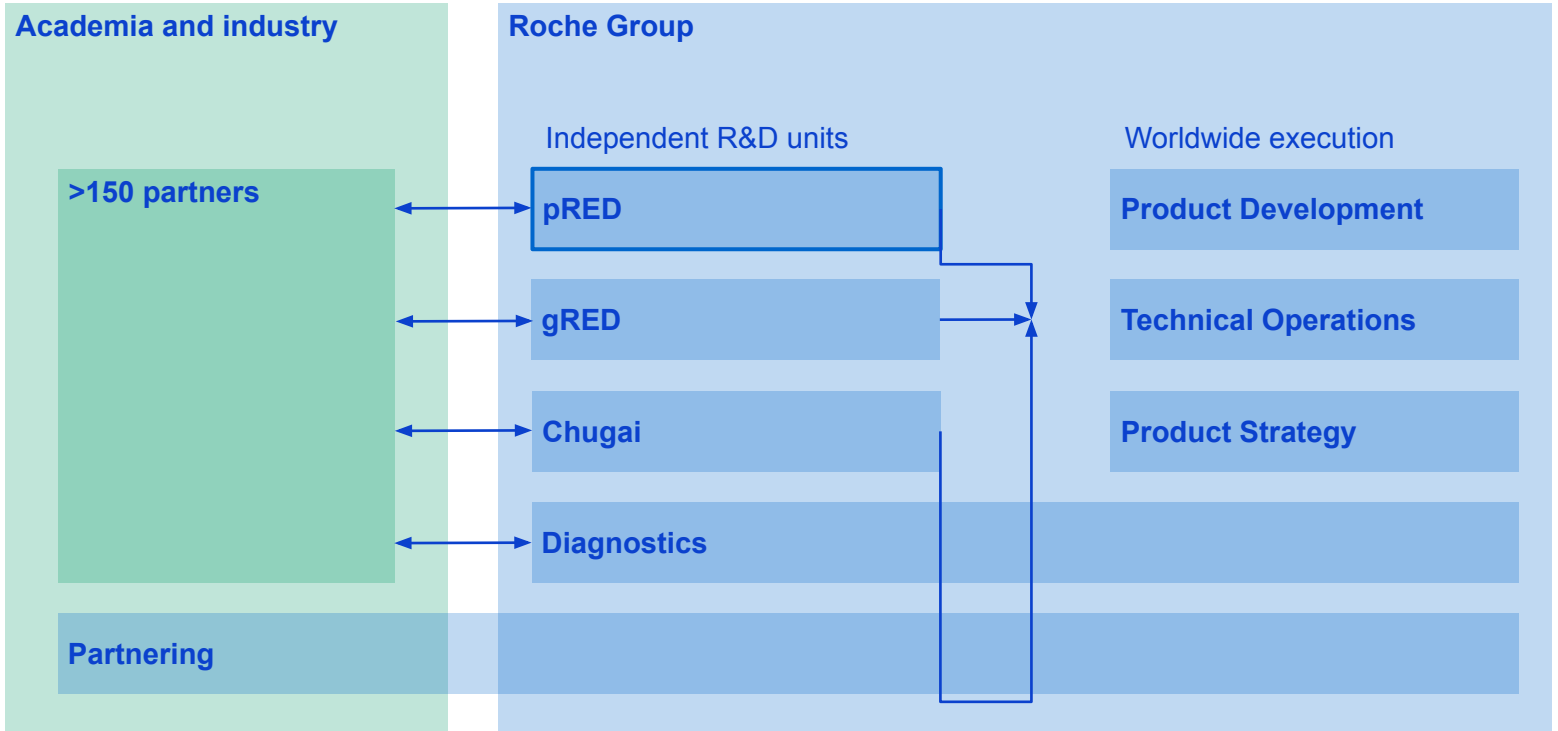
Roche Use Cases - Exploring QC's Potential for Disruption

@EuroHPC Summit Week 2022

Agnes Meyder
Roche pRED (Pharma Research and Early Development)

The Roche Group organisational structure

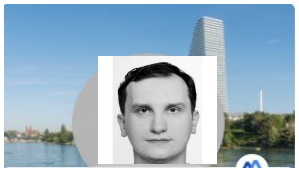
My team pRED Roche is one of three independent R&D units



