Quantum Innovation Challenge

QuSOP: a quantum learning–optimisation framework for robust dose selection in early clinical development

Team Pharm-Jij

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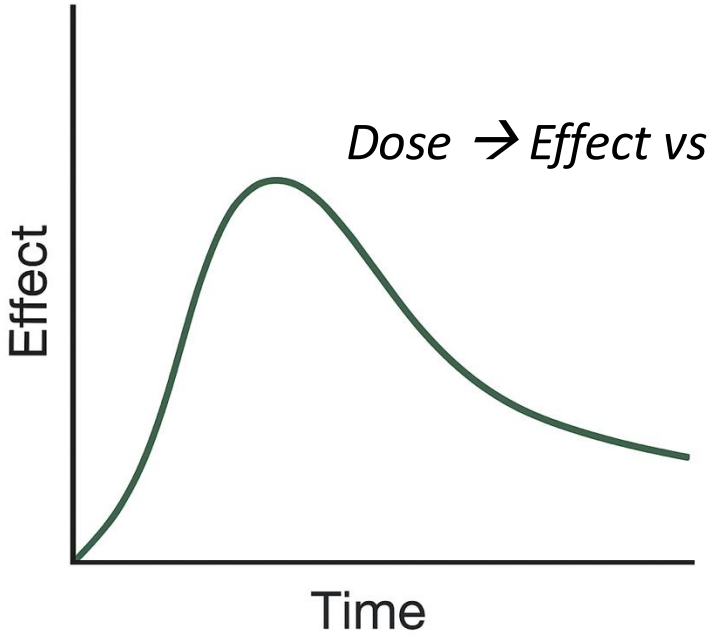
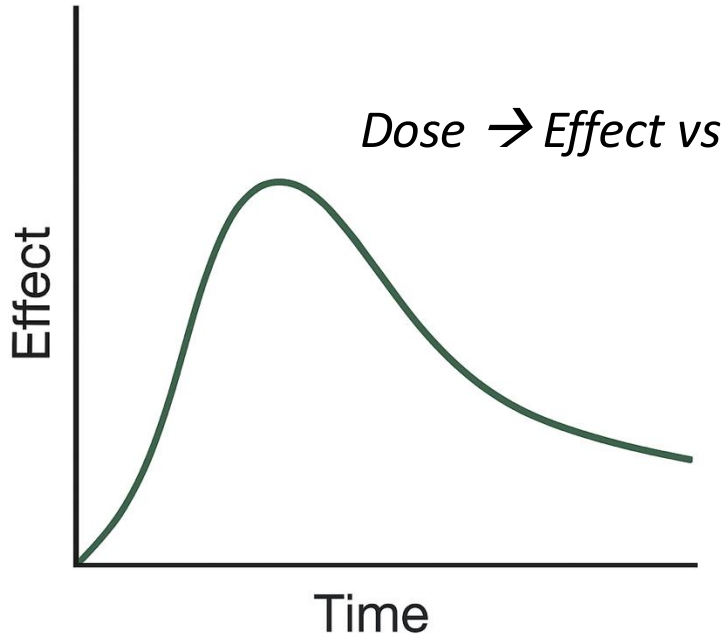
PK/PD models: key tool in accelerating drug development

- Utilizes preclinical and clinical pharmacokinetic and pharmacodynamic data to model exposure-response of drug in target disease
- Validated PK/PD models developed in early clinical trials can reduce doses evaluated in late-stage clinical trials, reducing costs and timelines



