Explaining an Empirical Formula for Bioreaction to Similar Stimuli (Covid-19 and Beyond)

Olga Kosheleva\textsuperscript{1}, Vladik Kreinovich\textsuperscript{1}, and Nguyen Hoang Phuong\textsuperscript{2}

\textsuperscript{1}University of Texas at El Paso, El Paso, Texas 79968
olgak@utep.edu, vladik@utep.edu

\textsuperscript{2}Division Informatics, Math-Informatics Faculty, Thang Long University
Nghiem Xuan Yem Road, Hoang Mai District
Hanoi, Vietnam, nhphuong2008@gmail.com
1. Bioreactions: general reminder

- Most living creatures have the ability to learn.
  - When we first encounter some stimulus – e.g., some chemical substance or some bacteria,
  - we do not know whether this stimulus is harmful or beneficial.
- This encounter – and several similar encounters – show us whether this particular stimulus is harmful, beneficial, or neutral.
- We learn from this experience.
- So next time, when we encounter a similar stimulus, we know how to react: e.g., fight or flee if this stimulus is harmful.
2. Bioreaction depends on whether stimuli evolve with time

- Some stimuli – e.g., smells associated with some chemicals – do not change with time.
- So, we learn to associate the smell with the corresponding stimulus; e.g.:
  - the smell of a dangerous predator with danger, and
  - the smell of juicy edible apples of mushrooms with tasty food.

Living creatures can become very selective in this association.

- They easily distinguish the smell of a dangerous wolf from a similar smell of a friendly dog.

- In such situation, an optimal strategy for a living creature would be:
  - to remember the exact stimulus – and
  - only react to exactly this stimulus.
3. Bioreaction depends on whether stimuli evolve with time (cont-d)

- Other stimuli vary in our lifetime.

- For example, many viruses – e.g., flu and Covid-19 viruses – evolve every year; in this case:
  - if the cells protecting our bodies from these viruses would only react to the exact shape of the viruses they encountered last year,
  - this would leave us unprotected against even a very minor virus mutation.

- In such cases, it is important to react:
  - not only to the exact same stimulus as before,
  - but also to stimuli which are similar to the ones that we previously encountered.
4. The closer the new stimulus to the original one, the stronger the reaction

- When we encounter the exact same dangerous stimulus, we are absolutely sure that this stimulus is dangerous.
- So we should react with full force.
- On the other hand:
  - when we encounter a stimulus which is similar to the original stimulus,
  - we are no longer 100% sure.
- This new stimulus may be harmless.
- We may be wasting resources if we immediately launch a full-blown attack against it.
5. The closer the new stimulus to the original one, the stronger the reaction (cont-d)

- These resources can be needed in the future, when a serious danger comes.

- So, the farther away the new stimulus from the original one, the weaker should be the bioreaction to this stimulus.

- Vice versa, the closer to the new stimulus to the original dangerous one, the stronger should the bioreaction be.
6. An empirical formula describing this dependence

- In many biological situations, there is a natural way to measure the distance $d$ between two stimuli.

- E.g., we can measure the distance between the two DNAs by the total length of the parts which are specific to one of them.

- The observations are in good accordance with the following dependence of the reaction force $f$ on the distance $d$:

  $f = F_0 \cdot \exp\left(-k \cdot d^\theta\right)$.

- The recent papers show that the observed biological values of these parameters are close to optimal.
7. Problem

- A natural question is: how to explain this empirical dependence?
- In this talk, we provide a possible from-first-principles explanation for the above empirical dependence.
- Before we consider this specific problem, let us recall where many from-first-principles explanations come from.
8. Numerical values vs. actual values

- What we want is to find dependence between the actual values of the corresponding quantities.

- However, all we can do is come up with relation between numerical values describing these properties.

- Numerical values depend not only on the quantity itself.

- They also depend on the choice of the measurement scale.

- For example, the numerical values depend on the choice of the measuring unit.
  
  - If we replace the original measuring unit with the one which is $\lambda$ times smaller,
  
  - then all numerical values multiply by $\lambda$: $x \mapsto \lambda \cdot x$.

- In particular, if we use centimeters instead of meters, then 1.7 m becomes 170 cm.
9. Numerical values vs. actual values (cont-d)

- For many physical quantities like time and temperature, the numerical values also depend on the selection of the starting point.
  - If instead of the original starting point, we choose a new starting point which is \( x_0 \) units earlier,
  - then all numerical values are changed: \( x \mapsto x + x_0 \).