Introduction to the Roche pRED Quantum Computing Team

Marielle van de Pol
pRED Informatics

Martin Strahm
pRED Informatics



Stanislaw Adaszewski
pRED Informatics

Agnes Meyder
pRED Informatics

Timothy Stitt
Group Informatics

Yvonna Li
pRED Informatics

Detlef Wolf
pRED Informatics

Clemens Wrzodek
pRED Informatics

Xavier Lucas
pRED TMo/CADD

Anna Vangone
pRED TMo/LMR

Wolfgang Guba
pRED TMo/CADD

Torsten Schindler
pRED Informatics

Our QC journey started in 2018 with a question…

How can Quantum Computing technology support drug development?

Explore

Hardware Industry

IBM

Superconducting
Gate based

Microsoft

Majorana (topological)
qubits

Google

Superconducting
Gate based

Intel

Superconducting in 2018,
Silicon spin qubits in 2021

Interviewing the Heads of Quantum computing, visiting their labs and teams to understand their QC strategy and testing our use cases with them.

This illustrates a snapshot of our journey only and is not an assessment of the companies. Technology is evolving rapidly.

Explore

Collaboration with academia

Constantin Schneider

- Quantum machine learning algorithms for the pharmaceutical industry

Dominik Schwarz

- Quantum Computing for Quantum Chemistry Simulations

Carlos Outeiral

- The prospects of quantum computing in computational molecular biology.
- Investigating the potential for a limited quantum speedup on protein lattice problems

- SABS CDT: System Approaches to Biomedical Science / Center for Doctoral Training / Oxford
- NQIT: Networked Quantum Information Technologies Hub

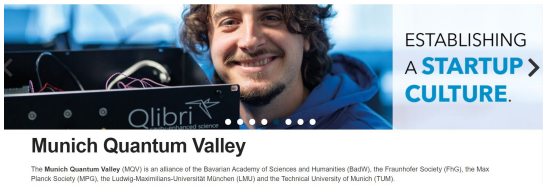
Expand

Membership and collaboration in different QC consortia worldwide

We are interested in pre-competitive collaboration for developing benchmarking, industry use cases, education and development of talent.

Memberships and collaboration:

- **Quantum Computing Industry Group - QCIG**
  DACH, since 2019
- **European Quantum Industry Consortium – QuIC**
  Europe, since 2021
- **Munich Valley**
  Germany, since 2021
- **Pistoia Alliance**
  Worldwide, since 2021



Quantum Computing Application for Pharma Research

Our scientific use cases

Covering pharmaceutical relevant applications

Chemistry	Optimization	Machine Learning
Chemistry Simulation	**Protein Folding**	**Image Classification**

The overall value of the uses cases lies understanding in what area QC will when and how much disrupt the R&D productivity:

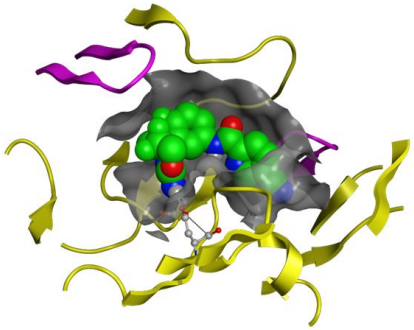
- **Chemistry Simulation:** Accurate binding affinity estimation would strongly influence efficiency in Lead Identification and Lead Optimization
- **Optimization:** Rapid identification of minima would strongly influence the whole pipeline of pRED and many other Roche units.
- **Machine Learning:** If Machine Learning is impacted by QC, better predictions would impact areas from Target Assessment to the Clinic.