Preclinical animal studies

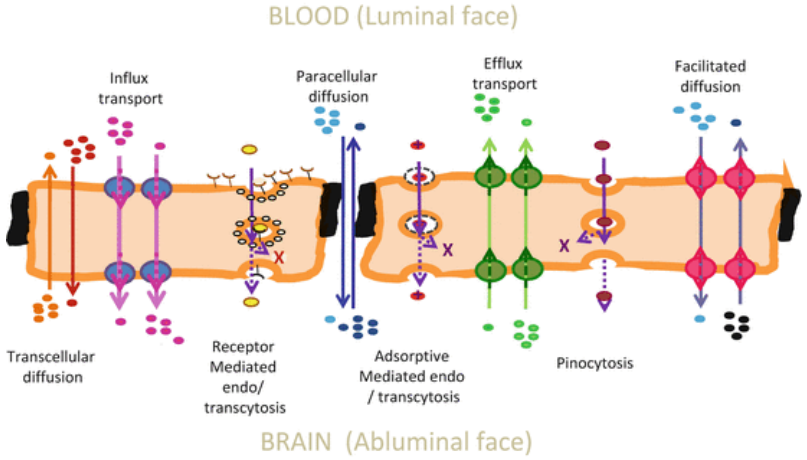


Clinical trials

Introduction and Problem Statement

1. How to accurately extrapolate to sub-populations?

2. How to describe non-linear biological processes?



From de Lange (2013)

- ML/AI approaches suffer from lack of data validation; sparse, unreliable data
- How can Quantum Computing address data limitations?
  - Propagate uncertainty as population-level attainment probabilities
  - Efficiently embed biological information from heterogenous, sparse data

Problem statement & Classical Monte Carlo

We would like to estimate the **probability of clinical success** $p(d)$ for a given **dose** d over the **discretised time window** for a **patient** $\zeta \sim P$.

$$p(d) = \mathbb{P}_{\zeta \sim P}\big(\mathcal{S}(d,\zeta)\big) \quad \text{where} \quad \mathcal{S}(d,\zeta) = \Big\{ \max_{t \in \mathcal{G}_{\text{qd}}} \hat{y}(t;d,\zeta) \le \tau_{\text{PD}} \Big\},$$

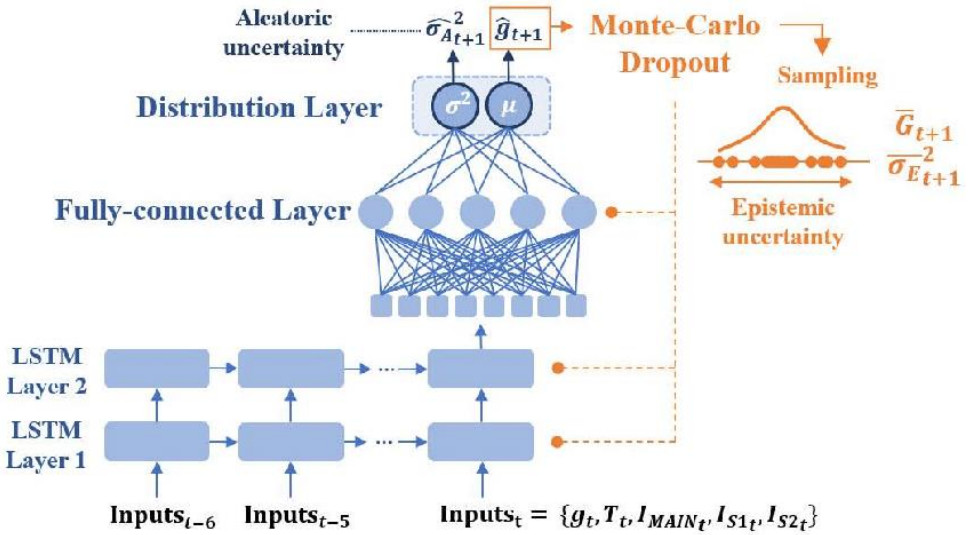
which indicates that for a dose d and a patient ζ, the **estimated biomarker path** $\hat{y}(t;d,\zeta)$ did not exceed the **safe dose** τ_{PD}.

Classical Monte Carlo is a computational method that uses **random sampling** to estimate quantities that cannot be computed analytically.

