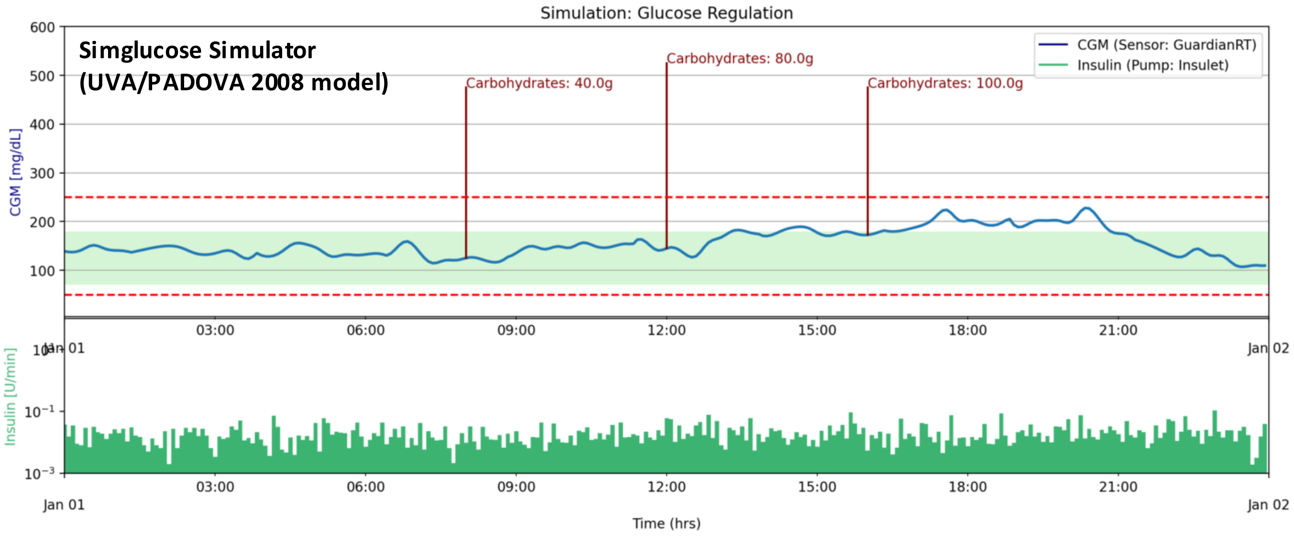
 **(A) Clinical Treatment (Basal - Bolus)**	 **(B) Reinforcement Learning Strategies**
Insulin Pump Therapy: Fixed basal & bolus setting • **Fixed basal insulin delivery** based on personalised Total Daily Insulin (TDI). • **Meal Bolus** based on the Carbohydrate to Insulin Ratio (CIR). • **Correction Bolus** based on the Insulin Sensitivity Factor (ISF).	A closed-loop system that monitors historical glucose trends to estimate insulin requirements.
Meal Announcement – 20 minutes in advance.	**No Meal Announcements.**
Manual Meal Carbohydrate (CHO) Estimation.	**No Meal Carbohydrate (CHO) Estimation.**
E.g., **BBI** – Ideal CHO estimates, **BBHE** – Human error in CHO estimates	E.g., **G2P2C** (novel algorithm), **PPO** (state-of-the-art RL algorithm adapted for glucose control)

1. Hettiarachchi, C et al. "G2P2C–A Deep Reinforcement Learning Algorithm for Glucose Control by Glucose Prediction and Planning in Type 1 Diabetes." *Available at SSRN 4226648*.

2.1 Quick Start

Step 5. Run Simulation

Adolescent0



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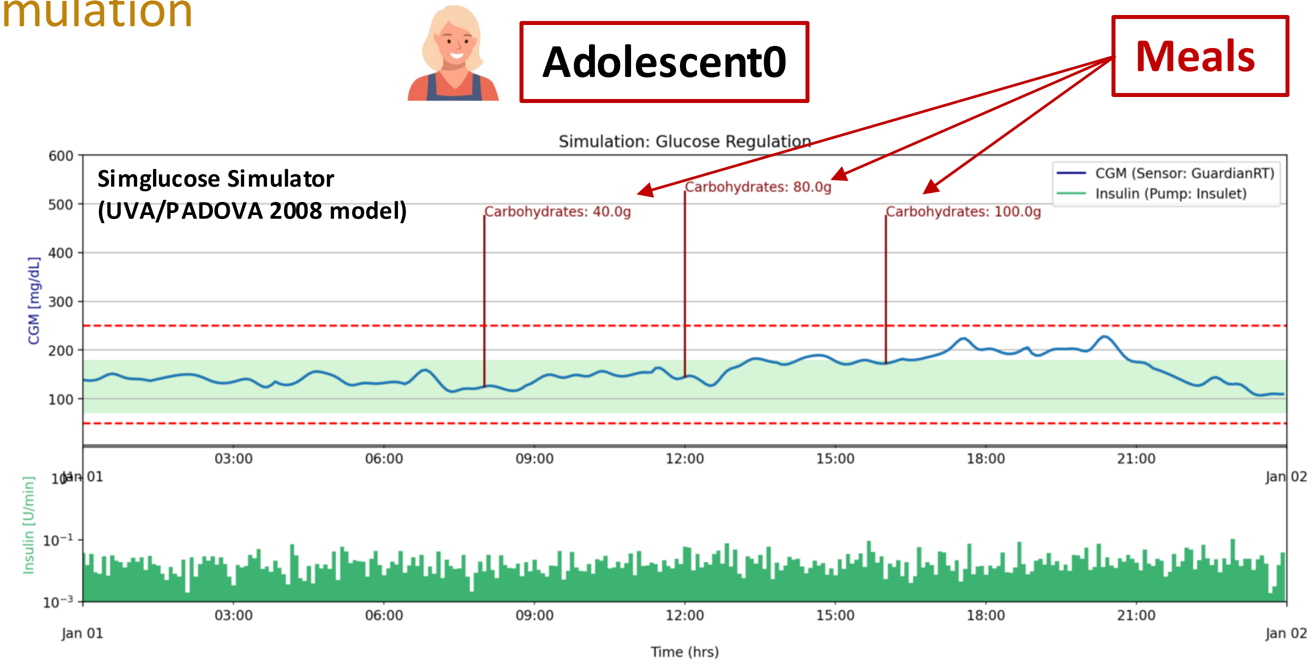
Step 5. Run Simulation



