



The Journal of the Palo Alto Institute

PAI is a 501(c)(3) nonprofit
creativity laboratory,
dedicated to the pursuit
and promotion of
unconventional truths
through research,
education and entertainment.

Vol. 6

June 2012

ISSN: 1948-7843

E-ISSN: 1948-7851



Twenty Blinks **1**

Keep the Buck: The Rational Basis of Irrational Exuberance **3**

Relationship Liquidity **5**

Therapeutics as the Next Frontier in the Evolution of Darwinian Medicine **7**

When I was young, the concept of a thousand years was too vast for my comprehension. When reading about historical events that long ago or hearing stories about our family that far back, they seemed too remote to be real. Thousand years seemed an interminable amount of time, not too different from epochs of geologic scale such as the Big Bang or the book of Genesis.

Now I am forty-four and, casually rounding up, have lived almost a half century. It sounds trite but some days it feels like those nifty near-fifty years went by in a blink. Then one day, as I was helping put on shoes for my six year-old son (wasn't it yesterday I was in his shoes?), he declared, "Daddy, it takes only twenty fifties to make a thousand. A thousand is really a small number." I barely recall finishing tying his shoes.

I now comprehend what fifty years feels like, and if I could link twenty of my lives end-to-end, that's a thousand years. Twenty blinks, that's all. Suddenly, a thousand years hardly feels long anymore. Rather, it feels shockingly accessible. Indeed, line up two hundred of my lives end-to-end, and that's already ten thousand years, which is just about the dawn of human civilization and by some calculation is before the book of Genesis.

It is often said that the longer we all live, the smaller the world feels. The longer I have lived, the smaller Time feels. I feel so much closer, not only to others on this planet today, but also to those who came before us and who will come after us.

All of civilization—roads, books, fusion reactors, cities, medicines, cell phones, languages, gazillion web pages, the Musée du Louvre, pizza, and moon rockets—have been rendered by the few billion (another now-small number) people in just twenty blinks. The human arc is nothing short of a miracle.

Keep the Buck:
The Rational Basis of
Irrational Exuberance

Joon Yun

Palo Alto Institute

June 2012

Modern Portfolio Theory (MPT), which earned its author Harry Markowitz the Nobel Prize in Economic Sciences in 1990 and is the basis of The Yale (or Endowment) Model, has been subject to criticism on various theoretical grounds and weak empirical validation in the real world. However, a significant deficiency of MPT remains overlooked. Whereas MPT assumes that investors who want higher returns must accept more risk, in the real world many market participants are in positions where they can chase higher returns because they can offload the risk onto others.

Take, for example, those who gamble with shareholder or client money. Performance fee structures typically enable profits to be shared between clients and managers during profitable periods, but clients alone bear the losses during down periods. Stock options work similarly in the asymmetric handling of return and risk. If the stock price of a company goes up, the shareholders and employees both benefit from the gain. If the price goes below the strike price, the shareholders disproportionately bear the loss since employees can choose to not exercise their options. The same can be said for the entire bonus culture of corporate America. All of these structures facilitate excess risk taking by money managers and corporate employees. Since agency risk can be high, high inside ownership is the best way to mitigate the misaligned incentives between managers and their clients or owners.

However, the decoupling of return from risk is far more prevalent in broader society than anyone realizes, such that it is essentially baked

into modern life. When an individual puts money into a savings account, a common misperception exists that the money is saved in a safe somewhere and that the depositor will receive interest payments. In fact, that deposit is invested by the bank into an asset that carries some risk. When those investments go sour—as we are frequently seeing during the current crisis—the depositors who should bear the loss for the risk they took are instead partially or completely bailed out by the Federal Deposit Insurance Company—which is funded by taxpayers. Such government guarantees incentivizes depositors, and therefore banks, to chase yield.

Risk and return are also decoupled in the housing markets. When housing prices rise, homeowners with mortgages keep the gains. Due to the non-recourse nature of the loans, when prices fall, homeowners can walk away and offload part or all of the losses onto the holders of these notes. During the current housing bust, the losses in many cases were passed onto Freddie Mac, Fannie Mae, or other financial institutions that had to be bailed out by the government. It seems that individuals as well as corporations are able to benefit privately from profits and push some of the losses onto society.

