

Response by Weinstein to de Grey's Rebuttal

Abstract

Doctor de Grey has done significant scientific work, but the entirety of his output runs the gamut from insightful to sophomoric—the burden of his worst efforts being concentrated around SENS. The extraordinary range is perplexing because serious scientific thinking doesn't typically emanate from minds with low logical standards.

Parsimony suggests that SENS began with conclusions, namely: (a) indefinite life extension is technologically tractable, and (b) we exist late enough in history to reap the full benefit. From there, de Grey assumes the simultaneous benefit of every doubt, adopts absurdly generous interpretations of all facts and re-imagines the universe to be maximally hospitable to his goal—all before cleverly shifting the burden of proof to his detractors.

Working backward from sacrosanct conclusions violates the most basic requirements of hypothetico-deductive inference, and blurs the distinction between logic and faith. For obvious reasons, treating such work as science is a precedent we can not afford to set.

In the unlikely event that perpetual youth becomes plausible in the near term, we will surely know from the fact that Dr. de Grey will no longer demand to be granted exemptions from minimum scientific standards.

Response

Our hunter-gatherer ancestors were keen observers of the world around them. Like modern hunter-gatherers they must have known that some plants could make you sick, and others could speed recovery, and that some behaviors were protective of health, while others jeopardized it. And they must also have recognized that, after reaching adulthood, a person's body becomes ever weaker and more vulnerable, as if taken over by some slow-acting, progressive disease. They would, from their vantage point, have been thoroughly justified in wondering if there were not behaviors and substances that might prevent the increasing vulnerability and decreasing efficiency that otherwise characterizes adult aging. And they would likely have had no reason to dismiss the idea that the aging illness might be halted or even reversed through clever human action.

But the long term pattern regarding such beliefs is clear: the more humans have come to understand about senescence and the structure that it degrades, the less plausible it has become that we will be able to halt, let alone reverse, the process.

Aubrey de Grey would like us to believe that the longstanding pattern—increasing knowledge resulting in decreasing plausibility—reached its end. In 1982.

That claim is based on the assertion that the list of senescence causes grew steadily starting in 1907, and that, since nothing has been added since 1982, the list must now be complete—and, as luck would have it, very short.

The claim that the list of causes is both short and complete is central to the house of cards that is SENS. And yet, as the back and forth between de Grey and myself makes clear, is utterly baseless. It assumes that the pattern of discovery is so regular that pauses can be quickly distinguished from end points. (Never mind that pauses are predicted to grow in length due to diminishing returns—de Grey, of course, is not a believer in diminishing returns). It assumes that nothing important remains to be discovered in the major chunks of human biology that have yet to be cracked (e.g. brain circuitry, epigenetic features of development). It assumes that potential causes of senescence that have entered the literature after 1982, but have failed to be discussed (e.g. histological entropy) are ignored because they are somehow already known not to contribute to the problem. It assumes that diligent gerontologists (the ones de Grey frequently accuses of overlooking the significance of his own work) can't have missed anything. And finally, it assumes that a daunting list of new problems would not be revealed by early increases in maximum longevity.

Given so many independent reasons to doubt the claim that the list of causes was completed in 1982, isn't the argument in favor of SENS dead on arrival?

Tractability

But even if we give SENS a pass with respect to the 1982 claim, it quickly finds new trouble surrounding the issue of tractability. Are all the problems on the current list amenable to technological remedies? Can all the remedies be used together? De Grey's beliefs on the matter are strange, but clear. The human body has a finite complexity. There are no natural laws or mathematical theorems that prevent indefinite maintenance. Therefore, the assumption of technological tractability is not only justified, but barring extinction, success is inevitable.