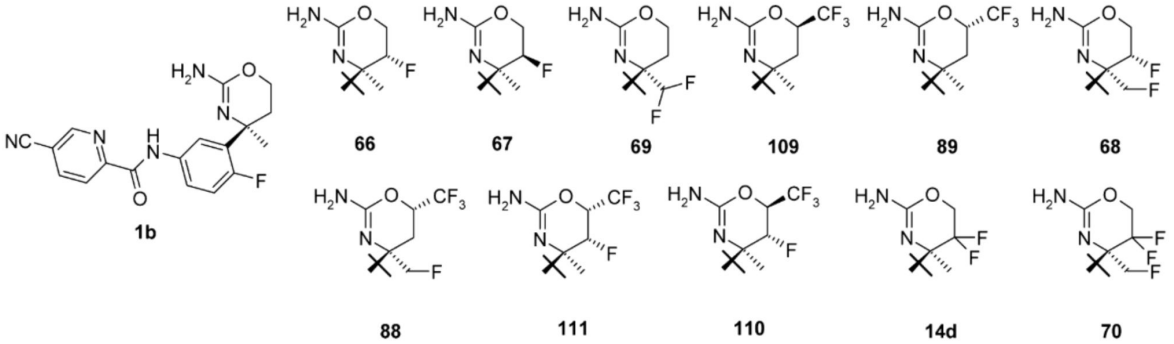
Chemistry Simulation: Protein/Ligand Binding

Binding affinity prediction for BACE-1

- Dataset published by Roche with enzymatic inhibition data for 12 ligands (pIC50 range: 6 to 8)
- X-ray protein-ligand structures publicly available for all molecules
- No significant changes in conformation of binding pocket (limited reduced fit)
- Ligand modifications only in oxazine head group (see below)

Goal: rank-ordering by calculated binding affinities and correlation with IC50 data

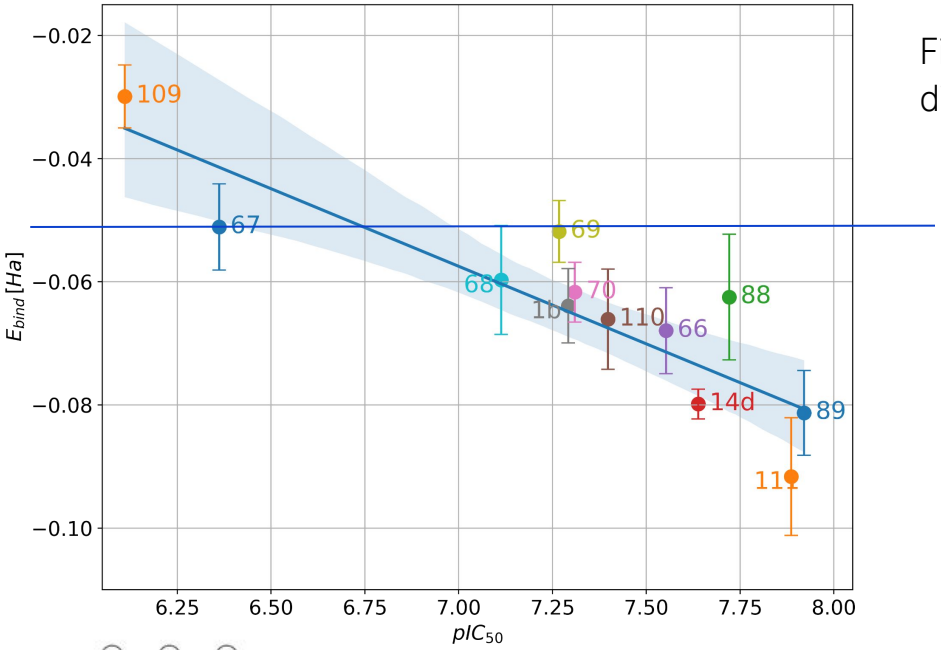


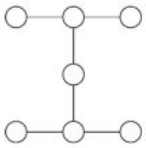


Hilpert, H. et al. (2013). β-Secretase (BACE1) Inhibitors with High in Vivo Efficacy Suitable for Clinical Evaluation in Alzheimer's Disease. Journal of Medicinal Chemistry, 56(10), 3980-3995. doi:10.1021/jm400225m