In essence, because of what amounts to personal protection from loss, contractual structures are in place for depositors, homebuyers, money managers, banks, and corporations to take high levels of risk while chasing yield. Now that the bust is in place, everyone is passing the buck. More accurately, everyone is keeping the buck and passing the losses. The decoupling of risk from return encourages recurrent speculative bubbles and forms a rather rational basis of irrational exuberance.

Social mobility enabled by innovations in technology, communication, and transportation has dramatically increased the liquidity of our relationships. Some of the hard-wired social traits that we inherited from our tribally-minded ancestors may be maladaptive and not properly suited to handle modern relationship dynamics.

Our attraction to new social opportunities was shaped when such opportunities were far more limited than they are today. Not unlike our attraction to sweet, fat, and salty foods, little selection pressure existed in the old world for evolving upper limits on our attractions for new social opportunities. But does a tendency to be intrigued by new social opportunities make us happier people in a world where access to new opportunities are virtually limitless?

Whereas our prehistoric tribal predecessors may have had access to a limited set of potential mates, friends, and colleagues, humans today can choose from a vast inventory of possible relationships in our mobile society and even meet distant partners through the internet. There are many beneficial aspects to rising number of relationship transactions. Access to more people, in life and in business, can increase the probability of finding better partners. On the other hand, rising relationship liquidity and transactions has resulted in higher quantity but lower average quality of human relationships. Furthermore, the cost of forsaking existing relationships for new ones has declined. In just the last couple of generations alone, divorce rates and job change rates have skyrocketed.

From a Darwinian perspective, agency risk today is probably much higher than our social brains were evolved to detect since the human tendency to trust counterparties was wired during the tribal era when there was a high degree of genetic alignment. A significant portion of interactions today are with non-relative individuals. This misalignment of interests increases the incentives for exploitation, and such violators of trust have more opportunities to start new relationships than ever before, thereby reducing the cost of being detected.

Indeed, agency abuse is prevalent in modern life. Corporate and political leaders are accused of enriching themselves at the expense of shareholders and citizens. Doctors are criticized for offering treatments that enrich themselves at the expense of making the best decision for their patients. The weak commitment of agents to principles can be seen as an outcome of low alignment.

Aligning interests as much as possible in human relationships may be the best way to adjust for the Darwinian maladaptation of our social brain in this era of vast relationship liquidity.

Therapeutics as the Next
Frontier in the Evolution of
Darwinian Medicine

Palo Alto Institute
June 2012

Joon Yun

Evolutionary medicine (also referred to as Darwinian medicine) is the application of evolutionary theory to the understanding of human ailments. It explores evolutionary mechanisms of disease, offering a complementary framework to the proximate mechanistic explanations that prevail in medicine today. In this paper, we consider the application of evolutionary theory to the treatment of ailments.

A major contribution of evolutionary medicine is the framing of human diseases as maladaptations of our prehistoric factory settings. Our physiologic processes were shaped during prehistoric evolution to meet the needs of the era, but those same processes may behave maladaptively in the modern environment and produce disease. We take that notion one step further and propose an overarching therapeutic paradigm for human ailments based on evolutionary theory—the induction of adaptations in the body as a way to treat disease. It is the idea of creating somatic traits in the body that evolution might otherwise need to create over many generations through the sheer force of variation and natural selection. In the same way that evolution has endowed us with traits that shield against biotic and abiotic stress to maintain homeostasis, we propose treating patients by endowing the body with buffers against ailments.

Most modern therapies provide relief in the short run, but chronic use can worsen the underlying condition, as the body remodels in the presence of the therapy and decompensates further. Caffeine stimulates acutely, but continued use leads to lowered baseline alertness. Virtually all drugs exhibit this phenomenon, known as

tachyphylaxis, to varying degrees. Modern medicine effectively provides the body with an adaptation, which ultimately de-adapts the body and creates dependence on further therapy. We suggest that providing therapy to induce an adaptation may represent an alternative model for relieving ailments .