- Given i.i.d. draws $\zeta^{(1)}, \ldots, \zeta^{(M)} \sim P$, the unbiased estimator of success at dose d is

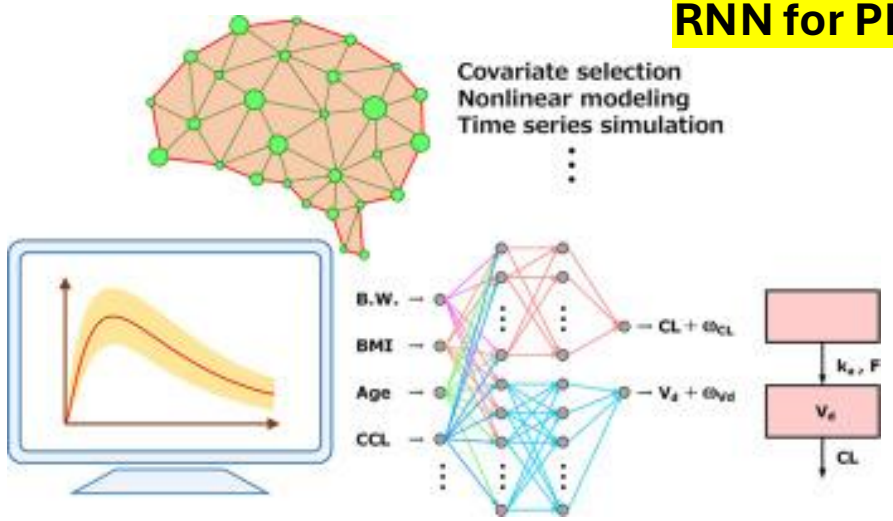
$$\widehat{p}_M(d) = \frac{1}{M} \sum_{m=1}^{M} \mathbf{1}\{\mathcal{S}(d,\zeta^{(m)})\}.$$

Probabilistic LSTM Model



Vien, et al. IWSHM 2021

RNN for PK-PD



Uno et al. Drug Meta. and Pharm. 56 (2024): 101004.

Classical vs. Quantum Monte Carlo estimator

To estimate $p(d)$ with **accuracy** ϵ, **Classical Monte Carlo** requires $O(\sigma^2/\epsilon^2)$ **samples**, where σ^2 is the **variance** of $\mathbb{1}_{\mathcal{S}(d,\zeta)}$. This yields to a **Computational bottleneck**.

- Evaluate ∼80 doses per grid
- Each dose simulated on 10^3–10^4 virtual subjects
- Hundreds of replicates for ±2–3 % confidence
- Each trajectory spans 24 h or 168 h

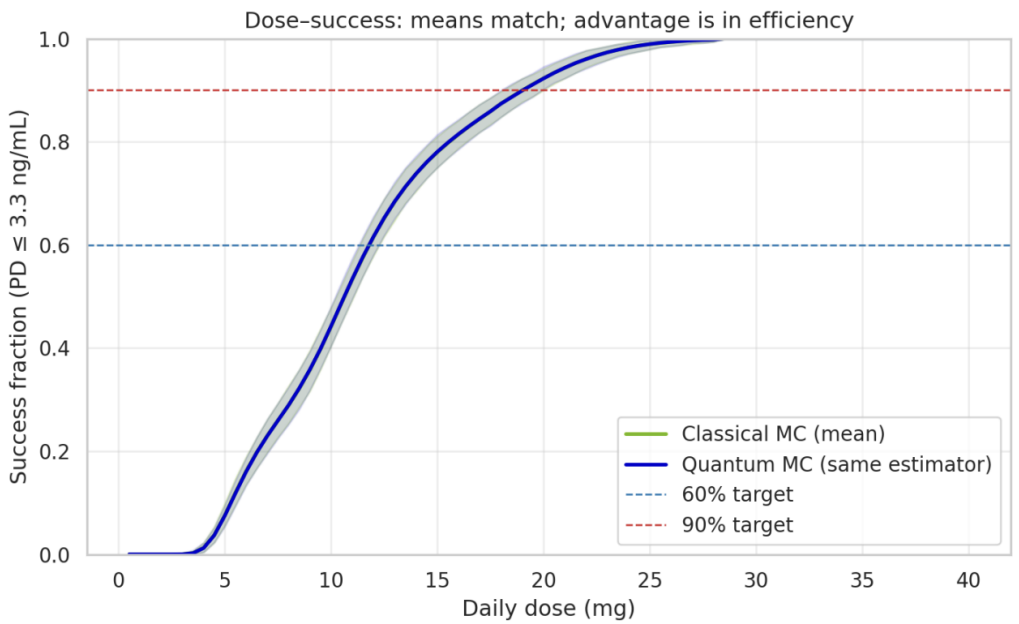
Total: 80,000 trajectory predictions

Quantum Monte Carlo: a quantum algorithm that provides a **quadratic speed-up** in the number of samples over classical MC.

