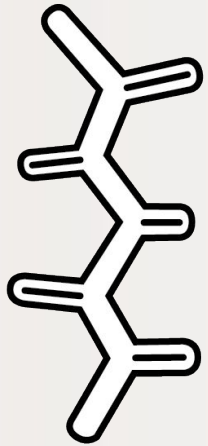


ProteinQure

The Quantum Landscape

ProteinQure

Computational drug discovery employing machine learning and quantum computing

Contact us!

lucas@proteinqure.com

Or visit our blog to learn more @ www.proteinqure.com

Comp. Methods in Drug Design Review

Structure-based

- Binding site identification
- Pharmacophore modelling
- De novo protein modelling
- Docking / virtual screening
- Molecular dynamics / FEP
- Protein-protein docking

Ligand-based

- Ligand similarity search / scaffold hopping
- Conformational search
- Ligand-based virtual screening
- Library design
- QSAR

Other algorithms (Structural biology, Quantum Chem, ML)

- ADME/Tox prediction
- pKa prediction
- Membrane permeability
- Decision-making algorithms
- Statistical modelling
- Electronic structure calcs.
- Sequence alignment / homology modelling
- Crystal structure prediction

Applications

What is a quantum computer good for?

Existing Quantum Algorithms

Algorithm	**Known Application Domains**
Factoring (Shor's Algorithm)	Cryptography (Cracking RSA encryption)
Search/Optimization (Grover Search)	Circuit design, Graph theoretic problems, Pattern Matching, Annealing
Quantum Simulation (Kivlichan/Babbush)	Dynamical properties of quantum systems, Quantum chemistry (predicting chemical properties)
Random walks (Quantum walk)	Markov chains, boolean logic, financial derivatives
Solving Linear Equations (HHL Algorithm)	Linear algebra (broad impact area), least squares fitting,
Machine Learning (Quantum-assisted Helmholtz machine)	Training neural networks, Autoencoders

Applications in Bio./Chem.

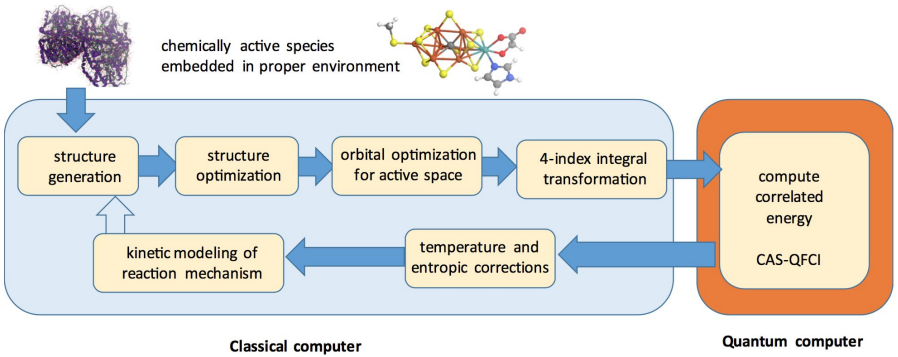
What are intersections for quantum computing in pharma workflows?

Quantum Chemistry

Elucidating reaction mechanisms on quantum computers

Markus Reiher[a,1], Nathan Wiebe[b,1], Krysta M. Svore[b], Dave Wecker[b], and Matthias Troyer[b,c,2]

[a]Laboratorium für Physikalische Chemie, ETH Zurich, 8093 Zurich, Switzerland; [b]Station Q Quantum Architectures and Computation Group, Microsoft Research, Redmond, WA 98052; and [c]Theoretische Physik and Station Q Zurich, ETH Zurich, 8093 Zurich, Switzerland



Encoding Electronic Spectra in Quantum Circuits with Linear T Complexity

Ryan Babbush,[1,*] Craig Gidney,[2] Dominic W. Berry,[3] Nathan Wiebe,[4]
Jarrod McClean,[1] Alexandru Paler,[5] Austin Fowler,[2] and Hartmut Neven[1]

[1]*Google Inc., Venice, CA 90291, United States*
[2]*Google Inc., Santa Barbara, CA 93117, United States*
[3]*Department of Physics and Astronomy, Macquarie University, Sydney, NSW 2109, Australia*
[4]*Microsoft Research, Redmond, WA 98052, United States*
[5]*Institute for Integrated Circuits, Linz Institute of Technology, 4040 Linz, Austria*
(Dated: May 11, 2018)