- There may also be non-linear rescalings.

- In all these cases, moving to a different scale changes the numerical value:
  - from the original numerical value \( x \)
  - to the new value \( T_c(x) \), where \( c \) is the parameter, and \( T_c(x) \) is the corresponding transformation.

- For example:
  - for changing the measuring unit, \( T_c(x) = c \cdot x \),
  - for changing the starting point, \( T_c(x) = x + c \). etc.
10. Invariance: general idea

- In many practical situations, there is no meaningful way to select a scale.
- All scales are equally reasonable.
- In such situations, it makes sense to require that:
  - the relation \( y = f(x) \) between the two quantities \( x \) and \( y \)
  - has the same form in all these scales.
- Of course:
  - if we re-scale \( x \), i.e., replace it with \( x' = T_c(x) \),
  - then, to preserve the relation between \( x \) and \( y \), we also need to re-scale \( y \),
  - i.e., to apply an appropriate transformation \( y \mapsto y' = T_c'(y) \).
Then, we can require that:

- for every $c$ there exists a $c'$
- for which $y = f(x)$ implies that for $x' = T_c(x)$ and $y' = T_{c'}(y)$, we have $y' = f(x')$. 
12. Invariance: example

- The formula $a = s^2$ relating the square’s area $a$ with its side $s$ remains valid if we replace meters with centimeters.

- However then, we need to correspondingly replace square meters with square centimeters.

- In this case, for $T_c(x) = c \cdot x$, we have $T'_c(y) = c' \cdot y$ with $c' = c^2$. 
13. How invariance explains a dependence: example

- Let us consider situations when:
  - for every $c$, there exists a value $c'(c)$ (depending on $c$)
  - for which $y = f(x)$ implies $y' = f(x')$, where $x' = c \cdot x$ and $y' = c'(c) \cdot y$.

- Now:
  - substituting the expressions for $x'$ and $y'$ into the formula $y' = f(x')$ and taking into account that $y = f(x)$,
  - we conclude that for every $x$ and $c$, we have $f(c \cdot x) = c'(c) \cdot f(x)$.

- It is known that every continuous (even every measurable) solution to this functional equation has the form $y = A \cdot x^b$.

- Thus, this ubiquitous power law can be explained by the corresponding invariance.
14. For our problem, what are the natural scales?

- Our problem is to find the dependence between the interaction force $f$ and the distance $d$.
- So, we need to understand what are the natural scales for measuring these two quantities: distance $d$ and force $f$.
- For distance, the usual distance measures are appropriate.
- So, a natural change in scale in the change of the measuring unit:

$$d \mapsto c \cdot d.$$
15. Case of force: analysis of the problem

• For force, the situation is not that straightforward.

• In a purely mechanical environment, we can combine several forces together.

• So we can easily see what corresponds to 2 or 3 unit forces.

• So, if we select a unit force $f_0$, we can talk about:
  
  – the force $2f_0$ which is equivalent to a joint action of two unit forces,
  
  – the force $3f_0$ which is equivalent to a joint action of three unit forces, etc.
16. Case of force: analysis of the problem (cont-d)

- In such an environment, the following will be a natural scale for measuring force:
  - the numerical value of the force \( f \) is the number \( n \) for which
  - the force \( f \) is equivalent to the joint action of \( n \) unit forces:
    \[
    f \approx n \cdot f_0,
    \]
  - i.e., in effect, the value \( n \approx f / f_0 \).
17. Case of force: analysis of the problem (cont-d)

- However, for biosystems, no such natural combination of forces is possible.

- The only thing we can do is compare two forces.
  - Of course, if the forces are almost the same, we will not be able to distinguish them.
  - So, if we select a unit force $f_0$, then the next natural value $f_1$ is the smallest value $f_1 > f_0$ that can be distinguished from $f_0$.
  - After that, the next natural value $f_2$ is the smallest value $f_2 > f_1$ that can be distinguished from $f_1$, etc.
18. Let us describe the above idea in precise terms

- To describe these values in precise terms, we need to be able to determine:
  - for each force $f$,
  - the smallest value $g = F(f) > f$ which can be distinguished from $f$.