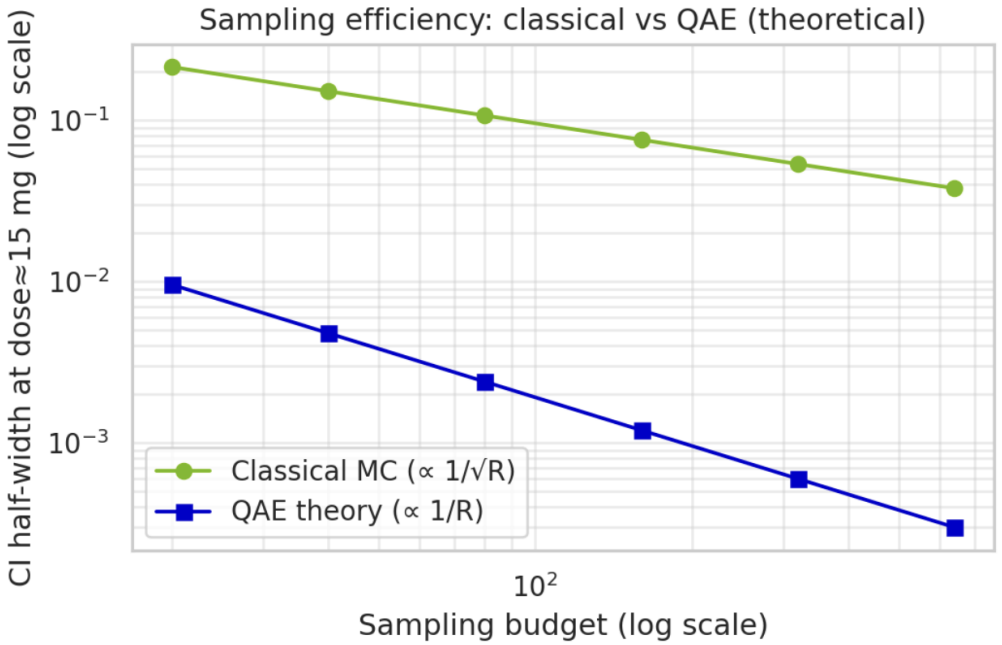
- Relies on **Quantum Amplitude Estimation**.
- To estimate $p(d)$ with accuracy ϵ, one requires $O(\sigma/\epsilon)$ samples.

Quadratic speed-up in efficiency.