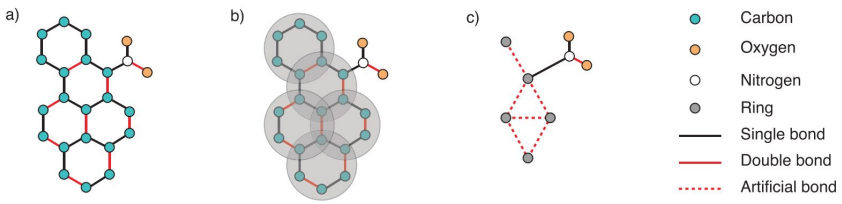
Very exciting capabilities to model electronic structure.

Google estimates 1 million qubit quantum computers would be required for electronic structure simulations. Not available in the near-term.

Molecular Similarity Search

A Novel Graph-based Approach for Determining Molecular Similarity

Maritza Hernandez, Arman Zaribafiyan, Maliheh Aramon, Mohammad Naghibi

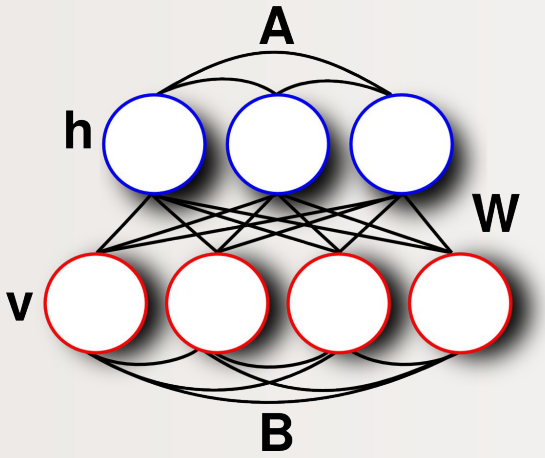


Biogen IQBit

Modelled search as quadratic unconstrained binary optimization, yielding higher accuracy when solved on a quantum annealing device (D-Wave)

Suppl. References:
Graph-based methods for molecular similarity search. Hernandez et et al. arxiv (2016)

Statistical Modelling (ML)



Quantum annealing versus classical machine learning applied to a simplified computational biology problem

Richard Y. Li, Rosa Di Felice, Remo Rohs ✉ & Daniel A. Lidar ✉

Quantum machine learning most valuable for applications with <u>sparse data and complicated probability distributions</u>

Big data approaches are far away (5+ years), but clever short term applications may exist

Quantum annealing for binding prediction
Li, Richard et al.
npj Quantum Info (2018)

Suppl Reference:
Biamonte et al. (2017). *Nature*, *549*(7671), 195.

Comp. Methods for Near-term QCs

Structure-based

- Binding site identification
- Pharmacophore modelling
- De novo protein modelling
- Docking / virtual screening
- Molecular dynamics / FEP
- Protein-protein docking

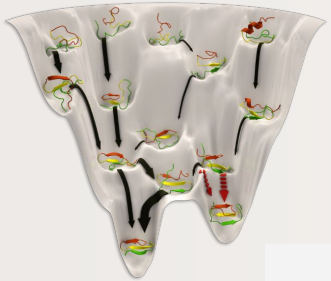
Ligand-based

- Ligand similarity search / scaffold hopping
- Conformational search
- Ligand-based virtual screening
- Library design
- QSAR

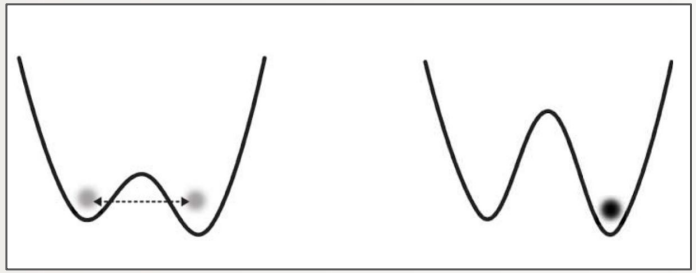
Other algorithms (Structural biology, Quantum Chem, ML)

- ADME/Tox prediction
- pKa prediction
- Membrane permeability
- Decision-making algorithms
- Statistical modelling
- Electronic structure calcs.
- Sequence alignment / homology modelling
- Crystal structure prediction

Protein Folding



Protein folding landscape



Quantum Annealing, D-Wave (2012)
Tunneling helps find optimal solutions

Use optimization algorithms to perform coarse-grained protein folding. Quantum annealing allows tunneling in rugged energy landscapes that speeds up folding.