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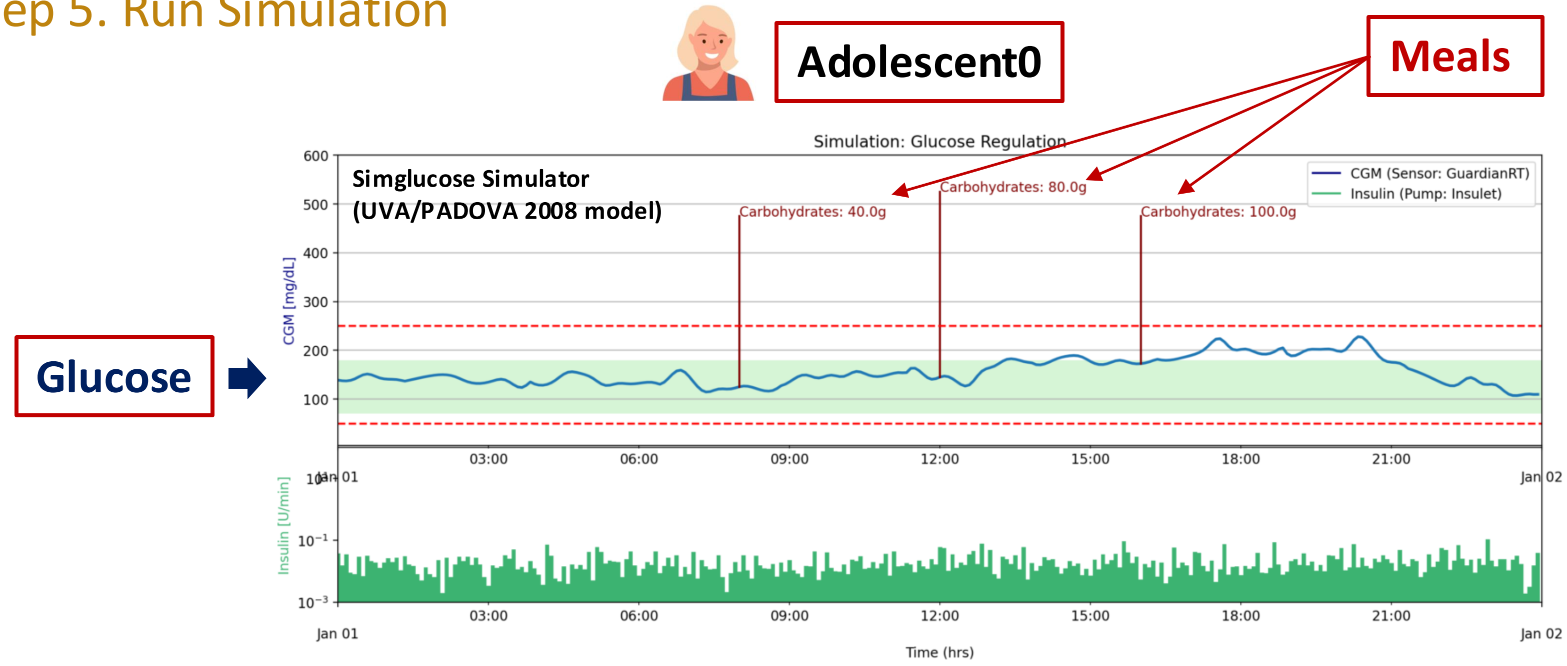
Step 5. Run Simulation



