White Paper

Medicine in the Age of AI

By Neal Solomon
CEO, Gemini Corp.

Gemini Corp.
1 Sansome St., Ste. 1400
San Francisco, CA. 94104

(415) 334-5600

The Era of Intelligent Medicine

Personalized medicine is defined as a set of technological tools applied to diagnostics and therapeutics that identify and treat the unique genetic sources of disease. In the case of oncology, for example, each individual's cancer has a different combination of unique genetic mutations; when these genetic mutations are diagnosed, specific targeted therapies may be designed for these unique mutations.

In recent years, we have observed parallel revolutions in information technology and genomics. In the case of genomics, bioinformatics provides valuable insights into genomics, proteomics and epigenetics. Genomics plays a role in ninety percent of the top causes of death. In the case of information technology, data analytics and artificial intelligent provide insight into complex problems and provided access to accelerated solutions. These fields are converging. As an example, AI is supplying tools for accurate medical diagnostics.

The application of AI tools to personalized medicine is a natural one. While bioinformatics analytics supplies insight into dysfunctional genes, structural proteomics and dysfunctional proteomics, applying AI to bioinformatics provides acceleration of observational patterns. Increasingly, biomarker tests are able to backward engineer the realization of individual gene mutations and their protein dysfunctions. AI applied to diagnostics is analogized to finding solutions to a complex puzzle with limited information.

In addition to bioinformatics analytics, imaging diagnostics supplies valuable observable insight into diagnostic solutions. Here, too, AI supplies valuable analytical tools for pattern recognition of observable imaging diagnostics. Without imaging diagnostics tools, early disease detection would be hampered.

Personalized medicine is increasingly focused on diseases that derive from genetic mutations, on orphan genetic diseases, on inherited diseases and on complex multi-variate diseases. Applying AI to solve these specific combinations of unique genetic challenges provides a clearer and more complete picture of the sources of diseases. AI also supplies tools for early disease detection.

The goal of diagnostics in personalized medicine is to obtain increased precision of the sources of diseases. In this sense, biomarker data supply genetic and proteomic dysfunction insights on the molecular and cellular levels. Only by understanding the source of a disease on a molecular and cellular level can precise therapies be identified. The unique details of each individual's specific health situation are identified by applying AI tools to precision medicine.

The paradigm case of the application of AI to precision medicine is the emperor of all maladies, cancer. Virtually all cancers are caused by some combination of genetic mutations. If we can identify these unique mutations, therapeutic solutions may solve the genetic dysfunction on the cellular level by applying corrected formed and precisely targeted proteins. Whereas it required millions of dollars to analyze an individual's genome twenty years ago as the field was emerging, it now costs less than a thousand dollars, with another similar test for relevant biomarkers.

But much of medicine, beyond oncology, requires the discovery of genetic or epigenetic mutations as the source of diseases. Several thousand conditions have a molecular origin. About fifteen percent of genes, out of 30,000 active human genes, cause perceptible diseases from genetic mutations. For example, 2-6% of the population have a genetic disease. These

diseases present a complex diagnostic challenge.

In many ways, the diagnostic medical challenges present only the initial set of problems for drug research. Once the genetic medical problems are identified, the solutions, in the form of medical treatments, become even more challenging.

What we need are tools from information technology in order to apply to biological challenges. Bioinformatics supplies analytical tools for assessing large data sets, including genomic data. Even data on a single individual's genome can be massive. More recently, AI has been applied to bioinformatic analytics in order to identify complex patterns in massive data.

One emerging technology that enables deep analytics of genomic and medical data involves digital twins. DTs apply tools to duplicate each individual's medical data in a digital model. Increasingly, AI is applied to DTs in order to supply insight on the molecular, cellular and system level.

DTs take individual biomarker and imaging data in order to build a model of each individual medical condition. AI tools enhance DT insights by building diagnostic models of specific diseases.

DTs are well suited to assess disease prognostics. DTs, guided by diagnostic inputs and by AI, are able to evaluate disease progression scenarios. Since diseases evolve in different directions and at different paces based on the behavioral or biochemical inputs, DTs are able to model the disease progression changes in models.

DT disease prognostics are able to develop complex time-elapsed prognosis representations based on various inputs and assess vectors of disease evolution. For instance, a DT on an individual disease can track biomarker assessment over time to evaluate disease progression.