First, it must be said that de Grey's belief can be partly rescued by taking it out of the realm of research proposals and taking it to the level of philosophical musings. In such a circumstance we can probably justify the claim that all finite problems are tractable given infinite time, so long as no natural laws must be broken to solve them—or something like that. But de Grey does great violence to the meaning of 'tractability' by dragging such justifications out of the realm of infinite typewriters and monkeys and into scientific discourse. Would it be justifiable to say, for example, that a problem requiring more time to solve than the universe is scheduled to last is technologically tractable? In de Grey's terms, yes. And while we are on the subject, why does de Grey feel entitled to count the finiteness of human complexity as win with respect to the tractability of senescence, while at the same time minimizing the corresponding loss associated having finite time to find a solution?

And what about the laws, limits and theorems that are emergent in complex systems? Humanity is only just beginning to understand these second order limits that arise in highly complex systems, and yet de Grey would have us believe that the least restrictive set of rules, the ones we already know, are the only ones with which we need to concern ourselves. Even still, he must caricature the first order rules in order to keep SENS alive.

To see what I mean, let's look at the second law of thermodynamics. De Grey portrays himself as a believer in natural laws in general and this one in particular, and he specifically uses perpetual motion machines to demonstrate that he recognizes intractability where it actually exists. But if you take literally his belief in the tractability of all things not specifically forbidden by law or theorem, then you will find perpetual motion machines are, for all practical purposes, coming. That's because the second law only prohibits perfectly efficient transfers of energy. It does not prohibit staggeringly efficient transfers, and by de Grey's logic, machines will cross every limit below 100%, up to and including, we must assume, the limit of our ability to measure the loss. Such devices may not be true *perpetual* motion machines, but in a universe of finite longevity no one will know the difference.

Doesn't the dependence of SENS on logic that also supports *de facto* perpetual motion machines place the proposal unambiguously outside the bounds of serious consideration?

Rates of technological progress

The next gaping hole surrounds the 'escape velocity' metaphor. In asserting that SENS has a potentially major significance to people alive today, de Grey has picked a strange analogy—a temporary positive feedback associated with the particulars of gravity and the launching of space craft. When I suggested that there was no reason to expect a rare escape-velocity-like process, and every reason to expect the ubiquitous diminishing returns pattern, de Grey fumbles spectacularly for a response. He renews his claim that diminishing returns are entirely about a loss of enthusiasm for progress. He connects gravity to aging by another seemingly unjustified metaphor, falling off a cliff. And focusing on exactly one factor in a complex system *where only the net effect is at issue*, he asserts that increasing use of primate models will make the process accelerate.

What can I say? The conclusion is sacred. Total rejuvenation and perpetual youth are foreseeable for people alive today. If escape velocity is required, then it must be justified. If diminishing returns is a impediment, then it must be entirely sociological.

If nothing else, doesn't the unjustified assertion that diminishing returns does not apply to SENS put the plan on ice as far as worthiness goes?

Disorder of mind and body

Then there are dual issues of memory fragmentation and histological entropy, two limits that might be expected to emerge in the relevant complex systems.

De Grey asserts that the brain couldn't possibly suffer from fragmentation because of the way memory is stored. But the reference he cites¹ shows a fair measure of desperation (as well as a good deal of chutzpah). Not only does the paper in question fail to make claims about how memory is in fact stored, it specifically warns the reader that the model presented is unlikely to be accurate.

And then there is the fact that everyday experience suggests that something very fragmentation-like is happening in healthy brains all the time. I wonder if de Grey has ever witnessed a situation like this:

Two people have an extended conversation. The next day, both have extensive recall of the conversation's progression. Five years later, each person has forgotten much of what was said, but when they talk about the event, each recalls things he had previously been unable to remember.

At the very least, this type of experience is common and matches exactly the predictions of the memory fragmentation hypothesis. Whatever the conversation participants are ultimately able to piece together must logically have remained stored in their brains, but had become inaccessible—seemingly as fragments isolated by what had been forgotten.

Perhaps memory fragmentation isn't the explanation, but given the amount of mystery that remains about the brain in general and memory in particular, and given the fact that the black box in question acts like it has issues with memory fragmentation, de Grey's protestations that fragmentation is impossible ring hollow. Maybe there is fragmentation, and maybe there is some other explanation for common fragmentation-like failures, but the suggestion that memory fragmentation in the brain is not worth worrying about is nonsense. It simply represents a pattern of dismissing completely any hazard to SENS' tractability that is less than fully certain.