2.1 Quick Start

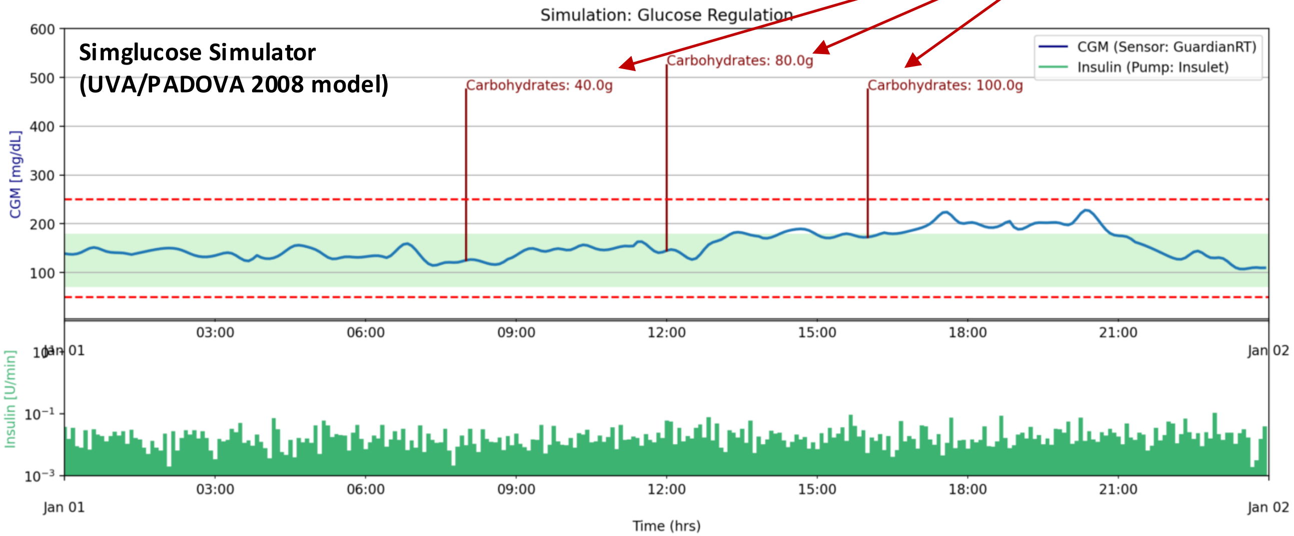
Step 5. Run Simulation

Adolescent0

Meals

Glucose

Insulin



Control Algorithm (e.g., *our G2P2C algorithm*[1,2])

1. Hettiarachchi, C et al. "G2P2C–A Deep Reinforcement Learning Algorithm for Glucose Control by Glucose Prediction and Planning in Type 1 Diabetes." *Available at SSRN 4226648*.
2. Hettiarachchi, C, et al. "A Reinforcement Learning Based System for Blood Glucose Control without Carbohydrate Estimation in Type 1 Diabetes: In Silico Validation." *EMBC*. IEEE, 2022.

2.1 Quick Start

Step 5. Run Simulation

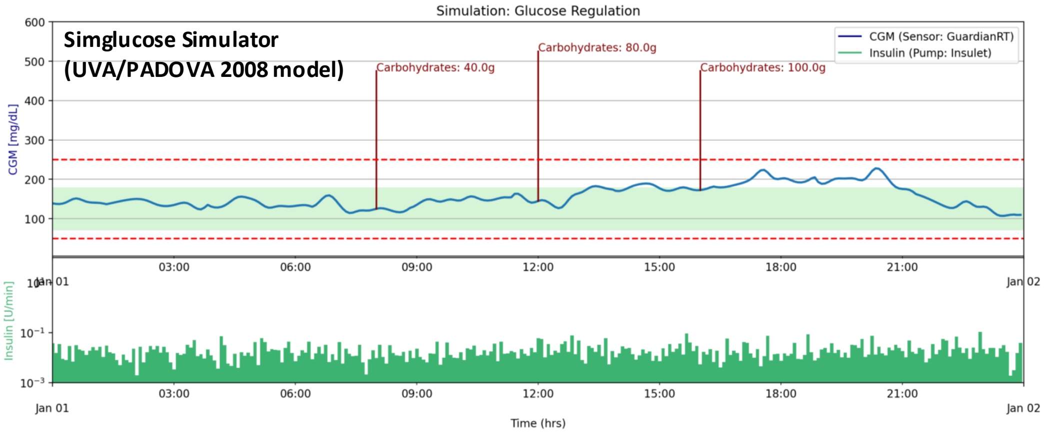
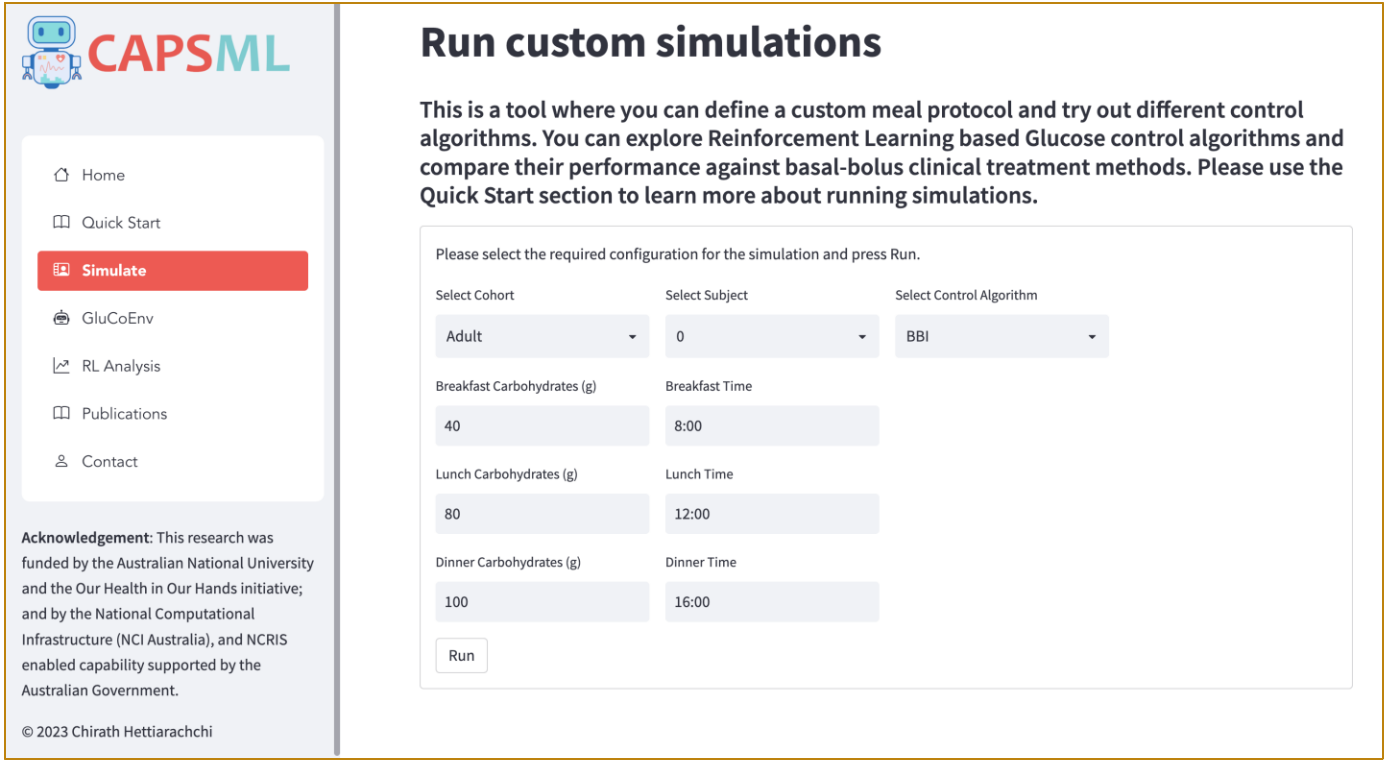


