On some problems in a very basic hosting model in biophysics

(*Rather humble attempt to synthesize Biology and Physics*:)

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Abstract. - In many biological disciplines dealing with cell structures, kinetics of enzymes or thermal adaptation, water is often implicitly treated as a stage, where all important actions are performed, but with its only passive involvement. This is not declarative but de-facto view and is for sure a result of a continued specialization. Nevertheless, when one plank of the stage is bent and dancers' heels often get stuck in this place, is it any wonder that the dance looks bizarre and at times enigmatic? The paper tries to explain some reasons for this enigma, which evidences are also given. The feature of water itself, one more abiotic factor is taken into consideration, providing a new explanation of many known facts. The paper examines the contribution of this water's characteristic to some details of enzymes kinetics and thermal adaptation.

[*Within this paper some comments, like this text, can be given in the square brackets*.]

Water is a *conditio sine qua non* for any cellular structure and enzyme operation. This is true to a such degree that almost any study of enzymes kinetics deals with the word "solution" (behind which the water lurks), but any specifics of the water itself are hardly considered, in contrast to the enzymes chemistry for example, where such properties of water as the hydrogen bonding, covalent bonding and high specific heat capacity are commonly used.
This brief survey will try to correct the situation, adding one more unaccounted abiotic factor to the studies of enzyme kinetics and thermal adaptation. The title of the article suggests the possibility of another view on water as a host, and the enzymes, cell structures, etc as a client, which not only performs its own tasks, but inherits some specific features of the host.

One, yet not alone water's peculiar characteristic is the fact of the minimum, which a specific heat capacity of liquid water (Cp) has at ca. 35°C-36°C [9], [10], there are slightly different values in different sources. It means the function Cp(T) of liquid water is not only far nonlinear but in mathematical terms not even monotonic. The heat capacities of most other liquids continuously rise with temperature.
Nevertheless, this fact is true for pure water, whereas the situation is so far unknown for any complex solution, typical when it comes to the enzymes' operation. However, the paper is based on the assumption that this is also true for a biological solution of a low concentration.
The paper examines the contribution of this water's characteristic to some details of enzymes kinetics and thermal adaptation.

By its very meaning this characteristic should be rather heavily involved either in a local (on-site) thermal balance, as in creating of a thermal heterogeneity in a nearby area. With this in mind, the question arises - does the factor of this peculiarity is strong enough to make a noticeable effect on the activity of the enzymes?
As the paper will try to show, this can be a factor, affecting at least the enzymes operation, reducing or promoting their activity.

Method

To confirm the hypothesis, albeit partly, it would be almost sufficient to reinterpret in this context an existing large volume of data on thermal adaptation and enzyme kinetics.
We temporarily postpone many possible consequences and predictions, our only goal for now is collecting of any confirming data.
So a search was performed to find any corroborations of the thesis. To boost and simplify the search it was Internet-oriented, i.e. carried out on the data most of which are available in the Internet sources. The difficulty of the method is the need to estimate as accurately as possible the temperature to which the specific event is attributed, this should be done to eliminate the most of false positives while missing no any false negatives. Taking into account the specific difficulties in accurately measuring the temperatures of various living beings, we'll take the tolerance interval as a zone of ±3°C around our point of interest (i.e. ca. 32°C - 38°C), and register only events with attributed temperature matching this range. There is also a subtlety concerning significant digits of a measured value: some experimental value, e.g. 34°C within a biological investigation very often by default means 34.0°C, whereas from the viewpoint of the measurement uncertainty (as is commonly in physics) it may be any value in the range (34 - 1)°C - (34 + 1)°C. This reflects the difference between the objects of research in biology and physics and should also be taken into account.

Further we'll specify the cases in the existing data where the effects of this factor come out; we'll do the job relying on the following more or less simple and even evident ideas:

1.The temperature at which the effect takes place (ca. 35°C) lies almost in the middle of the range suited for living objects, which implies the high significance of this effect for them. It's important also to emphasize the physical nature of the effect - its temperature domain is very narrow, on the contrary to biological events.

2. In the chain Water -> Solution -> Enzymes -> Behaviour (of the Host), any strong enough local anomaly translates onto the next level, where its "fingerprints" can be detected in the new context. The translation can be performed through all the chain.