Coarse-grained lattice protein folding on a quantum annealer

Tomas Babej,* Mark Fingerhuth,† and Christopher Ing‡
ProteinQure Inc., Toronto, Canada
(Dated: May 18, 2018)

A quantum alternating operator ansatz with hard and soft constraints for lattice protein folding

Tomas Babej,* Mark Fingerhuth,† and Christopher Ing‡
ProteinQure Inc., Toronto, Canada
(Dated: April 24, 2018)

ProteinQure Whitepaper I and II (http://www.proteinqure.com)

Hybrid (classical + quantum) approaches viable in the next 2 years

Docking

Pose generation using graph-based representation of pharmacophore and ligand (DOCK algorithm). Semi-flexible, no water.

Pharmacophore-based scoring function developed by ProteinQure being benchmarked.

Hybrid (classical + quantum) approach is viable here.

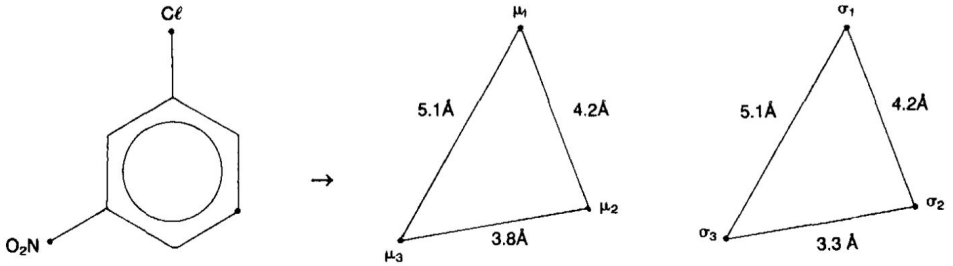


Figure 2. Example of site and molecule points.

Quantum algorithm for atomistic ligand-protein binding pose determination with electrostatic potential

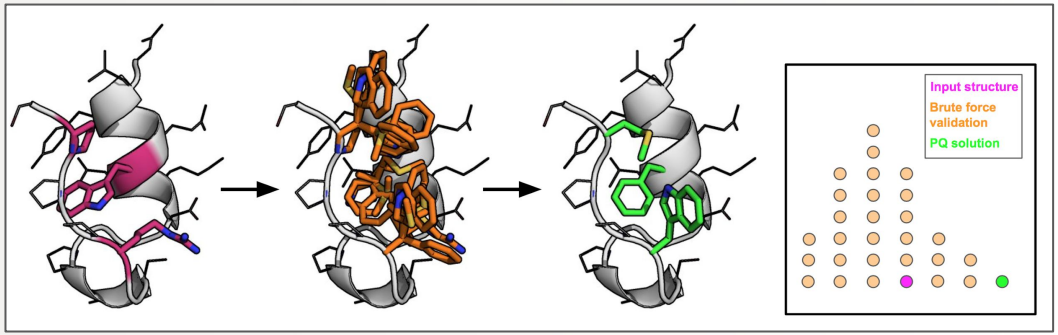
Tomas Babej,* Mark Fingerhuth,† and Christopher Ing‡
ProteinQure Inc., Toronto, Canada
(Dated: May 18, 2018)

A Combinatorial Algorithm for Calculating Ligand Binding
Kuhl et al.
J. Comp. Chem. (1984)

Conformational Sampling

Protein design algorithms require fragment assembly/sidechain packing which involve combinatorial optimization

Hybrid (classical + quantum) approach is under development, and will have applications for small molecule ligand binding projects



Quantum computational protein design

Aron Broom, Tomas Babej, Christopher Ing, and Mark Fingerhuth*
ProteinQure Inc., Toronto, Canada
(Dated: November 2, 2018)

Quantum strategy

How does the present and future look like?