Table. Clinical performance metrics.

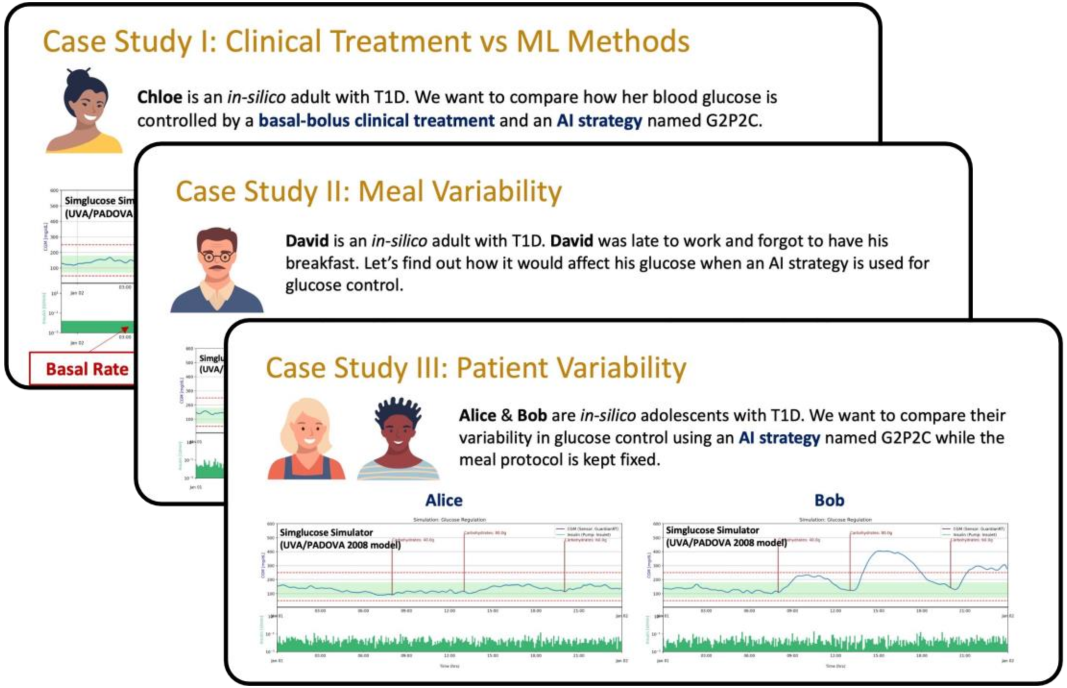
	Metric	Value
0	Time Above Range (TAR) - Level2 (>250 mg/dL)	0.0%
1	Time Above Range (TAR) - Level 1 (180 - 250 mg/dL)	14.93%
2	Time In Range (TIR) (70 - 180 mg/dL)	85.07%
3	Time Below Range (TIR) - Level 1 (54 - 70 mg/dL)	0.0%
4	Time Below Range (TIR) - Level 2 (<54 mg/dL)	0.0%
5	Risk Index (RI)	4.21
6	Low Blood Glucose Index (LBGI)	0.44
7	High Blood Glucose Index (HBGI)	3.77

2.2 Running Simulations…



(move to live demo…)

03 Diabetes Research:
Developing RL-based Treatment Strategies



03 (A) Case Study I: Clinical Treatment vs RL Methods

Chloe is an *in-silico* adult with T1D. We want to compare how her blood glucose is controlled by a **basal-bolus clinical treatment** and an **RL strategy** named G2P2C.