3. The "fingerprints" of the Cp anomaly are expected to be detected as irregularities, any significant disturbances in the data on enzymes activity, occurring in the temperature vicinity of the water anomaly (ca. 35°C).

4. Perhaps the strongest effect on the enzymes activity is achieved when the system pass the point of Cp-minimum in one or another direction, when the temperature increases or decreases, but not merely stays at this point. Some preliminary base for this assumption already exists.
A confirmation of the thesis-4 lies in the observations [3] and [5] of a difference in the properties of water at the same temperature - if one time the water goes to this temperature by heating, whereas another - by cooling.
"Certainly, water behaves differently, and possesses a different structuring, at the same temperature depending upon whether it is being heated or cooled" - [3].
In our context this means unavoidable additional costs for a hosting system to traverse this point. The costs can even depend on the direction the point is crossed. Not in all cases these costs would be prohibitive, but they should manifest themselves quite noticeably as a mass phenomenon.

5. The catalyzing ability of any enzyme is restricted on the thermal scale - too many conditions are to be met to operate effectively. Surely, it is true for any catalyzers, but in the case of enzymes we have a hosting system which could and had enough time to create and select the most appropriate ad hoc catalyzers.

6. An impact of this factor on the activity of various enzymes can be hardly described as inhibitive or promotive only, there are too many of them. But the predominant reaction of a hosting system - of a cell, or the whole organism - is expected to be more negative than positive because this temperature region is comparatively narrow and for many hosting systems would be cheaper not to develop some special means to get more adapted to it, but simply avoid this region using already existing ones.
Hence, for a brevity sake we'll sometimes call the point of our interest as *PV* (*Punctum Vitandi*, not confuse with *Punctum Vitarum*:).
The price, referred above, is the refusal to conserve the region of genes responsible for activation of the enzymes; sometimes this price seems to be very high:
"Because the active site of an enzyme requires very specific amino acids to promote covalent reactions, this region [of genes -P.D.] generally remains conserved during evolution. Instead natural selection favors mutations that alter the conformational stability of the enzyme" [1, p.41]. The last sentence shows some perspective for any creature when its adaptation ability is exhausted.

7. Any activity of poikilotherm creatures very strongly depends on the ambient heat. Higher temperatures favor the poikilotherm, until a some limit, of course. The theses 4 and 6 proclaim the very point of our interest - *PV* - as the point, which is better (cheaper) to avoid. On the other hand, according to thesis-1, the temperature domain of the effect is very narrow. Hence, we can't resist the temptation to make a prediction right now: seeking to get the maximum gain from an ambient heat, a poikilotherm often will shift the range of the most preferred temperatures up to the very point of our interest - surely, if his environmental temperatures extend to it.

We begin considering in this context any data from a recognized source of data on thermal adaptation [1]. The source is available through Internet as a preview.
The "fingerprints" of the Cp anomaly are expected to be detected as irregularities, any significant changes of the data on enzymes activity, occurring in the temperature vicinity of the water anomaly (i.e. ca. 35°C).

The graphs of anisotropy vs body temperature in Figure 3.10 from [1] illustrate the thesis-3. There are evident perturbations in the region of 30°C - 40°C, i.e. *in the PV-vicinity* - and only there. So this is the very first case "pro".

The graphs in Figure 3.6 from [1] are also of the same "pro" kind.

Some graphs from Figure 3.7 (the same source) comply with our theses whereas others do not. All the graphs display the activity of adenosine triphosphatase (ATPase) for different species of lizards. Surely, the hypothesis is not universal. Bearing in mind the sheer number of known enzymes (~ 5000 on year 2012 and much more expected in the long run), not to mention all live "platforms", where all these enzymes are working - any different result would be difficult to expect.

Figure 3.5 from [1] shows graphs for two statistical models of enzyme performance: a Gaussian and an exponentially modified Gaussian. In our context the both models comply with the thesis-1, showing a significant variations of the data near the *PV*.
The remark which follows the graph: "... the Gaussian model provides a better description of the data." is a valuable confirmation of our thesis-6. Really, here we have a performance curve of a whole hosting system (a lizard), not a single enzyme, and according to the Gaussian model we observe a continuous decrease in the region of interest - the hosting system can and do avoid it. On the contrary, the exponentially modified Gaussian model shows a narrow maximum at the point of interest, which, as we see, is not confirmed by the data.

