# Computational Infrastructure for Modern Pharmaceuticals

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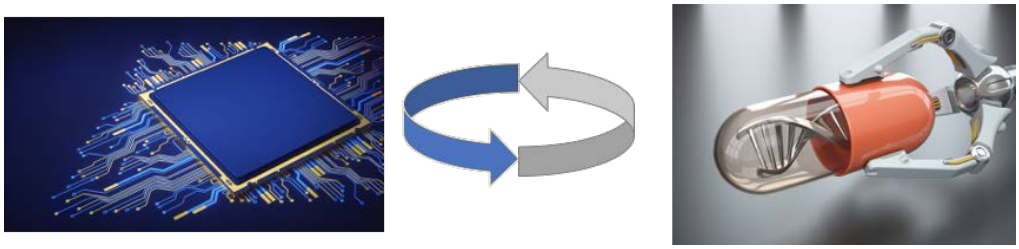
Over the last 150 years, the pharmaceutical industry has gone through different phases of transformation. Every phase incorporated new technologies of the time: Synthetic chemistry in the late 19th century, molecular biology after WWII, and bioengineering in the late 20th century. In the last few years, we have been observing the beginning of another leap that is incorporating advanced computing technology and robotic automation. The word *modern* in the title refers to another phase of modernization. Here we intend to have a brief look into how this transition is happening and why new computing technology is required to accelerate this transition. Specifically, we will discuss the role of special-purpose silicon and quantum processors.

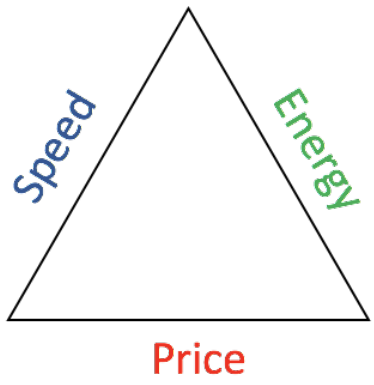
Pharma is a unique industry when it comes to reliance on new scientific development. A pharma business grows as its scientific discovery grows, in particular this is the case for first-in-class therapeutics. When a novel drug passes clinical tests, there is not much of a market barrier such as we see in other areas of technology (for instance solar energy), where pricing and production costs become marketing factors. In pharmaceuticals, the barrier is the science itself. The digital-robotic technology that is transforming pharma industry, at the fundamental level, is transforming scientific research in biology and chemistry. Massive automated collection of biological data boosted by AI and Machine Learning techniques is a powerful tool for the biologist to create and evaluate their hypothesis behind mechanisms of disease, leading to fast discovery of new therapeutic targets. On the chemistry side, computational simulation of macro- and small molecules have become a common workhorse for drug discovery/design. The question is whether the current computing infrastructures have the capacity and are designed to support the growth of pharma R&D? The answer is no, a paradigm shift is in need toward pharma-specific hardware-software infrastructure.



Digital-Robotic Technology for Pharmaceutical R&D

Let's look at some resource requirements for computational drug discovery/design where the whole scope of pharma R&D and its computational need is much broader. One fundamental and computationally demanding task in drug design is simulation of protein dynamics. Use cases are assessing drug molecule binding to a target protein, or studying protein misfolding in connection with neurodegenerative diseases. A typical simulation captures a system of tens of thousands of particles with an internal dynamics that spans 15 orders of magnitude time-scale from femtosecond to second, which is an expensive computation. Molecular dynamics simulations became commercially relevant (being employed in actual drug discovery projects) with the arrival of GPUs, where disruptive hardware technology brought known scientific methods into commercial use. The envisioned transition in R&D is about moving from expensive erroneous bench tests to reliable computer simulations and automated experimental verifications. We have just entered this paradigm shift which would form the backbone of pharma industry in the 21st century.

Further progress is impeded by three factors: cost, speed, and energy consumption of computing. Take the accurate prediction of a candidate drug binding to a cancer-causing protein. Such computation would cost ~$1-10 given $1 per GPU-hour on the cloud. This is about assessing one molecule in the chemical space of drug-like small molecules, a space with an estimated size of$10^{60}$ molecules. The global wealth is less than $10^{15}$ USD. Going beyond small molecules, more recent and more complex therapeutic approaches such as antibodies are more challenging for computational design. The ultimate goal is practical simulation of the whole cell to find the mechanism of diseases at the molecular level, a task that currently requires few months of simulation on the largest supercomputers. In order to reach our grails, we need to push the frontiers of computing power up and the price down.




Domain-Specific Computing optimizes for higher speed, lower energy consumption, and lower price

**New Computing Frontier for Pharma R&D:**

Post-GPU processors and domain-specific hardware/software co-design are seeding a new age in computing technology, what can impact pharma industry. How next generation processors find applications in pharmaceutical business is exemplified for ASIC and quantum chips:

**Application-Specific Integrated Circuit:** Building special-purpose processors could be the next step for pharma technology. If we want to mainstream molecular dynamics simulations of quantum chemistry calculations, we should think of ASIC chips. ASCIC and potentially FPGA bring speed and energy efficiency for computation. The cost of ASIC design and software development would not exceed a few million dollars and a one time cost. Even a few percent improvement in success of drug projects, and the investment is justified. This class of silicon processors can be readily employed for commercial applications.

**Quantum Computers:** Near-term quantum processors, computers that use quantum mechanics for computing, have one serious candidate application that is accurate modeling of molecules or finding their energy structure. Molecules are quantum objects and their accurate simulation on classical computers rapidly become impossible with the size of molecule growth. With our current method for simulating biomolecules, we are still struggling to model basic building blocks, such as water molecules or polarizable molecules. Quantum processors, if the hardware at a reasonable size (1000-10000) qubit becomes available, can come in as a game changer. Accurate simulation of biomolecules is the core of computational drug design, so quantum processors is a technology to follow closely. Front runners in quantum computing hardware technologies are superconducting circuits, trapped ion, and photonics, each with their own technological barriers for scalability.

**Computing for Pharma R&D:** We discussed some specific problems and solutions in the area of computational drug discovery/design. Digitization and automation of pharma R&D embrace a much broader spectrum of computational problems such as big data and biology discovery, intelligent experiment design, decentralized private data-sharing, precision medicine, etc. For all these, besides the hardware, we need to consider native softwares. Commonly referred to as hardware-software codesign, it adds another layer of efficiency and acceleration, which is another area that requires investment. We are entering the age of accelerated therapeutic discovery driven by digitization and robotics. The support technologies need to scale at a fast pace to modernize the pharmaceutical industry in the 21st century.