

“Fragility” and Complexity:

Why and how do we get worn out and what can we do about it?

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What's complexity?

There are many “definitions” of complexity. The problem is they don't discriminate very well - too many false positives.

Maybe some contain some necessary conditions but, certainly, not sufficient

Other common words and concepts in discussions about complexity

Emergence

Reductionism

Order/disorder/Edge of Chaos

Uncertainty, unpredictability

Auto-organization

Complejidad

Muchos grados de libertad

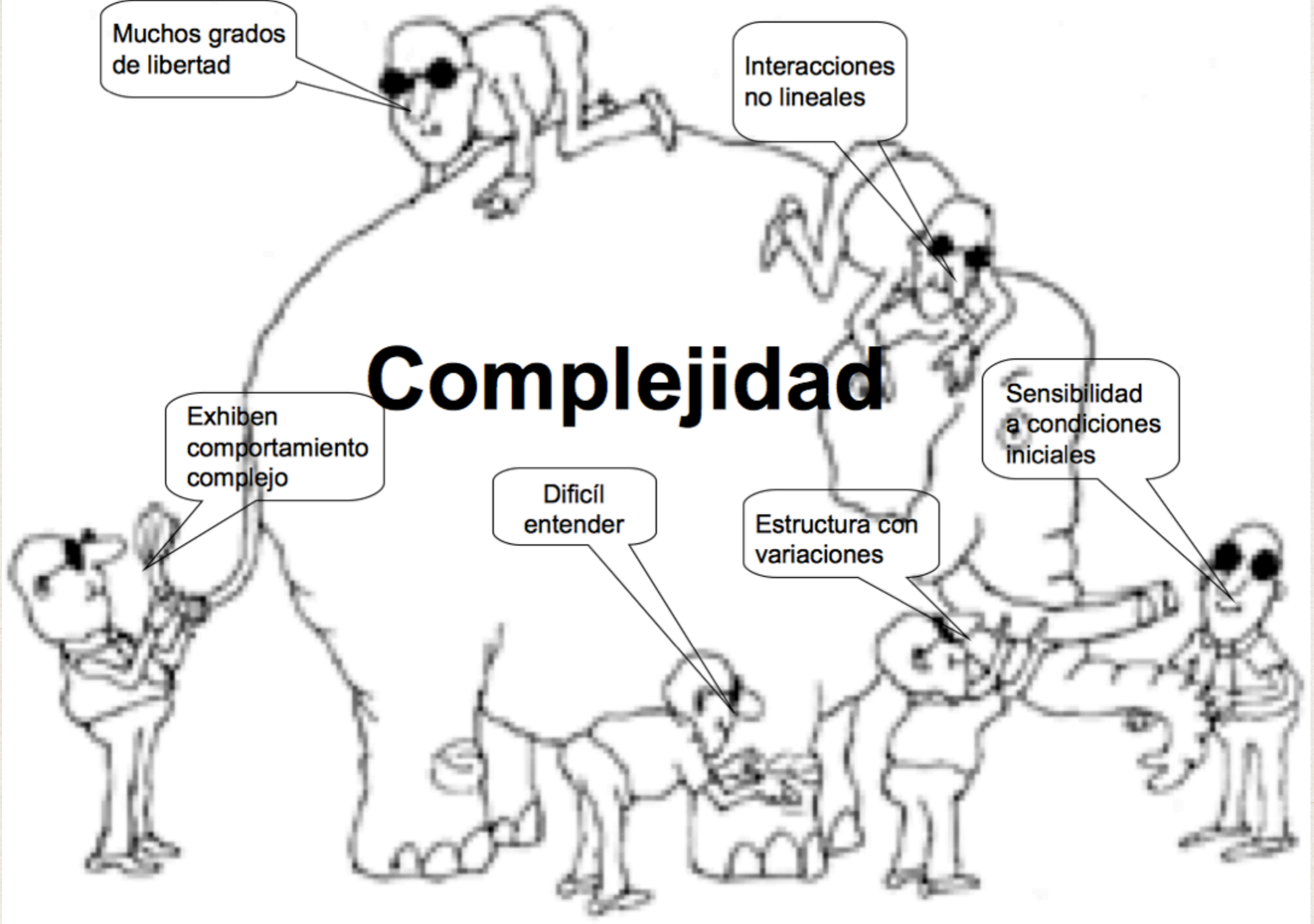
Interacciones no lineales

Exhiben comportamiento complejo

Sensibilidad a condiciones iniciales

Difícil entender

Estructura con variaciones



What distinguishes complex from non-complex phenomena?

❖ Structural properties

- ❖ A hierarchy of many different scales
- ❖ Qualitatively different degrees of freedom (“collectivity”) at different scales
- ❖ Hierarchy of building blocks (modularity)
- ❖ “Intra-block” interactions stronger than “inter-block”
- ❖ The “micro” and the “macro” are linked (fitness, semantics,...)

