

Rational Design Re-Emerges to Change Up Drug Discovery

"If we designed airplanes like we design drugs..." alludes Walter Woltosz, CEO and Chairman of Simulations Plus, then you probably wouldn't feel very safe on an airplane!

Rational drug design took the pharmaceutical industry by storm in the 1990s, a decade that spawned a series of fast and furious investments in the deserts of the Southwest.

The holy grail quickly turned into an elusive and dried up fountain of youth in the hot desert sands, leaving the area empty and desolate. The Billion-Dollar Drug was true, but mostly in cost and not in profits.

With new understanding from basic research and advances in molecular simulations, rational drug design now re-emerges, with the potential to shake up the pharmaceutical industry and provide benefits to both customers and drug developers.

The Old Way: Trial and Error in Drug Discovery

Most drugs were discovered through a series of trial and error, experimentation and desperation. Centuries before penicillin was accidentally discovered by Alexander Fleming in a petri dish in 1928, ancient Serbians, Chinese, and Greeks used moldy bread to rub into wounds to prevent infection.

Fast forward many hundreds of years, and scientists are still in the era of trial-and-error and accidental discovery, except that we've replaced humans with animals and biomarker experimentation.

It's important to draw the line between drug development and design. Common medicines used today, like Tylenol and penicillin, were never designed. We discovered and then manufactured them. In fact, we still don't know how these drugs work, but we can sure be grateful that they do.

A New Way: Drug Design

After a decade of Moore's law of computation rapidly increasing our ability to model complex systems, combined with nano-scale research on how molecules talk to each other, the trend of rational drug design re-emerges, poised to refine away the side effects of existing drugs and lay the groundwork for designing new ones.

Over the next 3 weeks we will discuss the trend towards design in drug discovery: first by reviewing basic research;

second by exploring novel techniques used to design drugs more effectively; and finally by observing how biotech startups are working to bring these treatments to patients.

Before we dive in though, let's check the water level and take a look at the current state of the pharma industry.

One of the largest drivers of cost in the pharmaceutical industry is the high rate of failure and cost of experimentation. On average, 19 out of 20 drugs fail and a human clinical trial, the last step to market, can cost up to \$100 million each. Successful drugs cost \$1-500 million to develop; if you take the other 19 failed drugs into account, the cost rises to \$2.6 billion per drug, with less than 20% of the cost dedicated to development of the successful drug itself. In general, the process often takes over 10 years in time, making drugs both a costly and high risk investment. The higher the risk, the higher the reward needs to be, which can lead to aggressive and hyper-competitive business behavior, often reflected back to consumers in terms of Shkreli-high prices for medicine.

Is there a way that we can reduce the experimentation phase by prefacing it with rational design? If only 2 out of 3 drugs fail, instead of 19 in 20, you can cut costs by a factor of 4, a savings of nearly \$2 billion per drug, enough to bring almost three other drugs to market. It's a buy-one-get-three-free deal.

Where's the Catch?

Our ability to design drugs is limited by a lack of fundamental understanding of the structures of molecules and the physics of drug interactions. Our understanding is limited by how fine our vision is and how fast our brains work. Technological advances allow our vision to become finer, our hands smaller, and our brains faster with the aid of computational power and molecular simulations. By using design and simulations, researchers and drug manufacturers can know which drugs will fail before spending costly human-hours and dollars in development and testing.

Up Next Week: Research in Medicine

Learn about the new nano-scale research exploring the common molecular and structural roots of diseases like Alzheimer's and Type II diabetes.

What is Compassionate Technologies?

Each Sunday we deliver to your doorstep an inspirational and educational piece describing a certain trend in technology and business.

We go from small to large throughout the year. This month focuses on Drug Design in Medicine, progressing up to topics in robotics, artificial intelligence, environmental and then space technologies.

Each month has four parts:

- 1st Sunday: Trends**
- 2nd Sunday: Research**
- 3rd Sunday: Technology**
- 4th Sunday: Business**

To keep our doors open, fund interviews with top scientists and industry players, and to continue hosting local events, we charge \$150 per year for 52 print weeklies.

While we're getting started, I'm doing free deliveries in my neighborhood for the month of June. Please enjoy and consider joining me on this journey!

Kindly yours,

Olivia Jeffers

Thoughts?

Email me at olivia@compassionate-technologies.org
Signup at www.compassionate-technologies.org

"Health is the greatest gift, contentment the
greatest wealth, and faithfulness the best
relationship." - Buddha