03 (A). Case Study I: Clinical Treatment vs RL Methods

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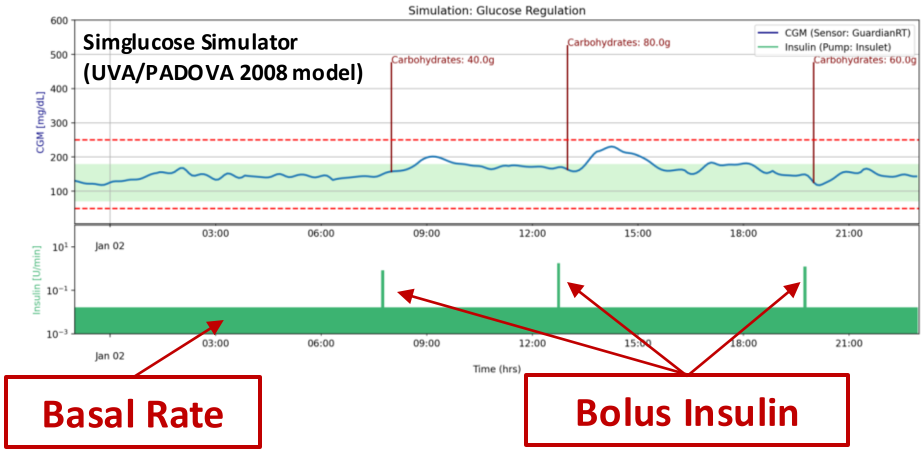
Basal-bolus Treatment

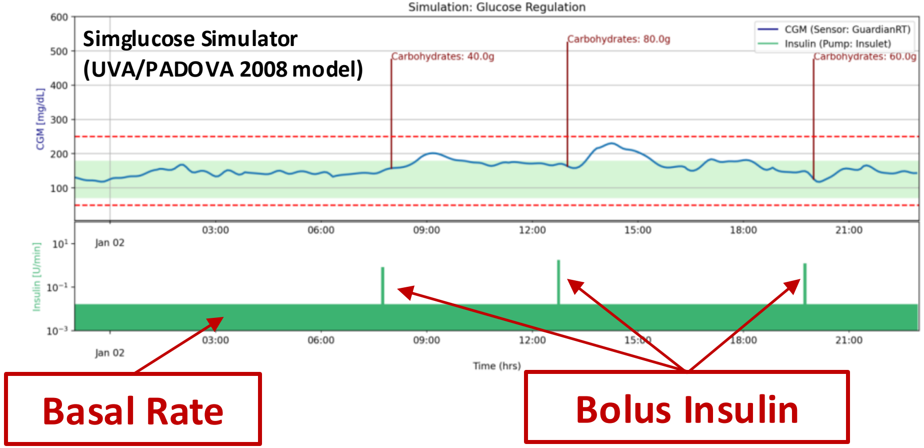


- Requires manual user input on meal announcements & carbohydrate estimation.
- Easy to understand.

03 (A). Case Study I: Clinical Treatment vs RL Methods

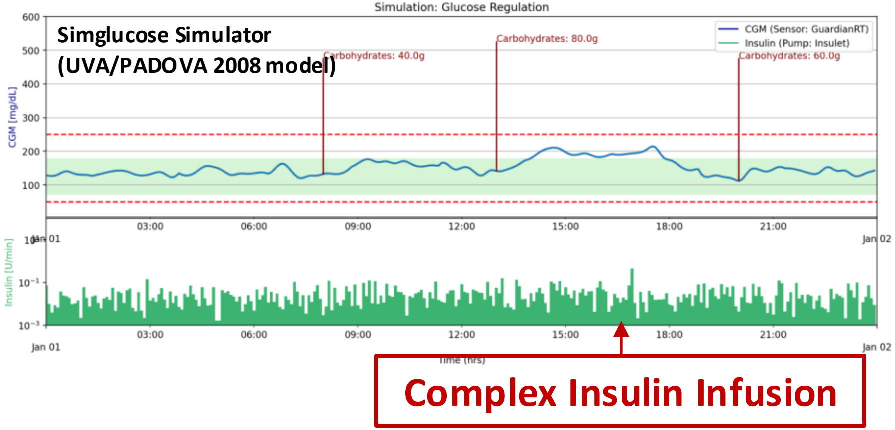
Chloe is an *in-silico* adult with T1D. We want to compare how her blood glucose is controlled by a **basal-bolus clinical treatment** and an **RL strategy** named G2P2C.

Basal-bolus Treatment



- Requires manual user input on meal announcements & carbohydrate estimation.
- Easy to understand.

RL Strategy



- The RL treatment strategy is more complex.
- Highlights the importance of collaboration & tools to improve explainability.

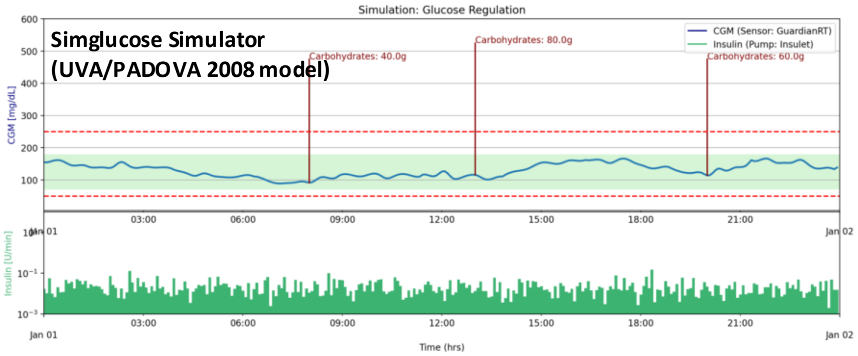
03 (B). Case Study II: Patient Variability


Alice & **Bob** are *in-silico* adolescents with T1D. We want to compare their variability in glucose control using an **RL strategy** named G2P2C while the meal protocol is kept fixed.