❖ Functional properties

- ❖ Systems are adaptative
- ❖ Their evolution depends on many different rules/strategies.
- ❖ Systems “learn” (environmental feedback to the system is used to update rules)
- ❖ The “micro” and the “macro” are linked (fitness, semantics,...)
- ❖ More complex behaviour (the “phenotype”)
- ❖ Better described by what they do than what they are

Sociólogos
Medialogos

Filósofos

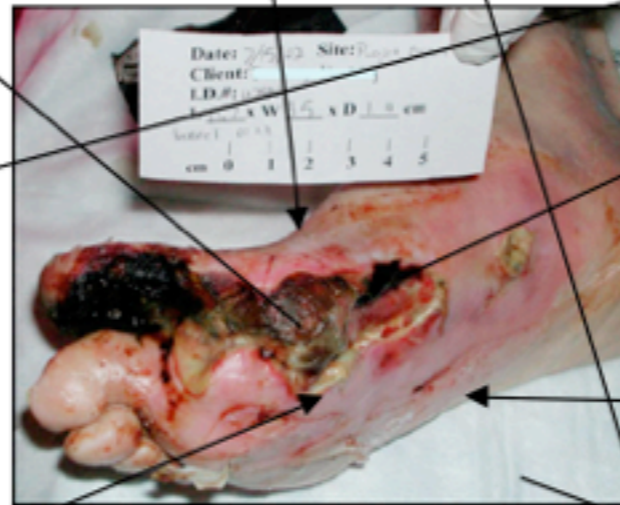
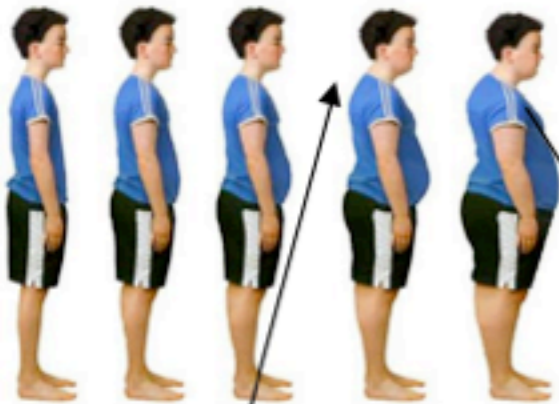
Geneticistas



The Complexity of Disease



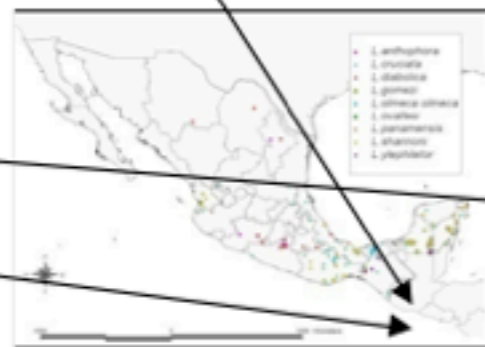
Nutrólogos
Psicólogos



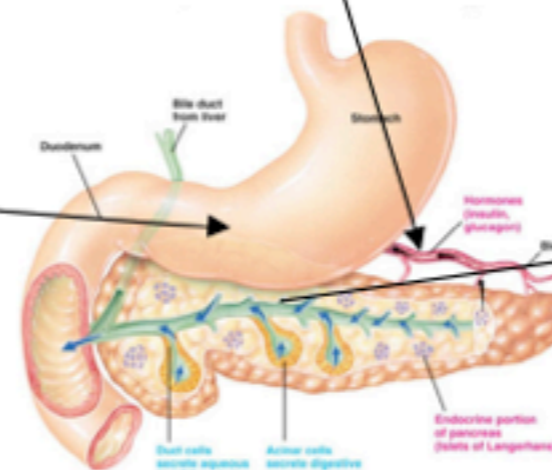
Bioquímicos
Biofísicos
Médicos

Médicos

Economistas



Demógrafos
Epidemiólogos
Data miners



Endocrinólogos



Políticos
Autoridades

Modularity

There is nothing complex that's not also highly modular

Structural modules - building blocks - (generally with spatio-temporal integrity)

Genes, cells, tissues/organs, teams, departments, tribes, neural structures, letters, words, sentences, books, hard disks, DVDs,...

In complex systems structural modularity is intimately linked to functional modularity. Each structure has a corresponding, particular function.