Guided by generative AI (GAI), DTs are even better able to identify risk scenarios – including the statistical chances of each scenario – very well. If a patient engages in unhealthy behaviors, a disease can be tracked in a negative scenario, whereas if a patient engages in healthy behaviors, a disease can be tracked in a positive scenario.

By inference, the DTs also supply risk-based predictions of patients and are able to supply healthy behavior recommendations. Disease progression scenarios can sometimes be contingent on specific inputs. DTs can then be applied to anticipate or predict specific disease scenarios based on different inputs. GAI is applied to DTs to recommend specific known therapeutic options. DTs can then update its prognostics scenarios with new data inputs.

DTs can also anticipate optimal health scenarios with application of precision therapeutics.

While DTs and GAI are useful for diagnostics and prognostics, they are also applicable to therapeutics.

Before the discovery of DNA, it was impossible to trace the source of a disease to its cause. But with the deciphering of the human genome, we now have the tools to observe the genesis of disease with great specificity. Each of thousands of genes can be damaged in different ways and thus embody mutations that generate uniquely dysfunctional proteins. These dysfunctional proteins manifest in each individual's unique disease manifestation. Without understanding precisely which gene is mutated and exactly how this mutation is manifest, it is not possible to find a solution to this disease.

This is where DTs and GAI are useful. DTs require insight from large data sets including libraries of genes and proteins. Not only do DTs model the diagnostic challenge of finding the genetic problem of diseases, but the DTs are also useful in helping to identify the therapeutic solutions.

To date, there are several novel therapeutic modalities that are applicable to personalized medicine. These include gene editing, cellular programing (and reprogramming), stem cells, mRNA, synthetic biology, immunotherapies and protein replacement. Each of these therapeutic modalities are nascent, yet each requires a precise solution configured from an accurate diagnosis of a patient's disease.

A patient's precise disease diagnostic is just the beginning. DTs and GAI are applicable to the diagnostics, but also to the precision therapeutics element. Once a diagnosis is precisely identified by a DT model, customized therapies are designed to solve the problem. A precision therapy is configured within the parameters of a personalized diagnosis.

Because precise genetic diagnostics with DTs present a complex anatomy of a disease, DT models are configured to recommend therapy solution options. Each scenario is supplied within a range of probabilities of potential outcomes. The challenge of DT models is a precisely match a precise medical therapeutic option to a very specific disease diagnosis.

Even the initial selection of a therapeutic solution option is just the beginning of attempts to solve the disease problem. DTs and AI are applied to tracking the therapeutics selection. New data on disease evolution, for example, from new biomarker data, are provided to the DT model, which is constantly updated as the patient therapies are tracked. Drug side effects and drug interactions are tracked in the model as adjustments are made.

Whereas the traditional model of selecting an off-the-shelf medicine is a convenient starting point for DT model therapeutic selection to a precise disease diagnosis, the more long-term and personalized therapeutic solution lies in identifying specific personalized therapeutic solutions targeted to the exact disease parameters. Ultimately, the DT model will be able to design a personalized medicine for each precise disease diagnosis. Specific therapies are tailored to individual genetic variations. This is the holy grail of medicine, which is made possible only with DT modeling therapeutic solutions.

The challenge is to reverse engineer a specific molecular medicinal therapy (genetic or proteomic) in order to develop a personalized therapy to solve a precise genomic variation model data. In some ways, this is a challenge of drug discovery with genetic precision on a micro scale. AI is well suited to apply to DT models to configure novel and unique biomedical or protein solutions to each specific unique genetic malady diagnosis. GAI in particular is well suited for targeted or tailored drug discovery by matching unique gene mutation combinations to precise gene or proteomic therapies.

On a macro scale, the challenge is to find ways to tailor medications to treat patient's individualized genetic variations. For example, a targeted therapeutic regimen may include tailoring known drugs to specific combinations and/or types of genetic mutations. DT models are useful not only for finding the best combinations of drugs for each individual's unique set of genetic anomalies, but they are also useful for tracking side effects, negative treatment outcomes and drug interactions.

Pharmacogenomics (PGx) is the study of how genome variations dictate a person's response to medications. DTs and AI are applied to PGx in order to assess medicinal outcomes as applied to specific targeted diseases.

When viewed from a macro view, there may be several types of breast cancer. But when view from a micro view of precise genetic mutations, there may be hundreds of different mutations which may result in

thousands of combinations of mutations that generate tumors. Each of these unique genetic mutation combinations requires precise targeted solutions. Viewed from this angle, breast cancer may be typified into hundreds of different categories, suggesting a very complex therapeutic challenge that require many different precisely targeted genetic or proteomic solutions.