Classical vs. Quantum Monte Carlo results

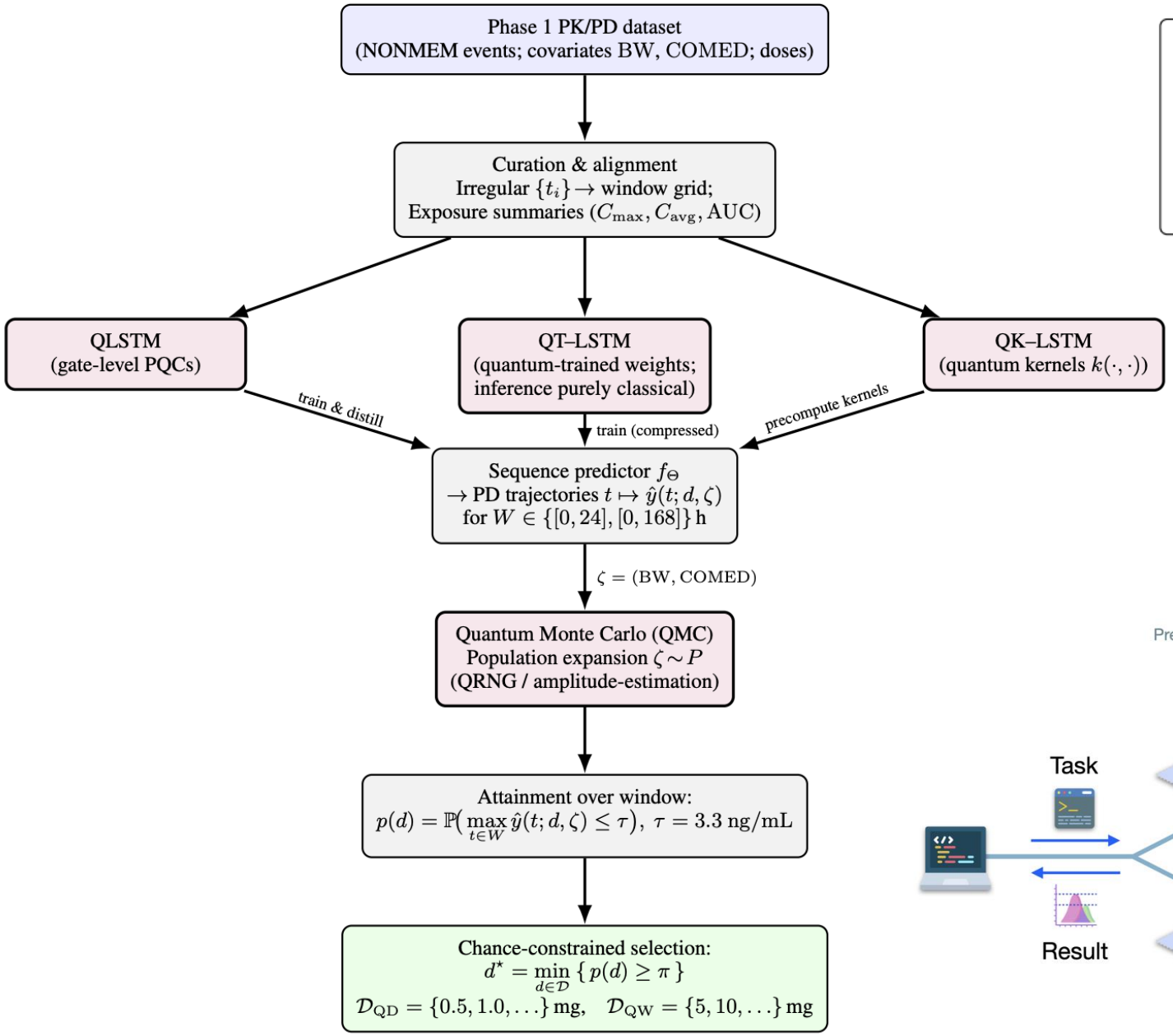


(a) Classical MC vs. quantum-augmented MC (QRNG): mean dose-success curves agree with Classical MC; efficiency gains stem from enhanced sampling (variance reduction) due to QMC.



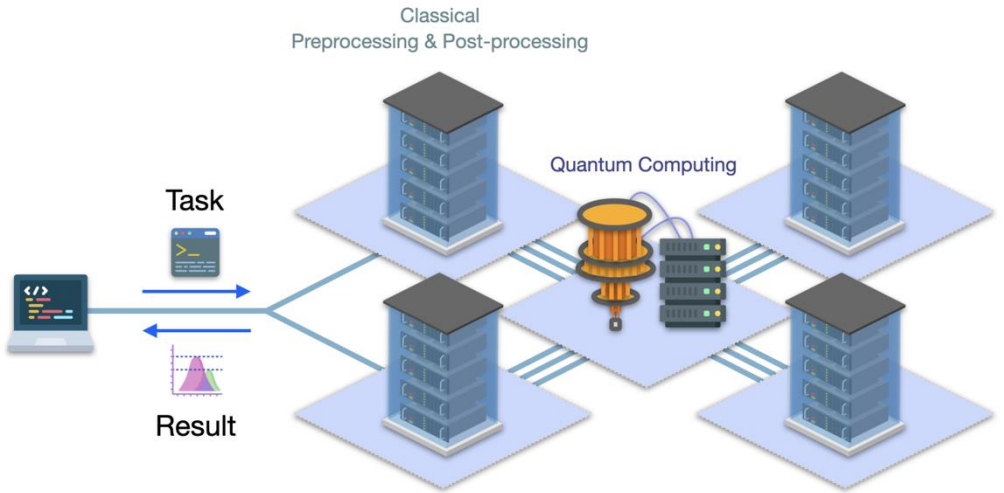
(b) Confidence-interval half-width versus sampling budget on a log-log scale. Classical MC exhibits $1/\sqrt{R}$ scaling; idealized QAE achieves $1/R$.