Results on current IBM and Honeywell Hardware Systems

Superconducting Transmon (IBM) and Ion Trap (Honeywell) devices were tried





IBM casablanca (7 qubit) machine

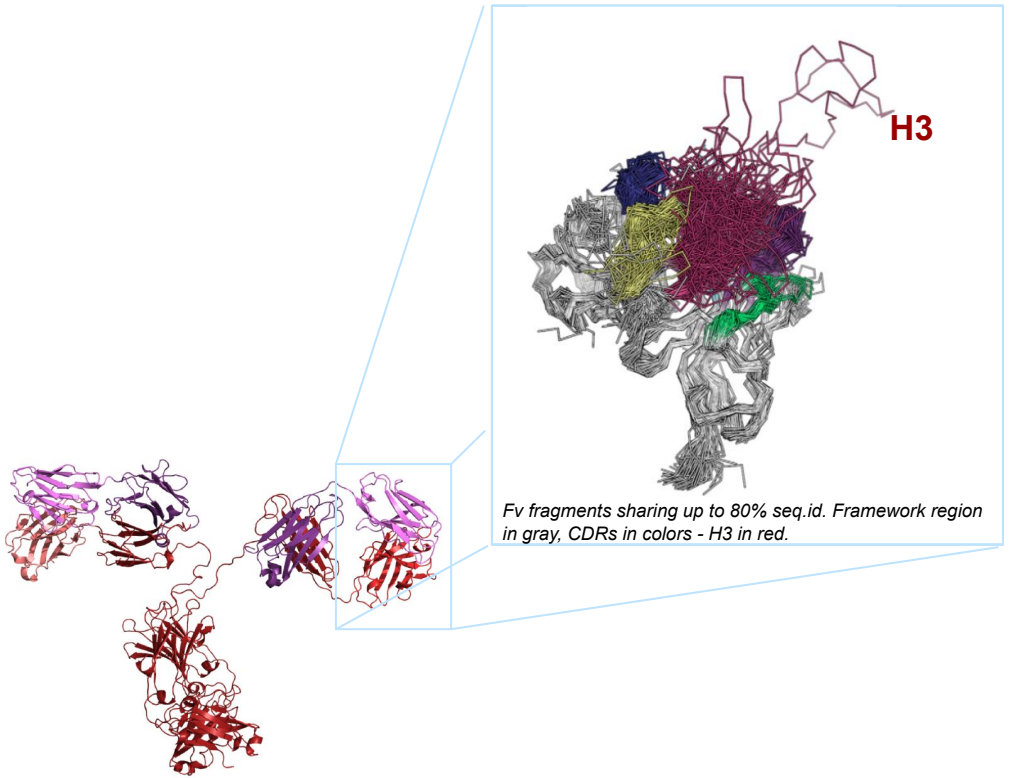
First evaluation of a data set relevant for drug discovery on actual Quantum Hardware.

- IBM: 7 qubit machine, 60 000 runs. One run takes 20 minutes.
- Honeywell: 13 qubit Machine, 8 000 runs. One run takes 1.5 hours.
- Error bars are based on defining 10 batches and taking their errors.
- The inhibitors can not yet be properly classified into two distinct groups (pIC50 < 6.5 vs. pIC50 > 6.5)

Public preprint: https://arxiv.org/abs/2110.08163

Use Case: Protein Folding

Modeling of H3 antibody loop



Fv fragments sharing up to 80% seq.id. Framework region in gray, CDRs in colors - H3 in red.

Maks & Deane, Comp and Structural Biotech. 2017

Antibody structure in drug development:

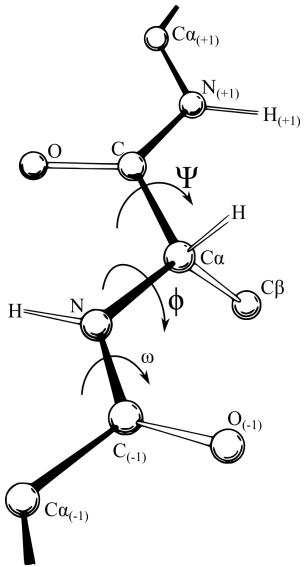
- Rational design and engineering
- Binding affinity modulation
- Improve stability
- Colloidal properties

In silico structure prediction:

- Experimental determination not suitable for large scale
- In silico prediction of Fv
- H3 loop the most variable in length and sequence

Classical methods to predict H3 properties

Finding the energy minima with Force Fields



Bond stretch | Bond Angles | Dihedral angles

$$E_{\mathrm{CHARMM}} = \sum_{bonds} k_b(b-b_0)^2 + \sum_{angles} k_\theta(\theta-\theta_0)^2 + \sum_{dihedrals} k_\varphi\left[1+\cos(n\varphi-\delta)\right]$$