But therapeutics can be seen as a dynamic process. Therapies typically require iterative solutions, including tracking, updating, analyses and scenario development. Consequently, medical therapies can be seen as an experimental process, i.e., iterative, with feedback and fine tuning. In a sense, this experimentation process with DT modeling – with trial and error and adaptation – typically continue until a therapeutic solution is found. DT modeling show therapeutic probabilistic scenarios that enable adaptation with the ultimate goal of curing the disease.

DT models are ideal for these sorts of therapeutic modeling of precision therapy scenarios that show progression with feedback and adaptation. The two goals of disease eradication and disease management are both fulfilled by DT models. While disease eradication is a clear goal, the most likely outcome of complex genetic diseases is disease management.

DTs and AI are useful not only for prognostics of a disease once it is diagnosed, but also therapeutic prognostics once specific therapies are initiated. Once a disease is tracked without a therapeutic intervention, the various scenario outcomes are probabilistically modeled in a DT model. But the disease is also tracked in DT model after specific targeted therapeutics options are applied, with various options detailed with different outcome probabilities.

Gemini's Digital Twins

The history of digital twins began with NASA in the 1960s in order to develop computer simulations of devices that could be computational tested before activated in space. Today, DTs are mainly applied to electronic and industrial products. Ansys (Synopsys) develops DTs for industrial devices and components in order to computationally test and simulate object mechanics and functions. Nvidia also applies its GPU-based modeling to DTs for industrial object simulation. Cadence and Synopsys construct software products for application to electronic data automation applied to semiconductor design and operational testing. Open Eye Cadence, a division of Cadence, develops software for pharmaceutical companies to perform molecular biochemistry simulations.

A variety of startups are developing DTs software for application to various industries, from industrial and semiconductor design to healthcare systems. These include Twin Health (DTs for chronic disease management), Q Bio (radiological diagnostic DTs) and Unlearn.ai (DTs for drug trials). However, none of these are focused on Gemini's areas of DTs for personalized diagnostics and therapeutics.

We are witnessing several converging technologies, including computing modeling (DTs) for molecular, cellular, tissue and systems simulations. These technologies apply to personalized medicine in order to identify precise genomic variations for each individual patient that pinpoint the source of disease.

AI, including generative AI, deep learning and machine learning, are applied to bioinformatics and to DTs as well. AI is particularly useful for identify patterns in big healthcare data sets, for learning about the behaviors of specific individuals and for predicting behaviors from past data analyses.

While the healthcare diagnostics field is becoming increasingly crowded, particularly with the advent of LLMs and GAI systems, these diagnostics approaches are focused on the macro level of general disease identification. For the most part, these systems are not focused on personalized medicine, which develops a precise data analysis of each individual's genome and genetic dysfunctions and may require intensive computational resources.

DT modeling for personalized medicine involves simulating biological molecular, cellular, tissue and systems structures and functions. The advantages of DT simulations include animating molecular and cellular interactions, identifying precise genetic mutations and their functional proteomics manifestations, developing customized biochemical or proteomic compounds to treat unique genetic diseases, identifying and testing therapeutic options, identifying drug side effects and interactions, identifying disease prognosis and predicting therapeutic effectiveness.

One of the advantages of digital twins applied to bio molecular models is that it enables the production of simulations to test therapy options before implementing these in the patient. The DTs enable experimentation of therapeutics in order to interrogate the data and to perform a trial-and-error process to eliminate less useful options. In addition, it is possible, with enough diagnostic precision, for DTs to design a customized therapy for a particular patient condition.

In addition to being useful for biochemical solution discovery, DTs are useful for tracking the therapy options in patients. Over time, the patient supplies updated tests to ascertain the efficacy of treatment options, which are then updated and optimized in the DT model in order to present supplemental treatment options.

While DTs for precision diagnostics is an invaluable component of the Gemini toolkit, the application of DTs to therapeutics is a crucial element of our system. One cannot develop a precise treatment without having the benefit of precise insight of the diagnostic source of a disease, but the development of unique custom therapies to individualized biomedical challenges is the holy grail of personalized medicine. Gemini's tools are uniquely suited to develop and test solutions to these complex biomedical problems.

Overall, DTs involve the interaction of AI and bioinformatics for application to personalized medicine in order to develop precise diagnostics and optimized therapeutics for disease management.