- Processes involving forces do not depend on the exact choice of the physical measuring unit for a force; so:
  - if we have $g = F(f)$ in the original units for physical force,
  - then in a new scale, for $f' = c \cdot f$ and $g' = c \cdot g$, we should have $g' = F(f')$. 
19. Let us describe the above idea in precise terms (cont-d)

- Now:
  - substituting the above expressions for \( f' \) and \( g' \) into this formula and taking into account that \( g = F(f) \),
  - we conclude that \( F(c \cdot f) = c \cdot F(f) \).

- In particular, for \( f = 1 \), we get \( F(c) = q \cdot c \), where we denoted \( q \overset{\text{def}}{=} F(1) \).

- Thus, we have \( f_1 = q \cdot f_0 \), \( f_2 = q \cdot f_1 = q^2 \cdot f_0 \), \( f_3 = q \cdot f_2 = q^2 \cdot f_0 \), and, in general, \( f_n = q^n \cdot f_0 \).

- So, a natural scale for measuring the bioforce \( f \) is the number \( n \):
  - for which \( f \) corresponds to the \( n \)-th element on this scale,
  - i.e., for which \( f \approx q^n \cdot f_0 \) and
  
  \[
  n \approx \log_q(f/f_0) = \frac{\ln(f/f_0)}{\ln(q)}.
  \]
20. Let us describe the above idea in precise terms (cont-d)

- It should be mentioned that this formula describes what is known in physiology as Weber-Fechner Law – that:
  - the intensity of each sensation
  - is proportional to the logarithm of its physical measure (energy or force).
21. From the above somewhat simplified description to a more realistic one

- In the above analysis, we implicitly assumed that for every two forces, we can either distinguish them or not.
- However, this implicit assumption is a simplification.
- When one of the forces is much larger than the other one, then, of course, this is absolutely true.
- However, as the forces get closer to each other, there appears a probability that we will not be able to distinguish these forces.
- The closer these forces to each other, the larger this probability.
- When the compared forces are very close, this probability becomes very large.
- Then, for all practical purposes, we cannot distinguish them.
22. From the above somewhat simplified description to a more realistic one (cont-d)

- In view of this fact:
  - to describe the scale,
  - we need to also select a confidence level with which we can distinguish the two forces.

- If we select this confidence level too high, then we will need a large value $q$ – the ratio of the forces $f_1/f_0$.

- The smaller $q$, the smaller the confidence level.
23. We arrive at different natural measurement scales for (bio)force

- There is no fixed confidence level, so there is no preferred value $q$.
- In other words, we can have different natural scales corresponding to different values $q$.
- What is the transformation between two different natural scales for measuring (bio)force?
- One can see that $n' = c \cdot n$, where we denoted

$$c \overset{\text{def}}{=} \frac{\ln(q)}{\ln(q')}.$$
24. Which dependencies are invariant with respect to these transformations

- We want to find out how force $f$ depends on the distance $d$.
- For biosystems, a natural way to describe this dependence is by using natural scale $n$ for bioforce.
- Thus, we want to describe how the bioforce $n$ depends on the distance.
- Both for the distance and for the bioforce, natural transformations have the form $x \mapsto c \cdot x$.
- Thus, a natural invariance of the dependence $n = N(d)$ means that:
  - for every $c$, there should exist some value $c'(c)$
  - such that $n = N(d)$ implies that $n' = N(d')$, where we denoted $d' \overset{\text{def}}{=} c \cdot d$ and $n' \overset{\text{def}}{=} c'(c) \cdot n$.
- We have already mentioned that this invariance implies that $n = A \cdot d^b$ for some constants $A$ and $b$. 
This explains the desired dependence between $f$ and $d$

- Our ultimate objective is to explain the empirical dependence between the physical force $f$ and the distance $d$.

- Let us therefore see how the above dependence between $n$ and $d$ will look like in terms of the dependence between $f$ and $d$.

- To find this out, let us plug in the above expression for $n$ into the above formula $f = f_0 \cdot q^n$, i.e., equivalently, $f = f_0 \cdot \exp(n \cdot \ln(q))$.

- This substitution leads to $f = f_0 \cdot \exp(A \cdot \ln(q) \cdot d^b)$.

- This is exactly the desired formula $f = F_0 \cdot \exp(-k \cdot d^\theta)$, for $F_0 = f_0$, $k = -A \cdot \ln(q)$, and $\theta = b$.

- Thus, we indeed have a from-first-principles explanation for the above empirical dependence.
26. Bibliography

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