Modularity implies quasi-independence of one structural/functional module from another and therefore environmental effects can act differently on one module than another

Structural and functional modularity in humans



Prominent Biological/Physiological Theories Of Aging

Antagonistic Pleiotropy Theory

Waste Accumulation Theory

Free radical damage

Insulin resistance

Advanced Glycation (AGE)

Telomeres and Hayflick

The Error Catastrophe Theory

Autoimmunity

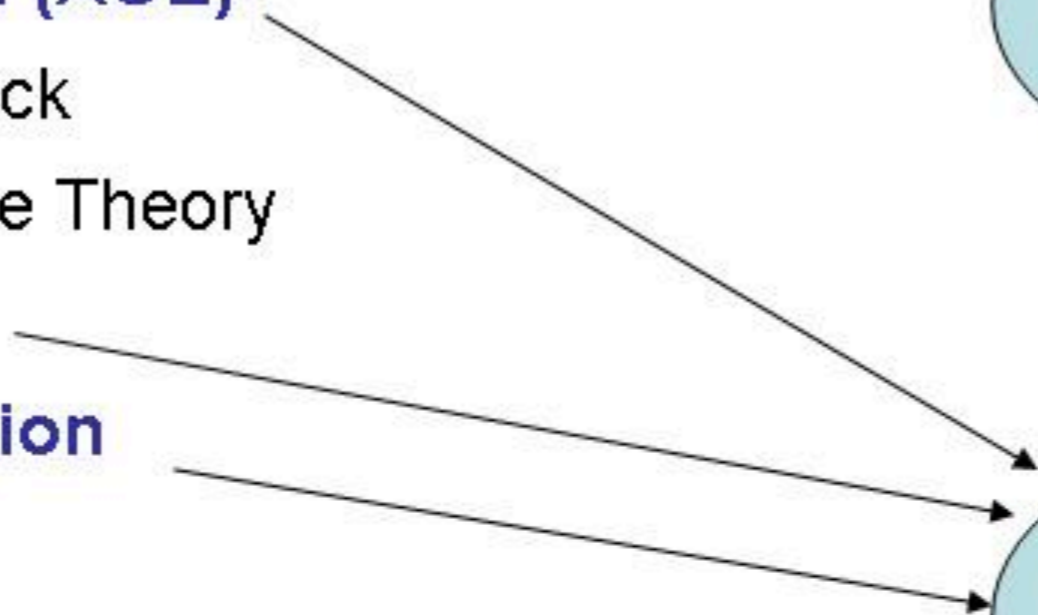
Circadian Deregulation

Evolutionary Theory

Genetic Mutation

Cellular Waste
Accumulation

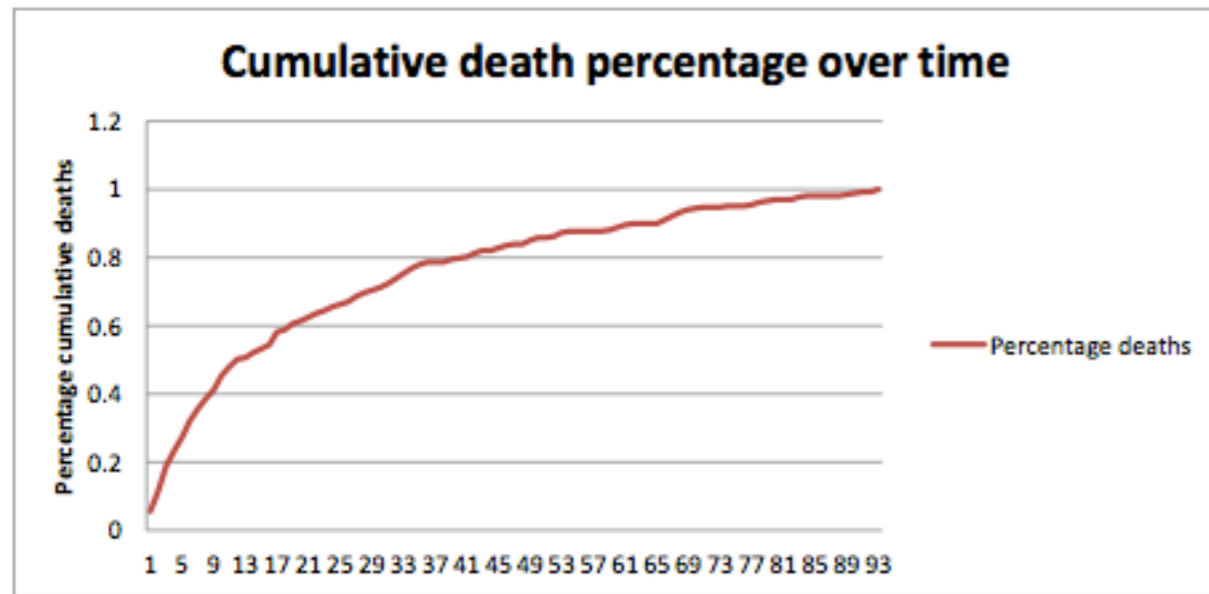
Wear and Tear



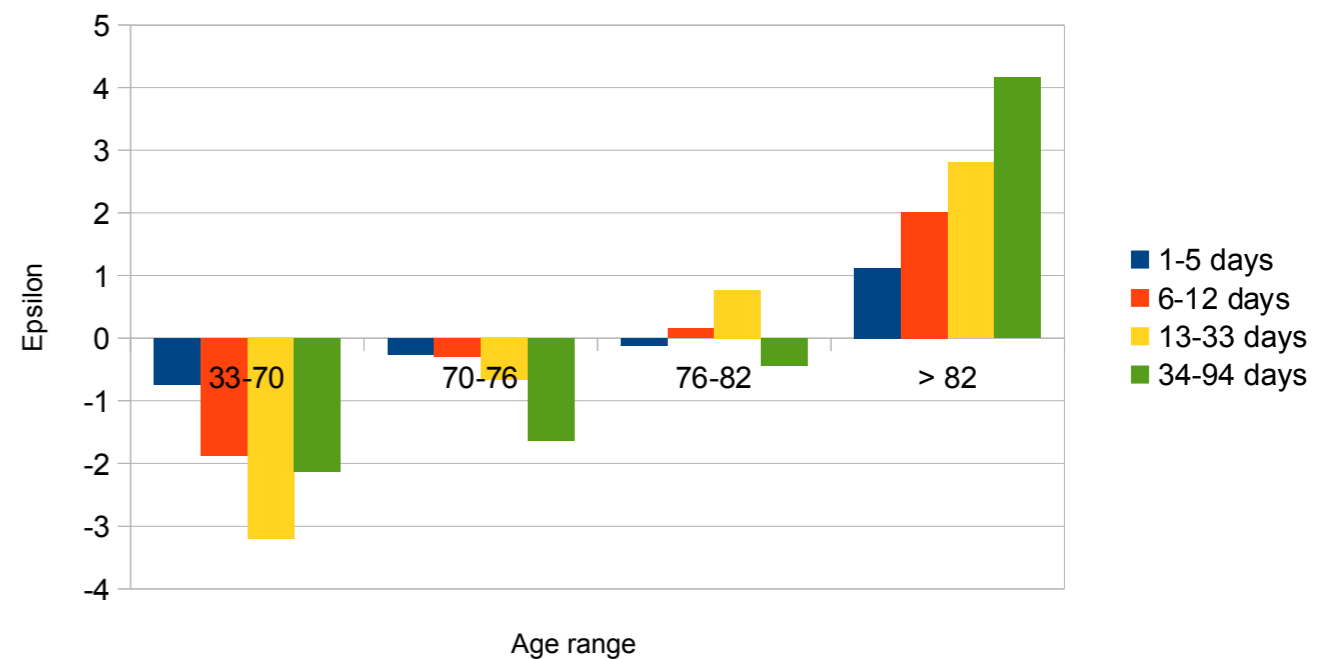
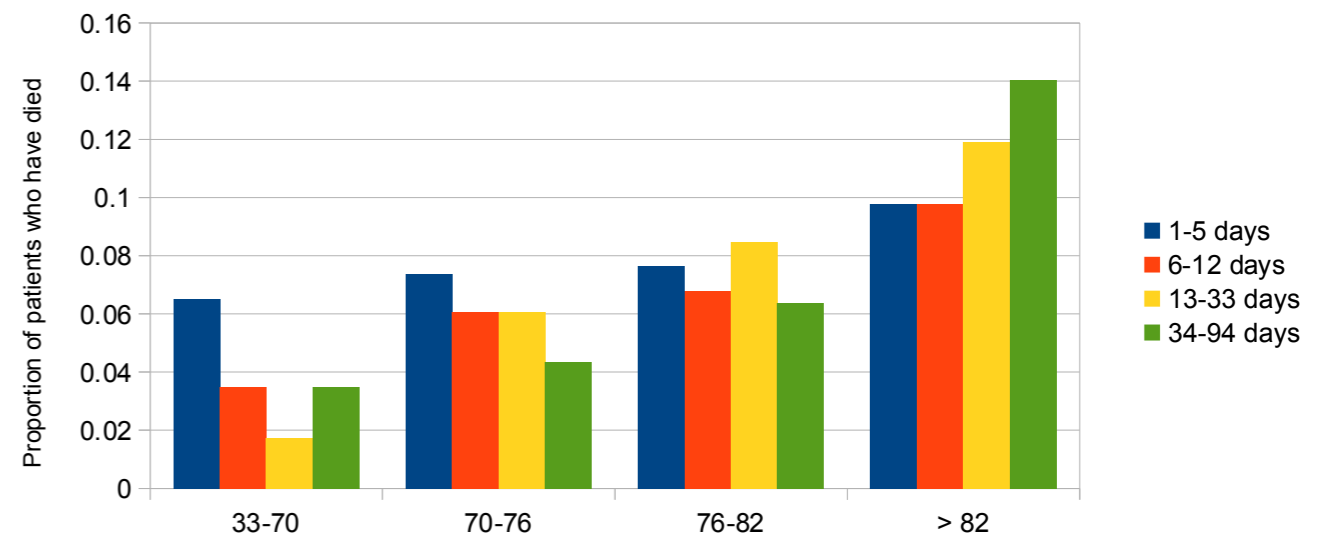
Modularity, Fragility and Complexity

- ❖ Humans are complex and therefore highly modular
- ❖ There are endogeneous (e.g., telomeric aging) and exogeneous changes (e.g. taking drugs) associated to these modules
- ❖ Environmental effects can and do act heterogeneously on structural / functional modules
- ❖ In particular, wear and tear can and will be heterogeneous
- ❖ Different modules will show different wear and tear (aging)
- ❖ Fragility arising from wear and tear can be thought of as the overall (emergent) effect of the wear and tear on the modules where the “whole” is not necessarily the sum of its parts
- ❖ Need (different) metrics to measure wear and tear for (different) modules. What is the relative “age” of a given module?