QuSOP framework

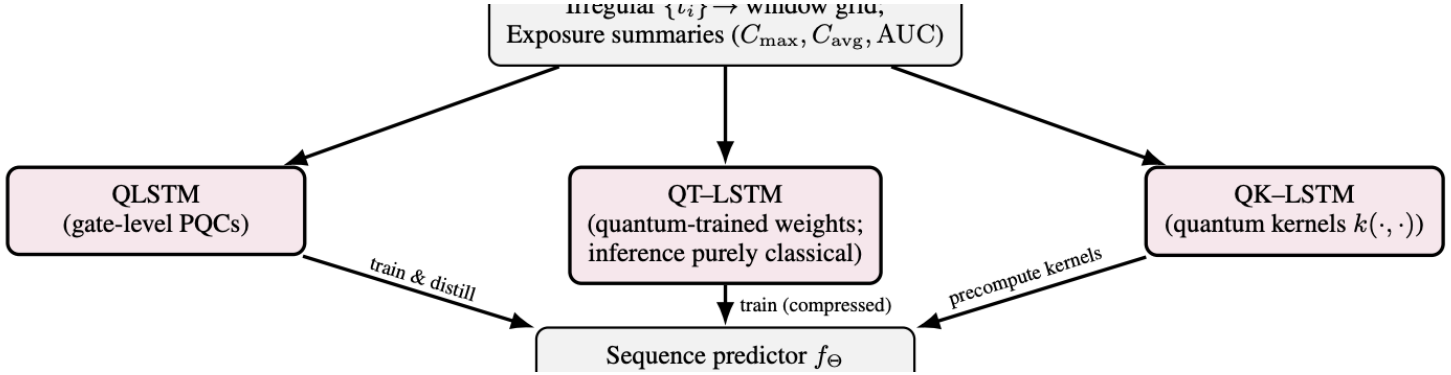


Legend

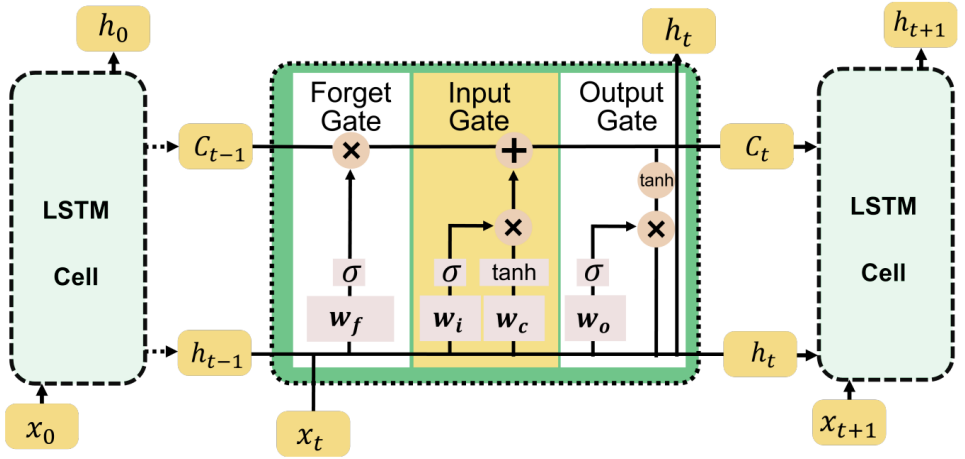
- Quantum modules (QLSTM, QT–LSTM, kernels, QMC)
- Classical preprocessing / inference
- Decision (dose policy)



