

Additional Notes For Antifragile

Note 1- Medicine and Convexity (Antifragility)

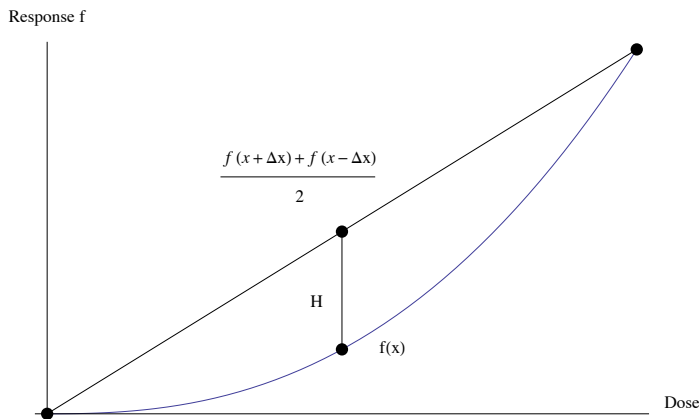
A brief explanation of nonlinearities as detection of risk in medicine (from antifragile), directly from mathematical necessities, or the ideas behind *Antifragile*.

Antifragility from Uneven Distribution (Explain How Things Benefit from Volatility/Variability)

Take health effect a function “response” from a single parameter, $f: \mathbb{R} \rightarrow \mathbb{R}$ be a twice differentiable, the effect from dose x .

If over a range $x \in [a,b]$, over a set time period Δt , $\frac{\partial^2 f(x)}{\partial x^2} > 0$ or more heuristically, $\frac{1}{2}(f(x+\Delta x) + f(x-\Delta x)) > f(x)$, with $x+\Delta x$ and $x-\Delta x \in [a,b]$ then there are benefits from unevenness of distribution: episodic deprivation, intermittent fasting, variable pulmonary ventilation, uneven distribution of proteins (autophagy), vitamins, high intensity training, etc.).

In other words, in place of a dose x , one can give 140% of x , then 60% of x , with a more favorable outcome.

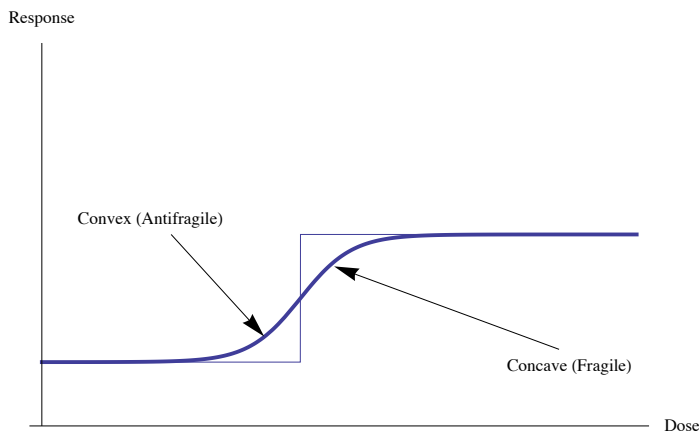


Proof: Jensen's Inequality.

This is a simplification here since dose response is rarely monotone in its nonlinearity, as we will see further down.

Mixed Nonlinearities in Nature

Nonlinearities are not monotone.