Fragility/resilience to stroke



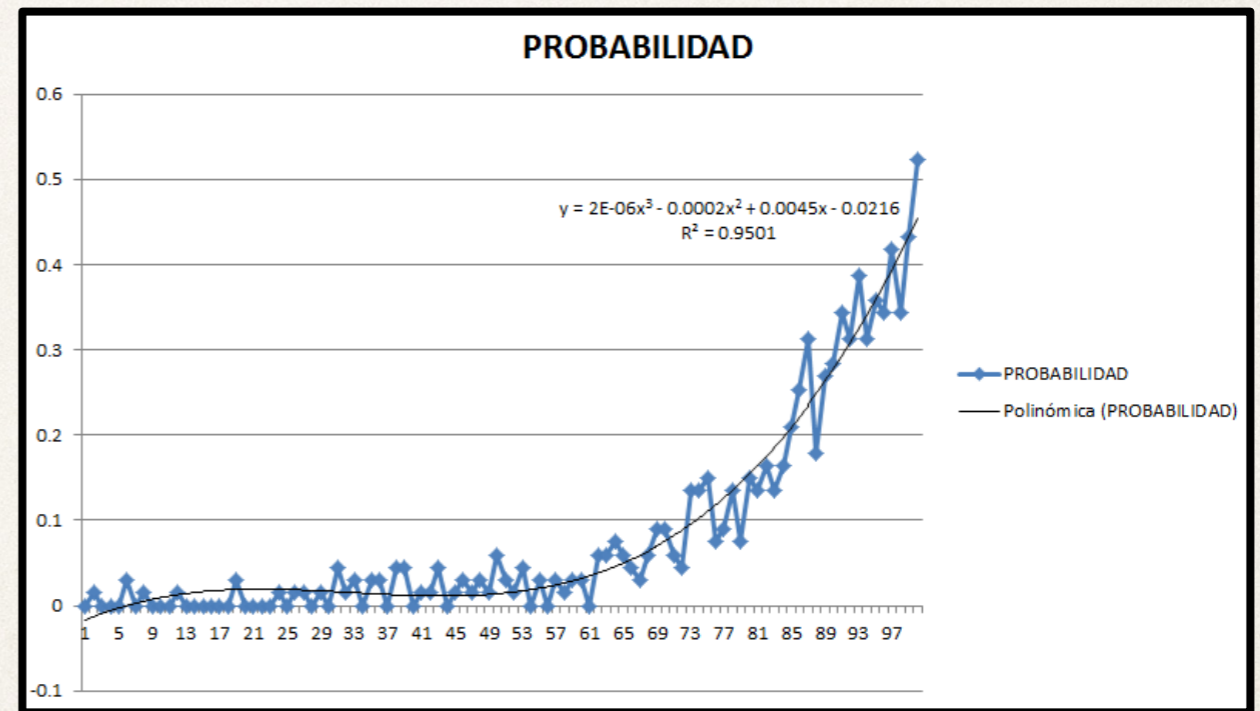
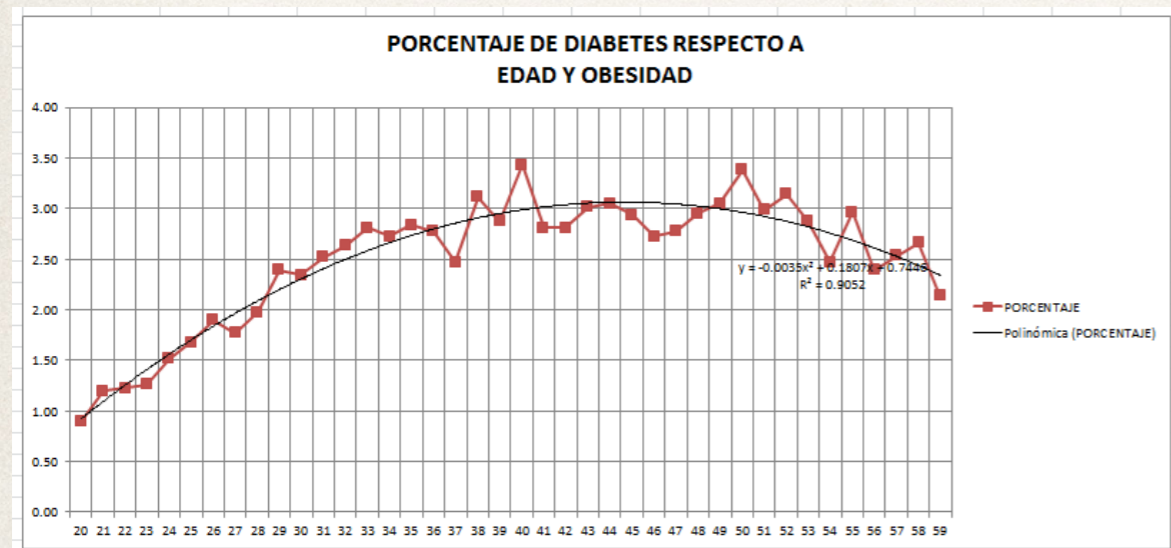
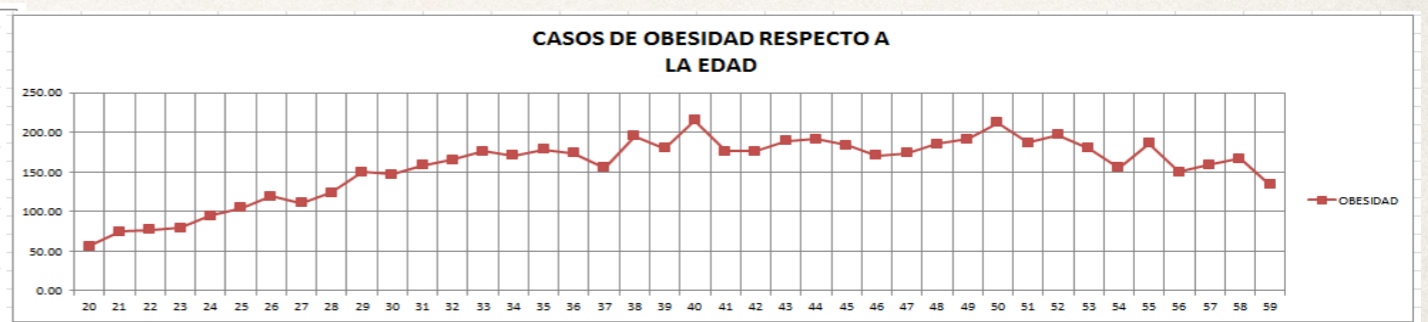
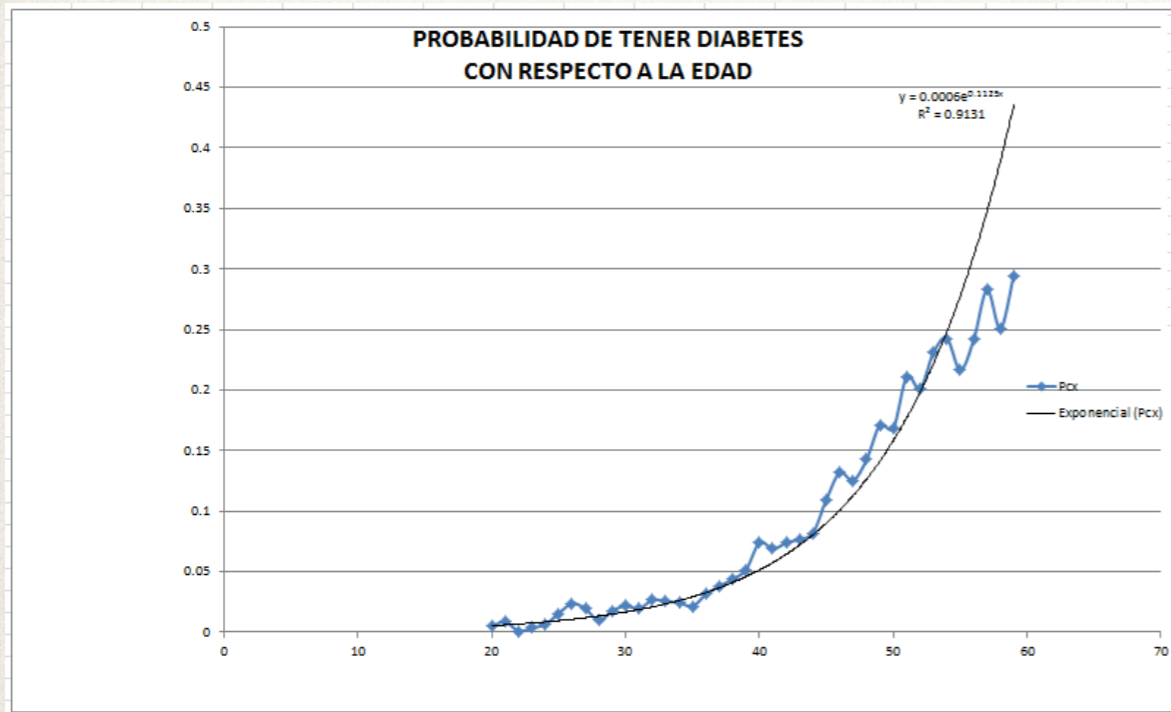
Analysis of stroke mortality should consider much shorter time intervals. Age effect is very strong but only plays a role for stroke victims > 82 . Death risk is same as for younger patients over short time scales (1-5 days) but very different over longer ones (34-94 days)