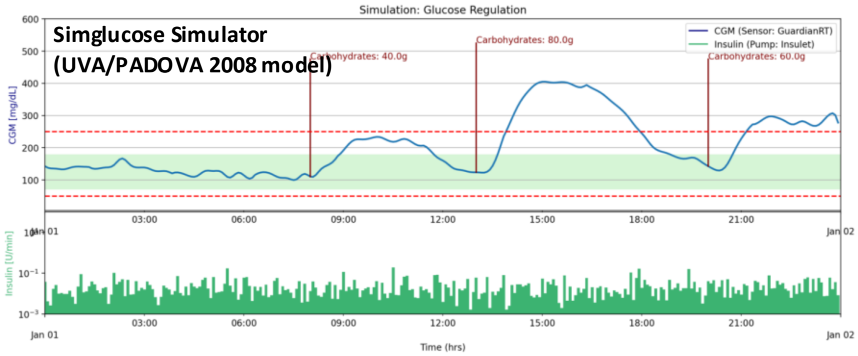
03 (B). Case Study II: Patient Variability

Alice & **Bob** are *in-silico* adolescents with T1D. We want to compare their variability in glucose control using an **RL strategy** named G2P2C while the meal protocol is kept fixed.

Alice



Bob



- Controlling blood glucose in Alice is easier compared to Bob.
- The RL strategies need to be carefully validated across all cohorts and subjects. CAPSML provides the capability to run simulations and visualise.

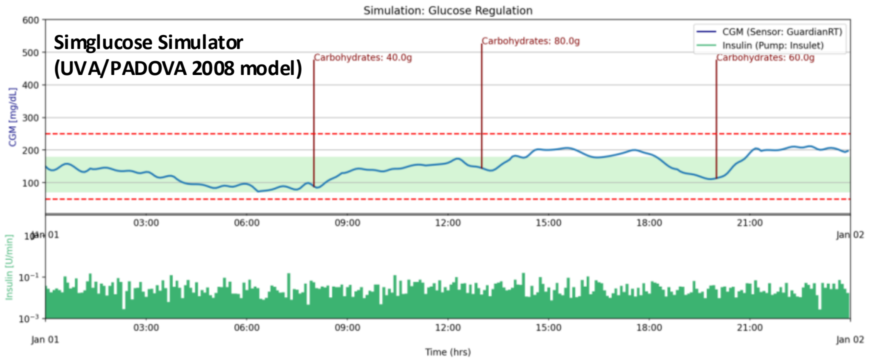
03 (C). Case Study III: Meal Variability

David is an *in-silico* adult with T1D. **David** was late to work and forgot to have his breakfast. Let's find out how it would affect his glucose when an RL strategy is used for glucose control.

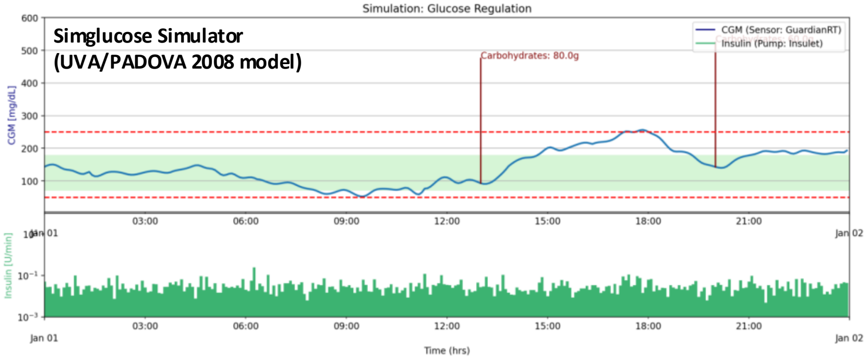
03 (C). Case Study III: Meal Variability

David is an *in-silico* adult with T1D. **David** was late to work and forgot to have his breakfast. Let's find out how it would affect his glucose when an RL strategy is used for glucose control.

Normal Day



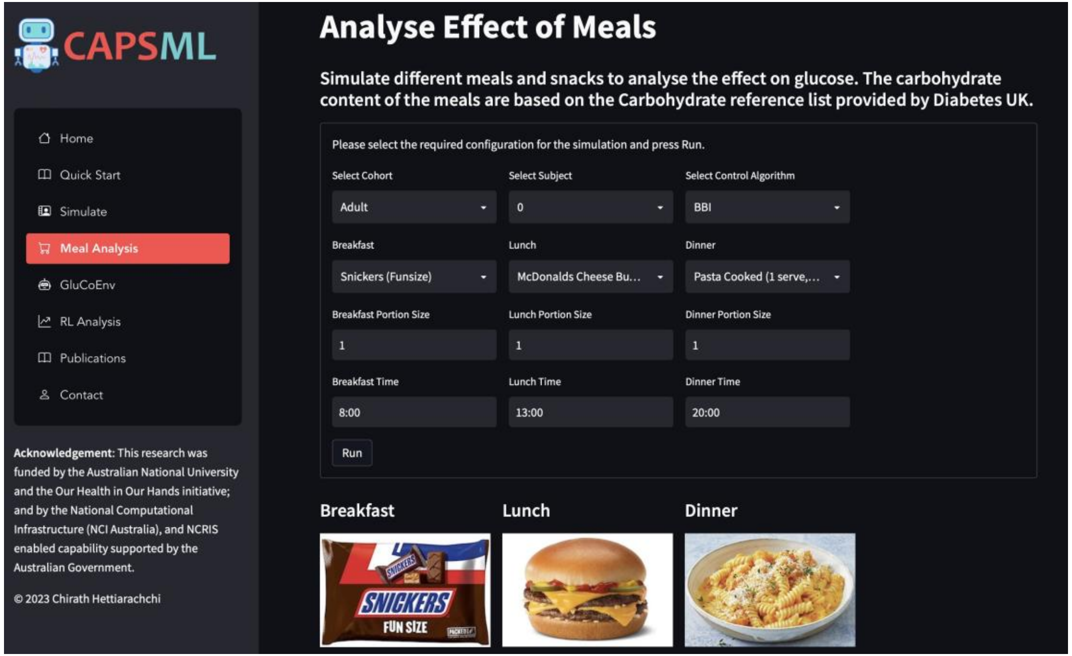
Forgot to have breakfast



- Simulating real-life events to evaluate potential failures of RL strategies is important.