Quantum hardware: the big players

Universal Superconducting Quantum Computers

Quantum Annealers

Digital Annealers

Other Universal QC Hardware

The hardware architectures are very different, need to experiment for your applications

It is difficult to do apples to apples comparisons (e.g. determining which is the best)

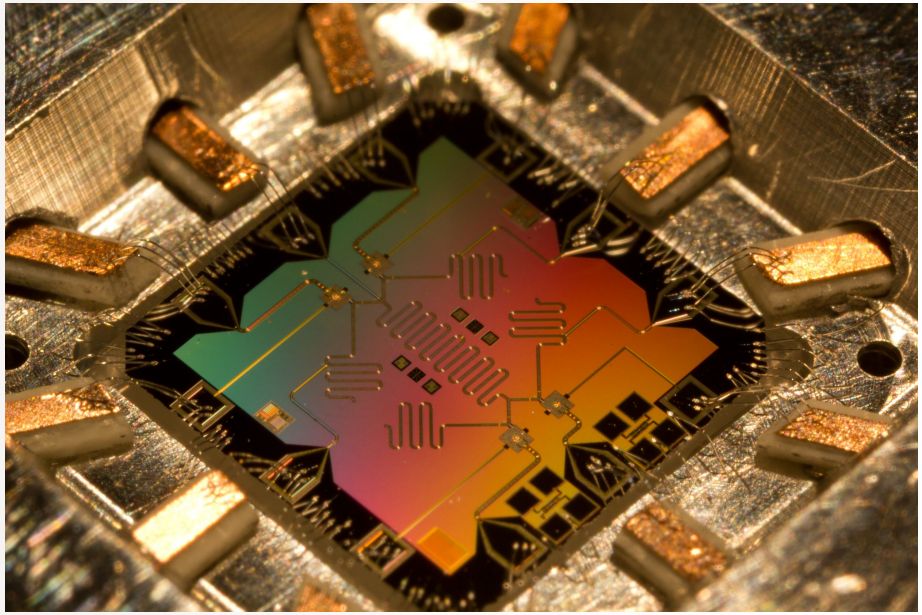
Quantum computing metrics

Key measurements of quantum ‘horsepower’

- # of qubits: How big a calculation can we do?
- Connectivity: How connected are the qubits?
- Circuit depth: How many operations can you perform on each qubit?
- Error rates: How likely are the calculations to be correct?

There are tradeoffs between attributes, but hardware providers are trying to demonstrate ‘quantum computational supremacy’

- E.g. find a problem where the quantum computer is better than classical computers
- Different problems require different performance metrics