Figure 3.2 shows slightly different case. Here the maximum is achieved at ca. 38°C, but the raw measurement steps, no less then 2°C, do not allow to consider this case as a serious argument against our thesis.
An explanation of such raw (only for our context!) steps can be found in the same source - the data would have been obtained through thermal mapping, and "these thermal maps have ... a mean error of less than 2°C!" ([1], p.32).   Which surely can be a great achievement collecting a data in the field, but can give only some weak additional confirmation of our thesis-3.

Figure 3.1a comply with theses 4 and 6, albeit indirectly. Here we observe a steep decrease in performance to ca. 30°C. The fitness curves on it belong to a hosting system, an aphid, so this is a true supportive fact for the thesis-6, because the aphids have a means to avoid this temperature region, so they "don't bother" to develop an internal adaptability in this temperature direction.

Figures 3.12 and 3.13 add more confirmation to the theses 3 and 6.

The graphs "Body Temperature vs Time" from Figure 2.11 also comply with thesis-4. Here both predicted and actual data do fluctuate around our point of interest, but the graph of the actual data, unlike the predicted one, traverses this point only once, without approaching close to it anymore. This is natural if it's better to avoid this point

Now let's see some data from another recognized source also available in the Internet [6].
The very first Figure 1 showing frequency histograms has this characteristic significant drop at 35°C (percentages for mammalian species). The text accompanying it is very interesting itself:
"Our results show that most [fungal - P.D.] strains grew well in the 12°C - 30°C range, but there was a rapid decline in thermal tolerance at temperatures >35°C". [- *Voila!* - P.D.]

Here is yet one respectful source [7]:
"Above 33°C many bees cooled their body via evaporation from their mouthparts."

We are changing the source of data again. Now it will be [2]. The Fig. 3 from it shows intersection of 2 graphs, one of a mean optimal temperature, with another, representing perfect coadaptation. The hosts - Australian skinks. The intersection occurs at ca.35°C, which is interesting enough.

Continuing to search through [2] we really stumbled upon the Fig.4 (Ancestral preferred temperature) which makes it clear that the most preferred temperature range for Australian skinks is ca. 32°C - 34°C.
This fact obviously complies with the thesis-7: the skinks, being poikilotherms, seeking to get the maximum gain from an ambient heat, shifted the range of temperatures, most preferred for them, up to the very *PV*. Can it be a simple coincidence? Surely, why not. But it seems, a traverse of this point even for a nimble skink is disadvantageously.
"Changes in thermal performance curves, though minor, may well be biologically significant." [2, p.1108] (Apparently the skinks vote "pro" - in our context:)

One more source of data [8]. Now the data on tadpoles of B. japonica from two different places (p. 42):
"Results showed that the upper water temperature selected by tadpoles [from Rushan -P.D.] was statistically similar, between 36-38°C"
And later, (p. 44):
"Field measurements at different seasons showed that tadpoles consistently selected water

temperatures lower than 37°C."
Moreover, (p. 44):
"The temperature selected by tadpoles [from Guoshin - P.D.] in the laboratory (ca. 28°C) was significantly lower than that selected in the field (34°C), suggesting that the temporal and spatial distribution of tadpoles in the field cannot be explained solely by heat avoidance behavior."
The similarity with the previous example should be noted. The tadpoles, which are poikilotherms alike the skinks, select the most preferred temperatures close to *PV*. Naturally, we are speaking not about laboratory data, but about the field data.
So one more abiotic factor can be added to the list of possible factors, which follows the last excerption in the source text.