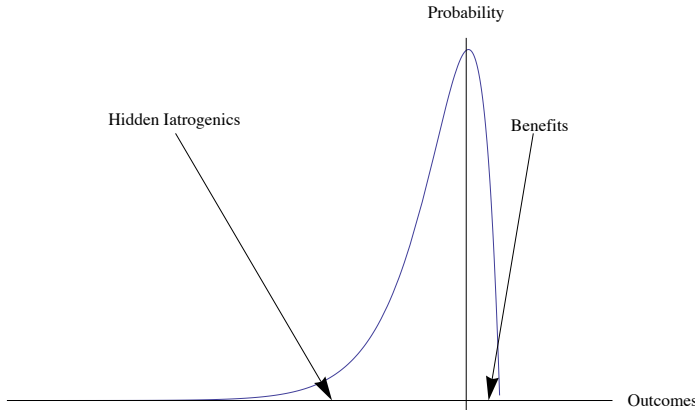


Nonlinearities in Biology- The shape convex-concave necessarily flows from anything increasing (monotone, i.e. never decreasing) and bounded, with a maximum and a minimum values, i.e. never reached infinity from either side. At low levels, the dose response is convex (gradually more and more effective). Additional doses tend to become gradually ineffective or hurt. The same can apply to anything consumed in too much regularity. This type of graph necessarily applies to any situation bounded on both sides, with a known minimum and maximum (saturation), which includes happiness.

For instance, If one considers that there exists a maximum level of happiness and unhappiness then the general shape of this curve with convexity on the left and concavity on the right has to hold for happiness (replace "dose" with wealth and "response" with happiness). Kahneman-Tversky Prospect theory models a similar one for "utility" of changes in wealth, which they discovered empirically.

Iatrogenics

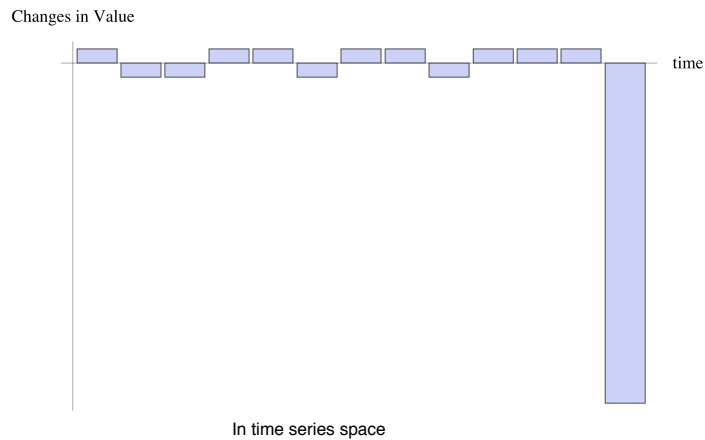
If $\frac{\partial^2 f(x)}{\partial x^2} \leq 0$ for all x (to simplify), and x is symmetrically distributed, then the distribution of the "outcome" from administration of f (and only the effect of f) will be left-skewed as shown in Figure 1. Further "known limited upside, unknown downside" to map the effect of the next figure.



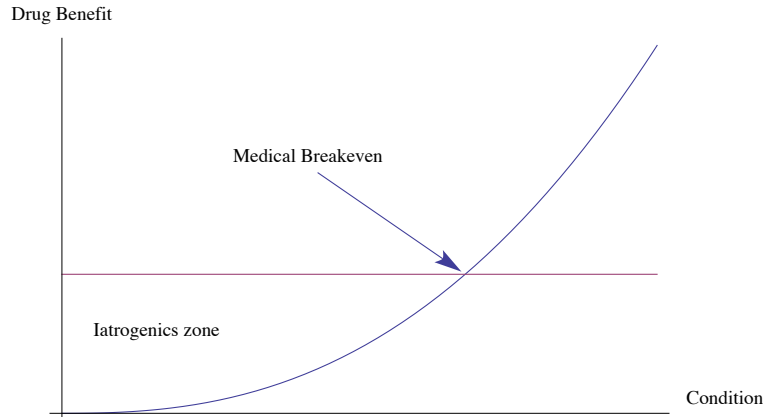
Medical iatrogenics: Probability distribution of f . Case of small benefits and large Black Swan-style losses seen in probability space. Iatrogenics occur when we have small identifiable gains (say, avoidance of small discomfort or a minor infection) and exposure to Black Swans with delayed invisible large side effects (say, death). These concave benefits from medicine are just like selling a financial option (plenty of risk) against small tiny immediate gains while claiming "evidence of no harm".

In short, for a healthy person, there is a small probability of disastrous outcomes (discounted because unseen and not taken into account), and a high probability of mild benefits.