Further, de Grey's assertion that all senescence problems in the brain are the product of processes within and between cells and have nothing at all to do with the interconnection of cells (i.e. circuitry and programming) serves only to rescue SENS from another likely hazard of the yet-to-be-discovered sort.

The question of histological entropy is similar. While the evidence is not overwhelming, what evidence exists suggests that tissues become increasingly jumbled with age². If de Grey would like to publish challenge to histological entropy, or present evidence that tissues remain consistently orderly with age, I would welcome the ensuing discussion. But until then, the preponderance of evidence supports the idea, and the burden rests with him to show otherwise. Given that, we must assume that even if all the cells of the body were themselves fully rejuvenated, and the space between them was cleared entirely of junk, increasingly disordered tissues would still become less efficient and more vulnerable over time, even if SENS accomplished everything it set out to do.

Again, de Grey sees nothing to worry about that won't be cured by intercellular and intracellular fixes. He sees no reason to think that cellular positional information—which is encoded during development—will be lost over time as the cellular lineages that store it are increasingly exhausted. Interestingly, he offers no explanation as to how such a seemingly inevitable loss has been avoided in our disposable evolutionary design.

From his reaction to issues surrounding brain circuitry and histological order it appears that de Grey has a paradoxical reaction to the systems and processes of the body that have

so far evaded thorough scientific understanding. Instead of fearing that the most difficult processes to study are likely going to be the hardest to fix, he simply assumes that nothing daunting lurks there.

Isn't his insistence on the completeness of the SENS proposal irreconcilable with the standards of common sense (not to mention science) given what remains to be learned about the brain and morphogenesis?

Costlessness

Finally, there is an issue that sits at the nexus of all the proposals that comprise SENS. Not only does de Grey believe he can halt, and even reverse, senescence. He believes he can do it without in any way compromising the functionality of the organism as it stands. As my *Mustangs to the Moon* proposal was designed to make clear, that simply doesn't add up. When a design is crude, like the 1903 Wright Flyer, it can frequently be improved without cost. But when a design is highly refined, increasing capacity in one place tends to require borrowing it from someplace else. The trade-off problem only becomes more severe when the capacity increases are extreme. It becomes still harder to imagine when the capacity increase has to be accomplished without taking the machine off-line.

The human organism, like all creatures, is nothing if not highly refined. And the capacity increase represented by the SENS proposal is nothing if not extreme. And yet, we are supposed to believe that, were it somehow possible, the only costs for infinite youth would be money spent on research and time spent on trips to the stem cell doctor. De Grey will not acknowledge that sizable costs to our normal physiological and psychological function would be all but inevitable. Oh well. I suppose if you're in the business of magical thinking, you might as well make the most of it.

References

1. Vogel DD. A neural network model of memory and higher cognitive functions. *Int J Psychophysiol* 2005;55(1):3-21.
2. Weinstein BS, Ciszek D. The reserve-capacity hypothesis: evolutionary origins and modern implications of the trade-off between tumor-suppression and tissue-repair. *Exp Gerontol* 2002; 37(5):615-627.

[Note to the judges: Aubrey de Grey did an odd thing with my submission. He responded to the abstract, claiming that the rest was redundant. I trust the judges will note the tactic and its various effects. On the other hand, it doesn't change the outcome of the analysis. De Grey says enough in his rebuttal to see SENS clearly for what it is.

I do not, however, want to abandon arguments as de Grey has done. Regardless of this contest's outcome, it is important that those who will undoubtedly continue to discuss SENS have a record of the progression of arguments. So I have made extensive comments on de Grey's rebuttal itself using the commenting features of Microsoft Word.

As you will see, my comments are informal, but I have endeavored to be complete and to credit de Grey's arguments wherever they prevail. I encourage the judges to read those comments, but not to get lost in the minutiae. What disqualifies SENS from serious consideration are the larger issues, which I believe are adequately covered above.]