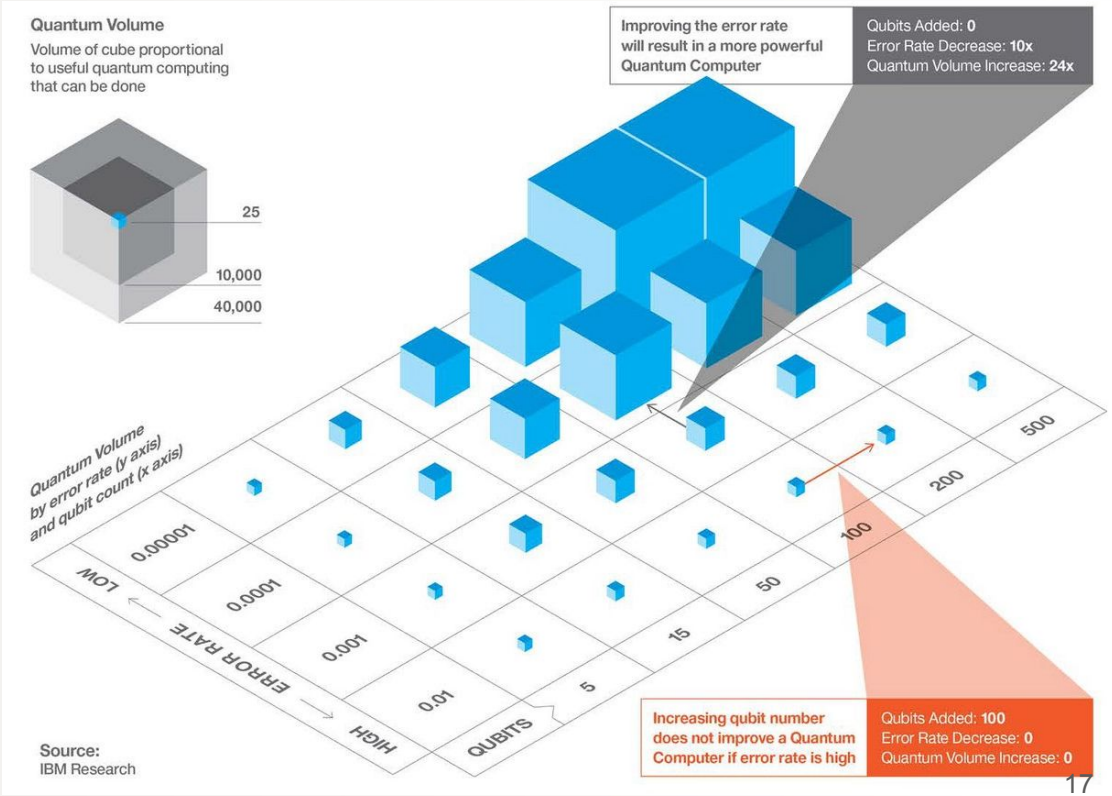


Quantum volume

(metric of performance)

IBM has tried to come up with a catch all term to represent computational power: "Quantum Volume"

- Combines many metrics into a single number representing computational capability
- Incorporates the ultimate goal of lots of qubits with low errors



Source: IBM Research

Current State (Nov 2018)

Metric	Current Best	Requirements for *Quantum Computational Supremacy*[1]
# of qubits	72[2]	200+
Connectivity	Pairwise	Pairwise connectivity likely to be standard for medium-term
Circuit depth	40	1500
Error Rates	0.5%	0.5%

[1] Estimates for commercial problems by PQ team (https://arxiv.org/abs/1805.05224, https://www.nature.com/articles/nature23458)
[2] Google's Bristlecone (https://ai.googleblog.com/2018/03/a-preview-of-bristlecone-googles-new.html)

Quantum computing - what's next?

What do the experts say (IBM Q conference - Dec 2017)?

Quantum chemistry large-scale application: **5-10 years until fruition**
Fully error-corrected quantum computer: **10-15 years until fruition**

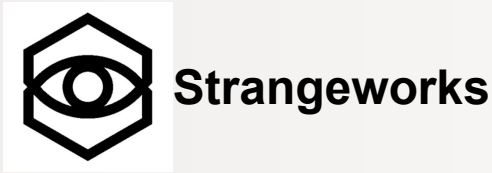
BUT!

Near-term quantum computing (2-3 years) can be powerful if you know what you're doing.

- clever hybrid algorithms
- treating it as a subcomponent for heavy lifting

Quantum software: the players

General quantum software:



Dedicated life science applications:

Advice becoming a quantum-ready company

Quantum developers are needed but almost non-existent

- Hard to convert classical programmers
- Super low-level programming (machine instructions)
- Combines expertise in multiple extremely technical fields
- Few dedicated courses, need to interact with the ecosystem to find talent

Within the next **2-3 years** be more focused on proof-of-concept and ensuring you are on the **frontier of high performance computing**

- advantage since no one knows when quantum supremacy will be achieved (advances are happening faster than people expected)

Technical Appendix: Classical vs. quantum

A short overview of computation

Resources to learn more

Quantum computing explained
http://www.wired.co.uk/article/quantum-computing-explained

Quantum computational supremacy explained
https://www.youtube.com/watch?v=90U_SmKyfGI

Quantum computing Q&A
https://quantumcomputing.stackexchange.com/

A gentle introduction to quantum mechanics
https://www.amazon.com/Quantum-Mechanics-Theoretical-Leonard-Susskind/dp/0465062903/ref=sr_1_3?ie=UTF8&qid=1524601465&sr=8-3&keywords=the+theoretical+minimum

Quantum machine learning incubator

Quantum Machine Learning Program

Mission

By 2022 the QML Program will have produced more well- capitalized, revenue generating quantum machine learning software companies than the rest of the world combined. The majority of these will be based in Canada.

CREATIVE DESTRUCTION LAB