Proof: Convex transformation of a random variable, the Fragility Transfer Theorem.



Mother Nature v/s Medicine



The hypertension example. On the vertical axis, we have benefits of a treatment, on the horizontal, the severity of the condition. The arrow points at the level where probabilistic gains match probabilistic harm. Iatrogenics disappear nonlinearly as a function of the severity of the condition. This implies that when the patient is very ill, the distribution shifts to antifragile (thicker right tail), with large benefits from the treatment over possible iatrogenics, little to lose. Note that if you increase the treatment you hit concavity from maximum benefits, a zone not covered in the graph—seen more broadly, it would look like the graph of bounded upside

From Antifragile

Second principle of iatrogenics: it is not linear. We should not take risks with near-healthy people; but we should take a lot, a lot more risks with those deemed in danger.

Why do we need to focus treatment on more serious cases, not marginal ones? Take this example showing nonlinearity (convexity). When hypertension is mild, say marginally higher than the zone accepted as “normotensive,” the chance of benefiting from a certain drug is close to 5.6 percent (only one person in eighteen benefit from the treatment). But when blood pressure is considered to be in the “high” or “severe” range, the chances of benefiting are now 26 and 72 percent, respectively (that is, one person in four and two persons out of three will benefit from the treatment). So the treatment benefits are convex to condition (the benefits rise disproportionately, in an accelerated manner). But consider that the iatrogenics should be constant for all categories! In the very ill condition, the benefits are large relative to iatrogenics; in the borderline one, they are small. This means that we need to focus on high-symptom conditions and ignore, I mean really ignore, other situations in which the patient is not very ill.

The argument here is based on the structure of conditional survival probabilities, similar to the one that we used to prove that harm needs to be nonlinear for porcelain cups. Consider that Mother Nature had to have tinkered through selection in inverse proportion to the rarity of the condition. Of the hundred and twenty thousand drugs available today, I can hardly find a *via positiva* one that makes a healthy person unconditionally “better” (and if someone shows me one, I will be skeptical of yet-unseen side effects). Once in a while we come up with drugs that enhance performance, such as, say, steroids, only to discover what people in finance have known for a while: in a “mature” market there is no free lunch anymore, and what appears as a free lunch has a hidden risk. When you think you have found a free lunch, say, steroids or trans fat, something that helps the healthy without visible downside, it is most likely that there is a concealed trap somewhere. Actually, my days in trading, it was called a “sucker’s trade.”

And there is a simple statistical reason that explains why we have not been able to find drugs that make us feel unconditionally better when we are well (or unconditionally stronger, etc.): nature would have been likely to find this magic pill by itself. But consider that illness is rare, and the more ill the person the less likely nature would have found the solution by itself, in an accelerating way. A condition that is, say, three units of deviation away from the norm is more than three hundred times rarer than normal; an illness that is five units of deviation from the norm is more than a million times rarer!

The medical community has not modeled such nonlinearity of benefits to iatrogenics, and if they do so in words, I have not seen it in formalized in papers, hence into a decision-making methodology that takes probability into account (as we will see in the next section, there is little explicit use of convexity biases). Even risks seem to be linearly extrapolated, causing both underestimation and overestimation, most certainly miscalculation of degrees of harm—for instance, a paper on the effect of radiation states the following: “The standard model currently in use applies a linear scale, extrapolating cancer risk from high doses to low doses of ionizing radiation.” Further, pharmaceutical companies are under financial pressures to find diseases and satisfy the security analysts. They have been scraping the bottom of the barrel, looking for disease among healthier and healthier people, lobbying for reclassifications of conditions, and fine-tuning sales tricks to get doctors to overprescribe. Now, if your blood pressure is in the upper part of the range that used to be called “normal,” you are no longer “normotensive” but “pre-hypertensive,” even if there are no symptoms in view. There is nothing wrong with the classification if it leads to healthier lifestyle and robust *via negativa* measures—but what is behind such classification, often, is a drive for more medication.