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PERSPECTIVE

Translational Therapeutics

The scienthetic method: from Aristotle to AI and the future of medicine

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While AI holds immense potential for accelerating advances in oncology, we must be intentional in developing and applying these technologies responsibly, equitably, and ethically. One path forward is for cancer care providers and researchers to be among the architects of AI and its adoption in medicine. Given the limitations of traditional top-down, hypothesis-driven design in an exponentially expanding data universe, on one hand, and the danger of spiraling into artificial ignorance (ai) from rushing into a purely 'synthetic' method on the other, this article proposes a 'scienthetic' method that synergizes AI with human wisdom. Tracing philosophical underpinnings of the scientific method from Socrates, Plato, and Aristotle to the present, it examines the critical juncture at which AI stands to either augment or undermine new knowledge. The scienthetic method seeks to harness the power and capabilities of AI responsibly, equitably, and ethically to transcend the limitations of both the traditional scientific method and purely synthetic methods, by intentionally weaving machine intelligence together with human wisdom.

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COR-055: Ways of Knowing was required of every freshman entering Coe College in 1989; for no matter the field of study, we must first learn the ways of knowing before embarking on our pursuit of knowledge. That was before the fourth industrial revolution, when knowledge was doubling every 25 years. Today, knowledge doubling is measured in months. To navigate this exponentially expanding data universe, our ways of knowing must undergo a profound transformation; one where artificial intelligence (AI) plays a pivotal role in the evolution of the scientific method. Pivotal, not singular, because in the absence of human wisdom, AI will inevitably spiral into artificial ignorance (ai).

But, per COR-055, to go forward, we must first look back; starting at the roots of the scientific method with the epitome of curiosity, because science is nothing if not curiosity. And who better symbolizes curiosity than the Greek philosopher Socrates with his *elenctic* way of knowing that surfaced new knowledge through didactic discovery? Introducing a new way of knowing did not end well for Socrates, one would hope that introducing a scienthetic way of knowing is received more favorably.

While Socrates laid philosophical foundations of curiosity, his student Plato, and subsequently Plato's student Aristotle, developed these into diametric frameworks for knowledge. Platonic dogma limits the physical world as an imperfect reflection of higher unobservable 'Ideal Forms' akin to shadows cast on cave walls by a more profound reality. In stark contrast, Aristotle elevates physical world observations as the gateway to knowledge. Aristotelian approach [1] begins with a hypothesis which is confirmed or invalidated through observations. Sound familiar? Remarkable isn't it that his approach, from over 2000 years ago, remains strikingly like our scientific method today.

Much has also changed since then. From the imprint of printing presses on the first industrial revolution to the electrification of human endeavor in the second, acceleration of new knowledge with information technology in the third, and internetworking of the globe in the fourth – humanity has engendered and harnessed exponential growths in knowledge. To the extent that shadows from Plato's cave are now casting shadows of their own on walls in digital caves; imperfect reflections of the physical world have become ideal forms of a synthetic world.

But the top-down, hypothesis-driven engine of the scientific method which powered many of these advances, is now becoming a rate-limiting factor under the crushing weight of the exponentially expanding data universe. This, at least in part, due to the vilification of bottom-up pattern-recognition in data analysis, driven by fears of data dredging and p-hacking. As we embark on the dizzying fast ramp to the fifth industrial revolution – with generative pretrained transformers, diffusion models, and talks of $7 trillion AI chip infrastructure – the scientific method is at risk of losing its Aristotelian grounding and veering towards Platonic idealism in asserting the top-down, hypothesis-driven dogma.

To be fair, the hypothesis-driven approach has not itself diminished; rather it is resource-constrained given the scale of emerging problem spaces. Consider cancer drug discovery, with virtually every gene implicated and chemical space exceeding

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10^{60} molecules, the molecule-to-medicine roadmap is littered with mostly similar drugs chasing a narrow set of hypothesis-driven pathways, ultimately resulting in 96% failed clinical trials. There just aren't enough researchers to cast a hypotheses net wide enough to encompass more effective cancer therapies. Is it time then to finally upgrade the 2000-year-old engine of the scientific method to an AI-driven, hypothesis-agnostic, purely 'synthetic' method?