Medical digital twins are likely to become the central – revolutionary – component of the medical industry as it evolves towards personalized medicine, yet are only beginning to develop in any useful way. DTs enable patient medical information to be collected, analyzed and interrogated in order to identify precise diagnoses of diseases and to find, develop and computationally test accurate and effective therapies.

DTs are biological models that are enabled by AI technologies. As AI is rapidly developing, DTs are positioned to be the indispensable element in the physician's and biological researcher's arsenal. The convergence of AI with personalized medicine is embodied in medical DTs. Much as internet search or the smartphone became strategic technologies, DTs are the single most critical strategic technology in a rapidly developing medical industry that could consolidate around medical digital models as the most important and indispensable feature. Yet, only Gemini has the vision for the potential of DTs.

Digital twins are applied to medicine by categorizing different types or levels in the Solomon Scale of biomedical digital twins.

Diagnostics: Levels 1-6

Level 1

Combine general patent health data into a single package. This may include a patient's genomic data, biomarker data, blood test results, medical digital imaging data and medical IoT device data. For the most part, this initial level captures and collects data for a patient medical DT.

Level 2

This DT level provides a deeper bioinformatics analysis of the patient medical data and provides a report of specific patient maladies over time. A physician can interrogate this model to ascertain general information about a known patient condition. This level of DT provides a physiological evaluation of a patient and provides a summary of their medical records.

Level 3

Building on the previous levels, this DT level provides a detailed view of a patient's cellular and molecular data. This level provides insight into anatomy and physiology of a known patient pathology on a cellular and molecular level.

Level 4

This DT level builds models in order to provide a diagnosis of a unique patient pathology. This level will include the three prior levels. Physicians can interrogate the model in order to identify a specific patient condition that was unknown before. The physician can run tests to verify the condition.

Level 5

This DT level is designed to ascertain a patient diagnosis of a specific pathology on a molecular or cellular level. This level also identifies molecular and cellular pathways in order to trace the mechanism of a disease. Since many genetic or hereditary conditions are based identifying a unique set of aberrant genes or dysfunctional proteins, this level is useful for clarifying these genetic sources of a patient disease.

Level 6

This level is designed to identify prognosis of specific disease pathways. The DT presents simulations in order to supply scenarios of possible disease progression based on various inputs. The DT is able to predict various scenarios of behaviors in its animations.

Therapeutics: Levels 7-10

Level 7

This DT level applies methods to identify therapeutic solution options to a particular patient disease on a *general* level. Once a general diagnosis is made, this DT level enables physicians to select a therapy based on similar common diseases. This level is also used to perform tests to ascertain a therapy's probabilities of success. Pharmacogenomics (PGx) is the study of how genome variations dictate a person's response to medications. DTs and AI are applied to PGx by providing simulations of drug interactions in order to assess medicinal outcomes as applied to specific targeted diseases.

Level 8

This level enables physicians to design unique therapeutic solution options based on the results of a diagnosis of a

patient's distinctive combination of genetic mutations. This advanced level can be useful in designing novel drug therapies. *DTs, AI and PGx are applied at this level.* In addition, this level conceives of a treatment as a solution to a multivariate genetic optimization problem. In a sense, the therapeutic solution to a multivariate medical problem requires fine tuning an optimal treatment.

Level 9

This level allows physicians to provide animations of advanced therapeutic options. This approach enables physicians to experiment with different therapeutic options in order to test viable therapies. DTs and AI are applied to PGx in order to assess medicinal outcomes as applied to specific targeted diseases.

Level 10

This level enables physicians to track different patient therapy solutions with feedback. With this level, physicians are able to update their therapy options. This level identifies drug interactions and side effects as well. DTs and AI are applied to PGx in order to assess medicinal outcomes as applied to specific targeted diseases. This level supplies DT simulations of predictive scenarios of various treatment options, enabling the modeling of prognoses relative to various therapeutic inputs.

Level 11

This level combines the previous levels into an integrated whole. The multiple levels reveal specific dimensions of insight into a specific aspect of the human body. This level views the body as a single comprehensive complete picture in which the individual layers can be disassociated in an analysis searching for an understanding of a complex multi-variate disease.

Level 12

This level combines multiple individual DTs into a single sociological map. This level can isolate unique sets of individual patients in order to identify group diseases. Epidemiological analyses can be performed on this DT level in order to trace causes and consequences of infectious diseases.