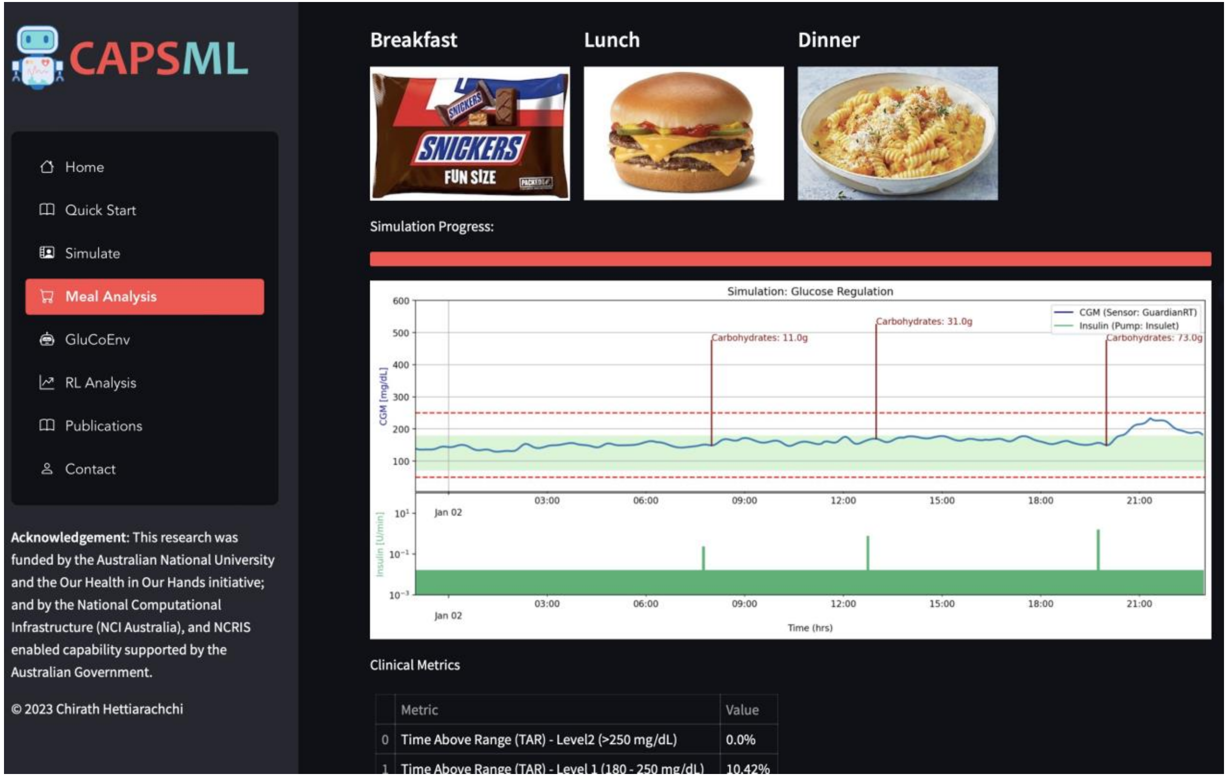
04 Diabetes Education

- Learn about glucose regulation and closed-loop systems.
- Learn about carbohydrate content of different meals/food and their effect on glucose regulation.



Note: The carbohydrate reference list by Diabetes UK is integrated in the tool (https://www.diabetes.org.uk/).

04 Diabetes Education



05. Impact & Potential of CAPSML

- CAPSML can be used on a desktop machine or mobile device without any specialised hardware to simulate RL-based control systems.

- Existing RL-based systems can be further improved by feedback from clinicians and health experience experts.

- A first step towards improving **trust/explainability** of the RL-based systems in glucose control.

06. Conclusion & Future Work

- CAPSML welcomes clinical and lived experience experts to experiment with an AI system and run custom simulations to learn about the AI system.

- Provide additional customisation capabilities for basal bolus treatment strategies.

- By conducting custom simulations, the strengths and weaknesses of the system can be identified to be continuously improved and fine-tuned based on the knowledge bases of clinicians and people with lived experience of T1D.

- In future, CAPSML (“**Controlling Artificial Pancreas Systems** using **Machine Learning**”) can be extended to allow researchers to test their AI algorithms for comparison and evaluation. It could address the currently limited benchmarking of different AI algorithms and systems in T1D if successfully used at scale.

THANK YOU

Acknowledgement: This research is funded by the Australian National University, School of Computing and Our Health in Our Hands (OHIOH), a strategic initiative of the ANU. This research was also supported by the National Computation Infrastructure (NCI Australia), an NCRIS enabled capability supported by the Australian Government.

Collaborators: We wish to thank **Dr David O’Neal, Dr Barbora Paldus, and Dr Dale Morrison** from the Diabetes Technology Research Group, St Vincent’s Hospital for their valuable insights towards this research.