Fragility/resilience to stroke

- ❖ Mortality here is more an emergent fragility in that it is not a direct effect of the stroke itself but rather an indirect consequence of a stroke on other “aged” modules.
- ❖ It would be interesting to see what are the other principle modules involved
- ❖ Deterioration of visual acuity would be an example of wear and tear that is much more modular, local and less emergent

Diabetes

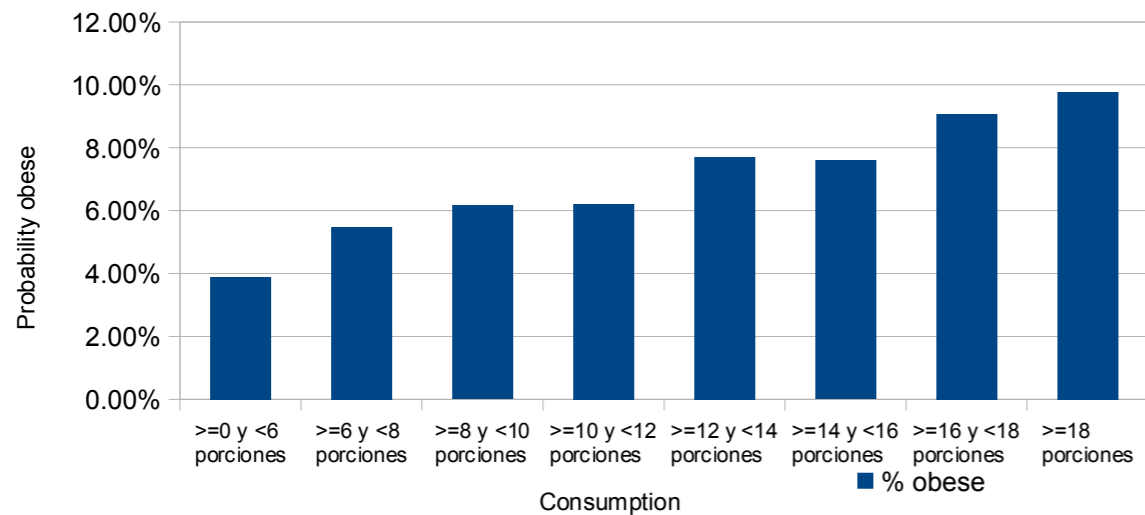


Diabetes

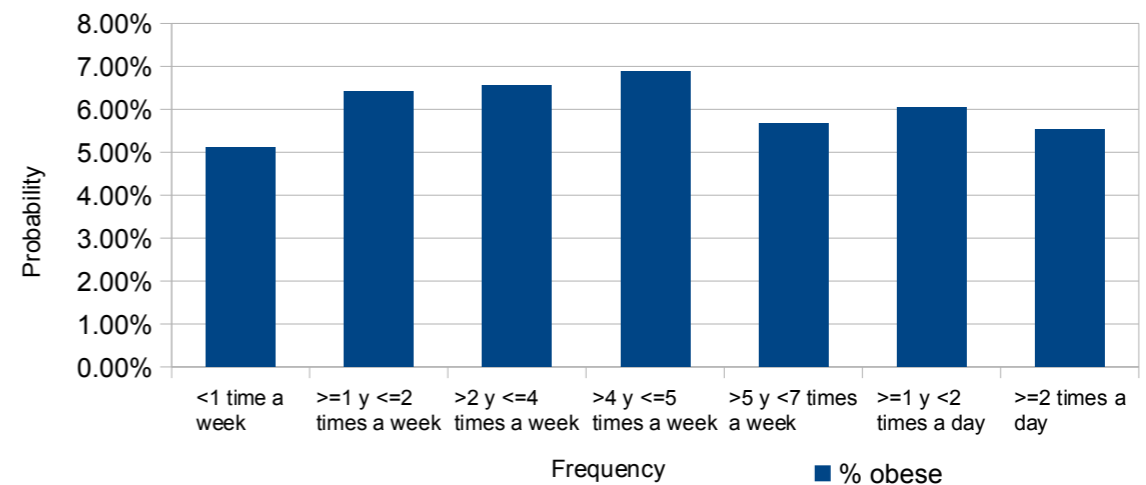
- ❖ Diabetes is a disease where risk increases as a lifestyle-dependent function of time
- ❖ An important one is nutrition - diabetes and metabolic load
- ❖ How do these factors influence aging / fragility through excess wear and tear?
- ❖ Distinct endogeneous / exogeneous factors can affect heterogeneously different modules
- ❖ Need to consider different metrics for different modules by considering the state of a module relative to what it should be or what it was