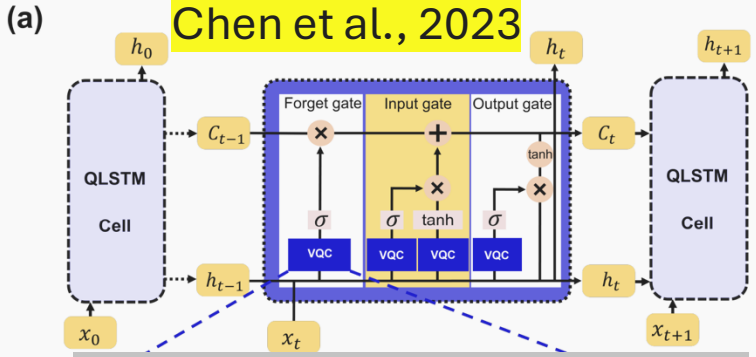
Quantum-Enhanced LSTM Model



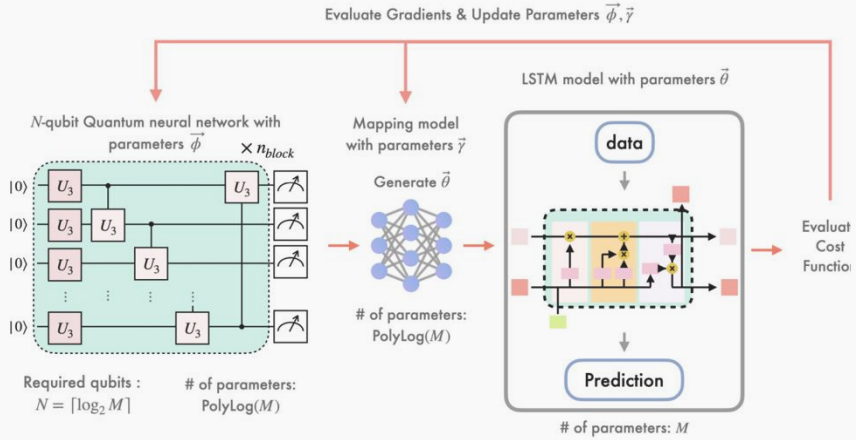
Classical LSTM Model



(1) QLSTM Model
Chen et al., 2023

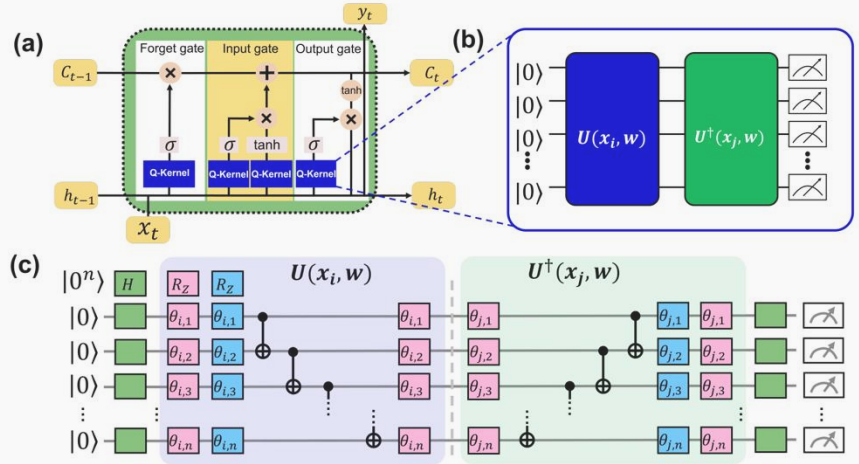


(2) QT-LSTM Model
Chen et al., 2024



Quantum advantage in space Complexity

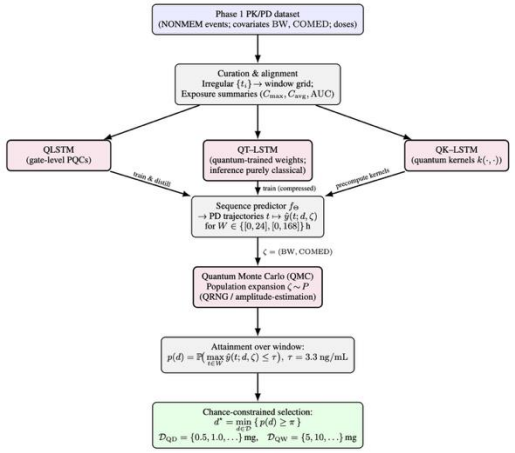
(3) QK-LSTM Model
Chen et al., 2025



Hybrid deployable architecture in Quantum-HPC

Current Result and Future Development

Decision Making Model for pharmaceutical companies:



Real-world and industrial level problems

What is the daily dose level (in whole multiples of 0.5 mg) that ensures that 90% of all subjects in a population similar to the one studied in the Phase 1 trial achieve suppression of the biomarker below a clinically relevant threshold (3.3 ng/mL) throughout a 24-hour dosing interval at steady state?

Which weekly dose level (in whole multiples of 5 mg) has the same effect over a 168-hour dosing interval at steady-state, if the compound was dosed once-weekly?