Applications of the synthetic method have yielded promising results. For instance, Eriksson et al. [2] developed mammography AI to predict disease progression in breast cancer. Similar AI models have been developed for other cancers. Manz et al. [3] AI for predicting short-term mortality risk in cancer patients outperformed routine diagnostic indices. Aklilu et al. [4] developed AI to predict laparoscopic cholecystectomy adverse events from videos of the procedure. Radiological imaging AI have already resulted in FDA approved AI. However, it can be argued that many of these are simply image-processing, curve-fitting, or similar statistical devices that narrow, perhaps overfit, rather than generalize training data. Even seeming creativity of ChatGPT and others is merely the most suitable next word, in a stream of words, calculated from streams of words in training datasets.

Therein lies a principal weakness of a purely synthetic method: garbage in, amplified garbage out [5]. AI systems integrated with bad data have resulted in several high-profile examples disproportionately disadvantaging the historically disadvantaged. What makes the synthetic method insidiously dangerous is the projected confidence – backed by volumes of data and smart algorithms – even when it is dead wrong. Recent AI from Google and Microsoft confidently reported patently wrong Super Bowl LVIII outcomes; Microsoft Copilot even crowned the losing team as the winner!

The expanding data universe mandates a new way of knowing but the obvious solution – a synthetic approach – is also the wrong solution. How can we avoid perils of artificial ignorance but deliver the promise of artificial intelligence? Funding is a reasonable ask but Microsoft and Google are well funded, and yet, here we are. Besides, funding does not always translate into optimal outcomes. One need dial back only a few years to see multibillion dollar investments in social media, purported to bring people together, deliver isolation and even deliberate harm [6].

Don't get me wrong, capital is essential. But what is needed even more is a 'scienthetic' method. A way of knowing that augments our capacity for making and analyzing observations but does not allow us to abdicate our responsibilities to scholarship, research, or ethics. A synergy in which AI analyzes datasets at scales beyond human capability to generate hypotheses – sound and hallucinatory – as springboards for human experts to assess and recommend for investigation. Such synergy was on display when mediKanren [7], an experimental AI, identified several unconventional options from which human experts selected isopropyl alcohol and put an end to Kelsea's years-long struggle. A simple, unconventional treatment resulting from the scienthetic method enabled Kelsea to live a healthy and full life. Another example of such synergy can be found in initiatives such as DeepMind's AlphaFold which has predicted over 200 million protein structures [8]. Protein structures can contribute not only to our understanding of cancer biology but also be used in designing corresponding targeted therapies and AI-driven drug discovery in general [9].

Although times, technologies, and our ways of knowing continue to evolve, the essence of our quest must remain the same: better understand, better care, and better serve. In 2015, OpenAI CEO Sam Altman quipped, "AI will probably most likely lead to the end of the world, but in the meantime, there'll be great companies." Citing "existential risk" from AI, Geoffrey Hinton, a godfather of AI, abruptly retired from Google in 2023. Others have raised similar alarms. However, with systemic therapy failure rates [5] near 75% and 95% in clinic and clinical trials respectively – despite US$90 billion investment annually – we don't have the luxury to retreat from AI in oncology. Instead, we must lead this evolution in our ways of knowing to synergizes synthetic intelligence with human wisdom. This is how we can mitigate Hinton's existential risk while buttressing translational advances in oncology. But for this to happen, we – cancer care providers and researchers – must be among the architects, not just end users, of AI in cancer care and research. It is my hope that the proposed scienthetic method is a means for such engagement which in turn not only mitigates risks but also unlocks untapped possibilities in finding effective treatments for solid tumors and a host of diseases and conditions that seem intractable today.

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COMPETING INTERESTS

KIB's work has been funded by the NIH, the NSF, the Breast Cancer Research Foundation of Alabama, and Innovate Alabama. He is CEO-Scientist of CerFlux and is co-inventor of issued (and pending) patents pertaining to in vitro, in silico, ex vivo, and cancer supermodel technologies.

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