Obesity and Nutrition

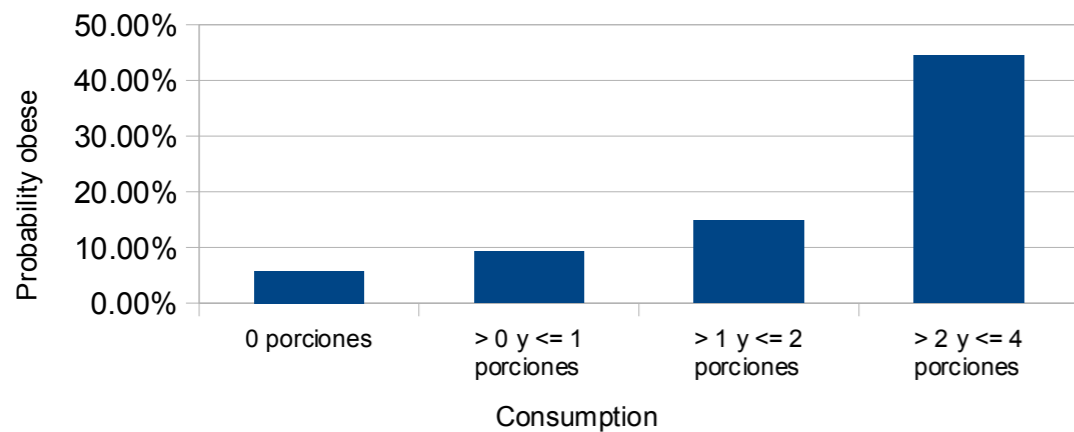
Graph of Probability of obesity vs average daily consumption



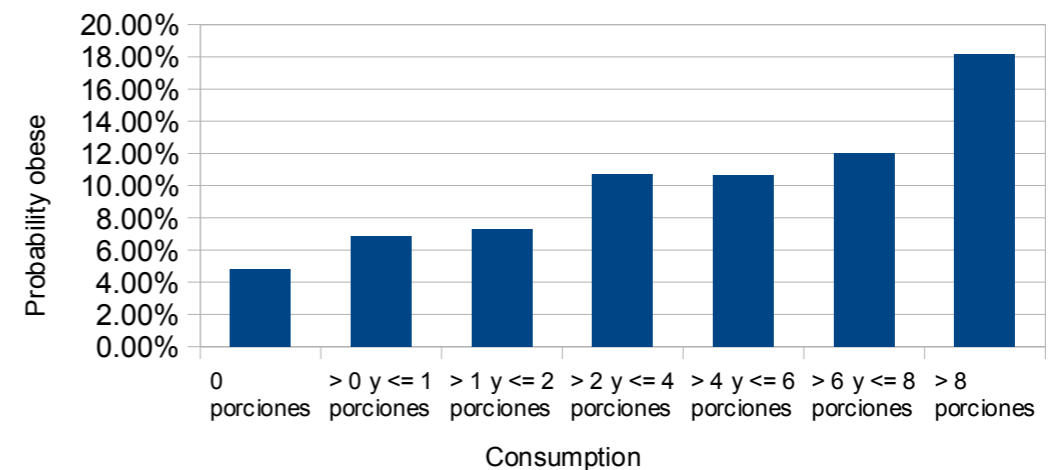
Graph of probability of obesity vs consumption frequency of fast food



Graph of probability obese vs daily consumption of diet drinks



Graph of probability obese versus daily consumption of lettuce



Obesity and Nutrition

- ❖ These results show how lifestyle (what and how much you eat) creates an environment that leads to a condition (obesity) that is associated with excess wear and tear
- ❖ It is not so obvious what factors most influence metabolic load - quantity versus quality

“Extreme” Lifestyle effects

Ideas from and work
with Ali R. Coronel

- ❖ There are particular groups where lifestyles are extreme and exogenous wear and tear can be very different than the average
- ❖ e.g. homeless people, drug addicts,
- ❖ Individuals in these groups can exhibit wear and tear far above the normal. e.g. effects of “thinner” on the lungs and cognitive capacity; malnutrition on development and the digestive system
- ❖ To what extent can an extreme lifestyle lead to a module that looks like a much “older” one
- ❖ To what extent can an extreme lifestyle lead to fragility

Conclusions

Fragility by definition has to be complex and an emergent phenomenon

Complex systems are modular

Need to consider fragility / aging at the modular level

Need metrics that establish the expected state of a module given the past state and the state for a given baseline life history

The modules undergo changes due to both endogenous and exogenous effects

A multitude of factors are associated with the exogenous part many of which can be thought of as causing “excess” wear and tear

Need to understand the dynamic process by which, for example, lifestyle affects modular conditions

Conclusions

- ❖ Need to get cause and effect right
- ❖ e.g. stroke mortality as a function of time is influenced by fragility
- ❖ Diabetes and other chronic diseases cause excess wear and tear which can cause fragility