Suppose we change the body-weight distribution of the population to be treated to 70–140 kg, how does that affect the optimal once-daily and once-weekly doses?

Suppose we restrict that concomitant medication is not allowed. How does that affect the optimal once-daily and once-weekly doses?

How much lower would the optimal doses in the above scenarios be if we were to ensure that only 75% of all subjects achieve suppression of the biomarker below the clinically relevant threshold (3.3 ng/mL)

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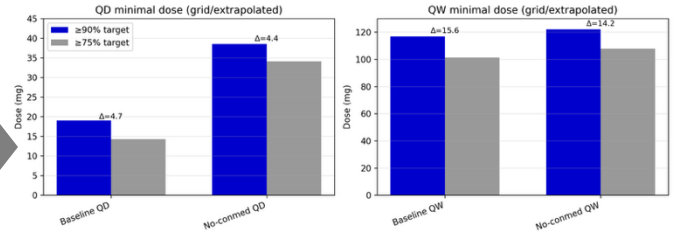
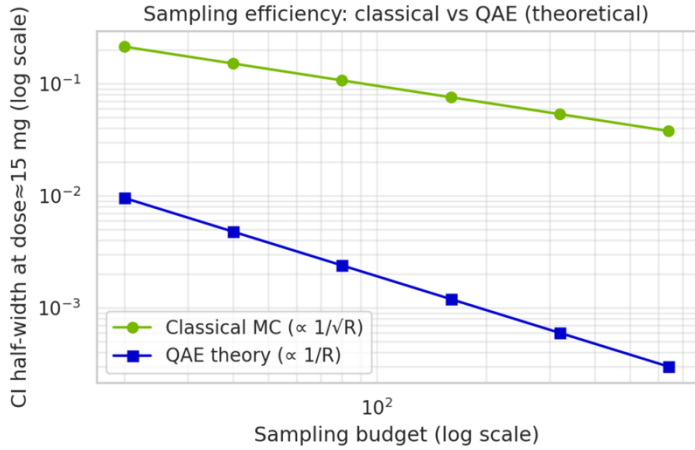
Industrial level solution

Scenario	Regimen	Dose at 90% (mg)	Dose at 75% (mg)	Reduction (mg / %)
Baseline QD	QD	19.0	**14.3**	**4.7 / 25.0%**
No-conmed QD	QD	38.5	**34.1**	**4.4 / 11.5%**
Baseline QW	QW	116.9	**101.3**	**15.6 / 13.4%**
No-conmed QW	QW	122.1	**107.9**	**14.2 / 11.6%**





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