Contact Us





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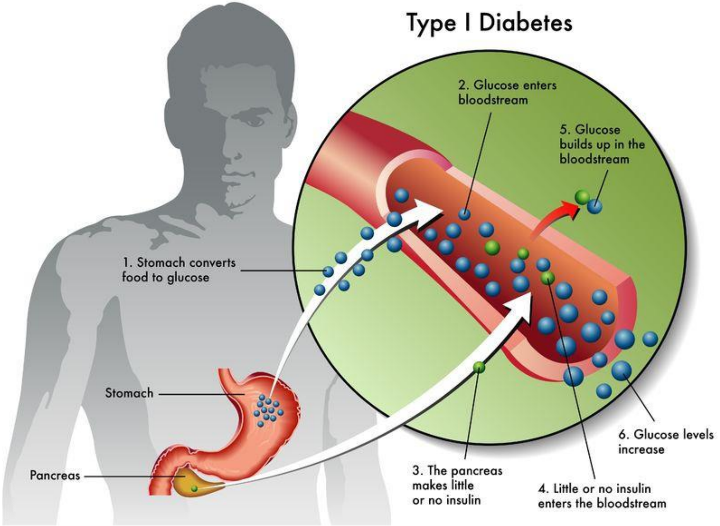
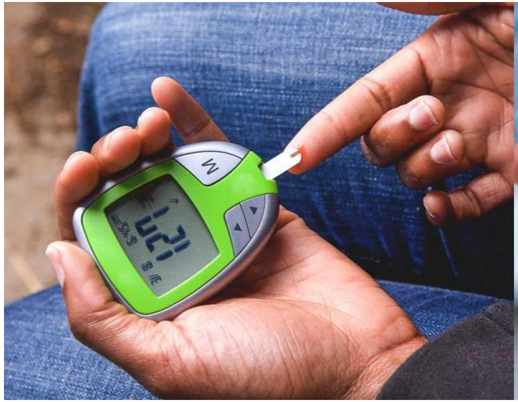
Australian National University

1.2 Background: Type 1 Diabetes



Autoimmune destruction of insulin producing β cells in the pancreas.



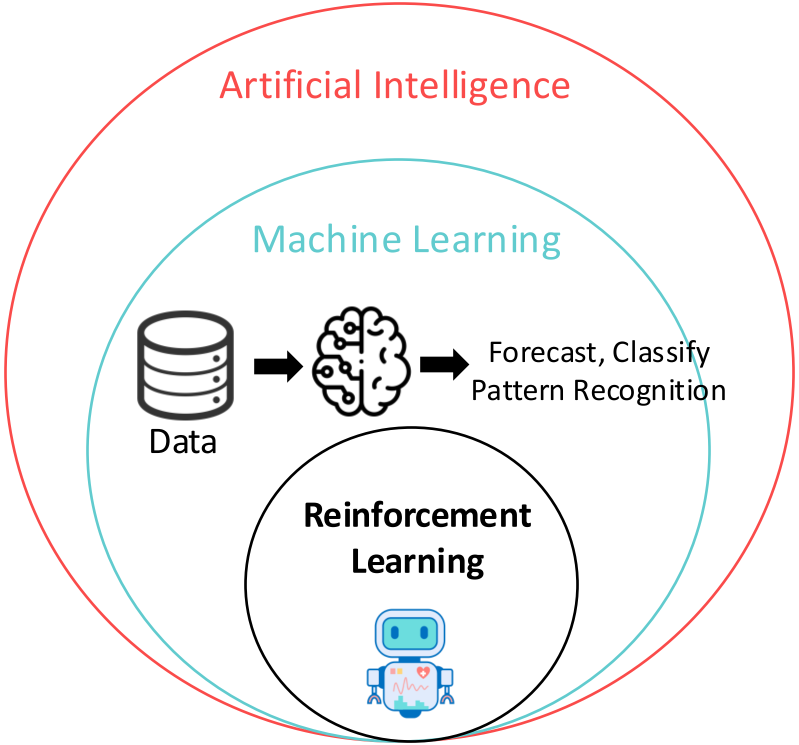
Measure the glucose level.

External insulin delivery is required!

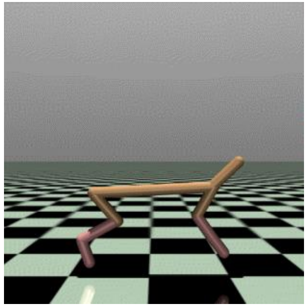
Clinical insulin administration strategy is based on clinical heuristics using personalised metrics.

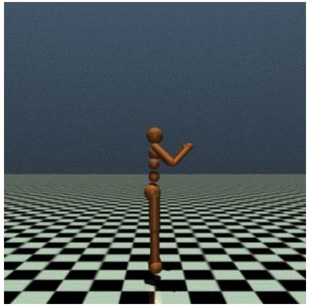
Image Credits: https://www.healthline.com/, https://diabetesvoice.org/

1.4 Background: Machine Learning & Reinforcement Learning



Reinforcement Learning Applications:





Images/Gif Credits: Mastering Atari, Go, Chess and Shogi by Planning with a Learned Model, DeepMind , 2020; MuJuCo

02. Introduction: CAPSML

Human vs AI **Human-AI Collaboration**

Photo by Andy Kelly on Unsplash and Stable Diffusion

Alice Bob

Chloe David

Step 1
Select an in-silico subject

Midnight

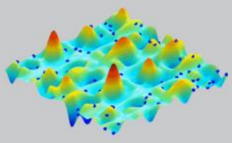
Breakfast 8am 40g

Lunch 12pm 80g

Dinner 7pm 100g

Step 2
Setup a meal protocol

Control Algorithm



Step 3
Select the control algorithm

Ru