8. Chemistry of enzymes effectively maps any hosting creature to a temperature range. Due to thesis-4, including of the *PV* into this range will imply additional costs to traverse it. Hence, to reduce these costs, an average host would be interested to expel this point from its temperature range.
So all living creatures that have formed over billions of years would have to have such an impact - at least in the appearance of present-day temperature limits.
A drawing from [4] so impressively hints on the final result of this long process, that it is reproduced here (Figure 1, courtesy of P. Bøckman [4]). Figure of the same kind can be found in [1]. This is Figure 3.14, [1] but it lacks such a definitive indication of the temperature.
So the point of Cp-minimum also can be proposed as a point separating most cold-blooded and warm-blooded creatures.

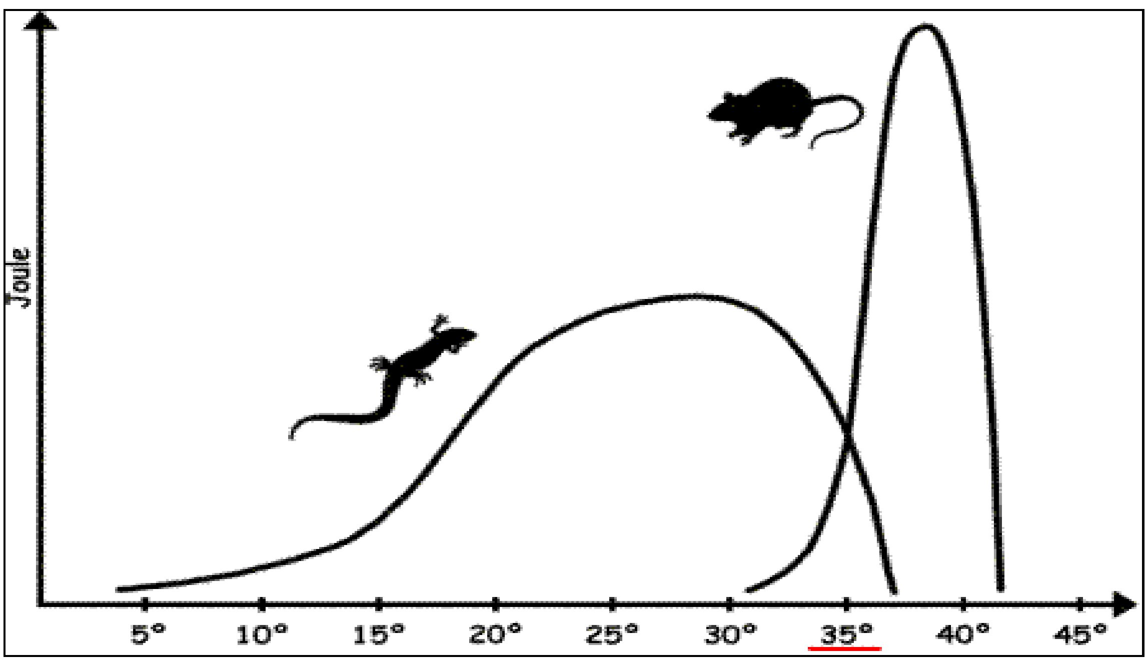

Figure 1. The result of the translation from thesis-2, performed through all the chain. The extremely long processing resulted in a superposition of very many individual curves, describing performances of various enzymes in an environment that varies over space and time, and in the presence of the stable and independent factor.

Results.

Surely, comparing to a vast amount of a relevant data, the number of evidences may seem insufficient yet. However, it should be understood: these were all sources studied so far. I.e. any source with a relevant data - the data on events which can be attributed to the temperature region of our interest - contained one or more data, which could be interpreted in a favor of our hypothesis. And this interpretation was performed with ease, which well represented data provide.
Not to mention a large volume of data being not studied yet.
The true goal of the paper is to draw possible attention to a manifestations of some specific features of the host (water) on the level of "client" (chemistry of enzymes) - which manifestations are expected to find.
The paper shows that almost any living creature should try to avoid very narrow range of temperatures around the point of water's thermal anomaly. Crossing this range brings some additional costs, yet apparently not fatal. Here we can only to reiterate:
"Changes in thermal performance curves, though minor, may well be biologically significant." [2, p.1108]
Obviously, the region around the Cp minimum is interesting enough to make direct experiments and collect data more specifically.
More refinements here would be needed due to the importance of Cp for thermodynamic aspects of enzymes' operation and local (in-site) heat generation.

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