In this model, hypertension would be treated by offering patients drugs that elevate rather than lower blood pressure. This is effectively how exercise works. During exercise, we raise our blood pressure and heart rate, such that in the long run our baseline blood pressure and heart rate go down. An appropriate autonomic stimulus, whether physical activity or sympathomimetic drug, would induce vagal strengthening—thereby leveraging preexisting capacities within the body instead of overriding or replacing them.

These types of solutions would reverse the current trend of greater dependence on medicine, which is expensive, inelegant, and ultimately, ineffective. Induced adaptations may offer far superior therapies at a fraction of the cost, exactly the kind of outlier solution needed in this time of crisis in the healthcare system.

In some ways, the idea is hardly new. Vaccination induces a somatic adaptation. Priming the immune response prepares the body for potential future exposure to a dangerous pathogen. Vaccination is arguably one of the greatest inventions in medical history in terms of its efficacy and impact.

While vaccination provides the most sweeping example of induction of adaptation, a number of recent examples suggest the idea can be more broadly applied. Asthma is a pulmonary condition where insufficient sympathetic response in the smooth muscles of the respiratory tract predisposes to spasm and closure of the airways. For a century, symptomatic relief of asthma has featured the use of sympathomimetic drugs. However, chronic use of beta-agonists

induces down-regulation of beta receptors and furthers autonomic dysfunction. On the other hand, Richard Bond has shown that administration of beta-blockers may be a way to treat asthma by inducing an appropriate adaptation.

Similarly, administration of the antigen in small doses has been shown to induce adaptation to cope with both environmental allergies and food allergies. Positive pressure ventilation for respiratory dysfunction can produce not only diaphragmatic weakening, but also a host of other physiologic dysfunctions. On the other hand, diaphragmatic pacing promotes negative pressure ventilation and strengthening of the diaphragm, which becomes an adaptation for the patient. Exercise, which has been associated with amelioration of many chronic diseases, is a natural example of adaptation induction.

The progression of life is defined by the accumulation of buffers (traits) against stresses over evolutionary epochs. As advances in technology enable them to live to unprecedented ages, modern humans are now facing many unprecedented stresses, both externally from the environment and internally from within their own bodies.

Evolution has not kept pace with these changes; in many ways, diseases can be viewed as maladaptations awaiting the forces of evolution to eventually endow adaptations over the generations. We believe that human innovation can harness knowledge of evolution theory and accelerate the induction of adaptations within generations rather than across them.

In the final analysis, adaptation is the end, and evolution has been nothing more than the means to that end. Over the very long haul, if humans learn to create adaptations to maintain homeostasis, human evolution itself could be at risk for extinction.

References

- ¹ Williams GC, Nesse RM. *Why we get sick: the new science of Darwinian medicine*. New York: Vintage Books. 1996.
- ² Weiner H. *Notes on an evolutionary medicine*. Psychosom Med 1998;60(4):510–20.
- ³ Williams GC, Nesse RM. *The dawn of Darwinian medicine*. Q Rev Biol 1991;66(1):1–22.
- ⁴ Yun AJ, Lee PY, Bazar KA. *Paradoxical strategy for treating chronic diseases where the therapeutic effect is derived from compensatory response rather than drug effect*. Med Hypotheses 2005;64(5):1050–9.
- ⁵ Hanania NA, Dickey BF, Bond RA. *Clinical Implications of the Intrinsic Efficacy of Beta-Adrenoceptor Drugs in Asthma: Full, Partial and Inverse Agonism*. Curr Opin Pulm Med. 2010;16(1):1–5.
- ⁶ Burks AW, Laubach S, Jones SM. J Allergy Clin Immunol. *Oral tolerance, food allergy, and immunotherapy: implications for future treatment*. 2008 Jun;121(6):1344-50.
- ⁷ Yun AJ, Lee PY, Doux JD. *Negative pressure ventilation via diaphragmatic pacing: a potential gateway for treating systemic dysfunctions*. Expert Review of Medical Devices May 2007;4(3):315–9.



431 Florence Street, Suite 200
Palo Alto, California 94301

650.641.8947 /T
paloaltoinstitute.org

©2012
Palo Alto Institute