Tetrahedron angles

$$+ \sum_{impropers} k_\omega(\omega-\omega_0)^2 + \sum_{Urey-Bradley} k_u(u-u_0)^2$$

1,3 non-bonded angles

$$+ \sum_{non-bonded} \left(\epsilon \left[\left(\frac{R_{ij}^{min}}{r_{ij}} \right)^{12} - \left(\frac{R_{ij}^{min}}{r_{ij}} \right)^{6} \right] + \frac{q_i q_j}{\epsilon r_{ij}} \right)$$

Most time consuming → Atoms in the vicinity of any atom

Equation minimization will take years on Quantum Devices

... when using the classical approach on Quantum Hardware

	n_{steps}	t_{step}	**Total time**	**Logical qubits**
Classical[1]	$4x10^{9}$	$2.3x10^{-4}$s	10.6 days	-
Quantum (serial)	$8.9x10^{4}$	25.2 hours	256 years	~ 10^{4}
Quantum (parallel)	$8.9x10^{4}$	16.4. mins	2.8 years	~ $4x10^{4}$

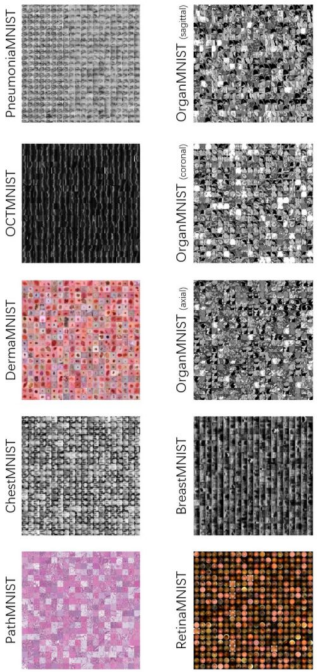
(10 amino acids with each 20 atoms and a 16 bit angle representation)

Public preprint: https://arxiv.org/abs/2105.09690

1: Jakob et al, JACS 2004.

Quantum Machine Learning on Medical Data

Image Classification



Medical imaging is an area of active research in the machine learning community; deep learning delivers promising performance in classification, segmentation etc.

- Disadvantage: very large architecture, compute intensive and require large amounts of training data

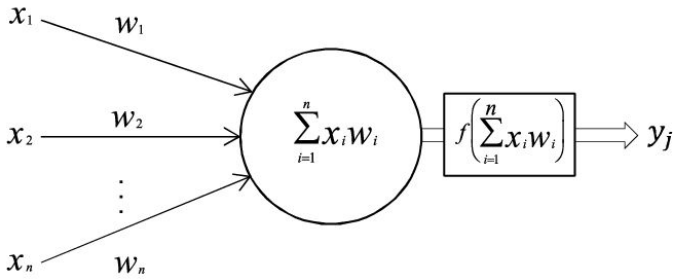
Goal: does QC offer the potential to improve the efficiency and accuracy of DL algorithms?

Supervised Machine Learning with Quantum Circuits

Experiments

Artificial neural networks:

- Model as series of matrix multiplications
- Leverage QC's inherent advantage in linear algebra operations and higher dimensional Hilbert space



Approach:

- Evaluate our data set on state of the art quantum computers on quantum assisted NNs (QANN)
- Explore the capability of orthogonal NNs (ONN) on current quantum computers

Architecture:

- QANN: 4,4,2 and 8,4,2 with sigmoid activation function
- ONNs: 4,2 and 8,2 (no hidden layer)

Results in QML

Currently:

- Comparable accuracy on small scale
- Validated polynomial speed up on orthogonal NN
- Also developed quantum inspired classical algorithm with speed up on training

Challenges:

- Hardware is still too noisy to train deeper/larger networks
- Competing against highly efficient GPUs

Public preprint: https://arxiv.org/abs/2109.01831

Conclusion

- The benchmarks from our use cases make it possible for us to compare new developments against our needs and understand where we need to focus our efforts.
- More investment into fundamental QC research is necessary. Cooperation with QC industry and users of QC technology is vital.
- We need to ensure that our understanding of the QC algorithms is complete when the HW is ready for commercialization.

Chemistry

https://arxiv.org/abs/2110.08163

Optimization

https://arxiv.org/abs/2105.09690

Machine Learning

https://arxiv.org/abs/2109.01831

Doing now what patients need next