

From:

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Report on a Ph.D. thesis by Dr. Stanislav Matousek*General comments:*

In this thesis Dr. Matousek has produced an in depth analysis of the three competing methods for calculation and clinical evaluation of acid-base physiology, including the bicarbonate approach, "traditional" base excess approach, and "modern" Stewart approach using a detailed theoretical framework and computer simulations analyzing these approaches and their limitations.

He has clearly elucidated why the modern approach is flawed, with an especially good discussion of why the diagnosis of hypoproteinemic alkalosis is actually an artifact of the choice of coordinates. At the same time Dr. Matousek has pointed out the value of the value of precise correction to the anion gap afforded by the modern approach and the importance of the buffer value as a neglected acid base parameter.

He has described the concept of linearization of protein buffer curves and the importance to physiology. The standard linear approximation used for the van Slyke equation viewed as a Taylor series correction to the value at physiological pH has not been commented upon previously.

The candidate has described in detail the limitations of the single monoprotic acid approximation in the description of plasma and provides the first rigorous comparison of the Watson and Figge-Fencel models for implementation of the modern approach.

Dr. Matousek has derived various transformations between physiological acid-base parameters. Equation 3.32 relating the change in strong ion difference to the base excess is a particularly important new result.

Finally, he has implemented a rigorous acid base model into a physiological simulator for clinical and educational use.

Typographical errors, comments, and suggestions:

Page 10, paragraph 1, line 4. "ballance" to "balance"

Page 10, paragraph 1, line 5. "pneumology" to "pulmonology"

Page 10, paragraph 3, line 4, Poul instead of Peter Astrup

Page 11, paragraph 2, line 1. Do you mean "amended"?

Page 14, paragraph 2, line 6. Do you mean equation 1.5?

Page 15, paragraph 2, line 6. What is "OH remark"?

Page 18, paragraph 2, line 1. I am not sure I would consider Wikipedia a reliable source.

Page 30 below Eq. 1.46. An important point to make is that equilibrium concentrations can be measured from the analytical concentration and the pH, which are usually measurable.

Page 31, figure 5 caption. Should this be alfa3?

Page 37, next to last line. Should there be something in the ()?

Page 38, Eq. 1.88. Should there be a C_b on both sides of the equation? In other words, should there be a different font on one side?

Page 41, paragraph 2, line 4. At some point prior to this, you probably want to define electroneutrality as applied to aqueous solution.

Page 44, figure caption. The connection of all buffers through H^+ concentration is called the isohydric principle.

Page 51, paragraph 1, line 7. Should be "don't know how".

Page 53, third paragraph from bottom, last line. Should be "denature".

Page 62, last paragraph, line 5. Should be "pKA"

Page 70. Should there not be a factor of 2 in front of calcium and magnesium if concentration is in mM?

Page 82, paragraph 1, line 4. Should be "Wrenn"

Page 91, caption of Figure 36. Might not the similarity on the right compared with the left be related to the scales on the y-axis?

Page 94, last paragraph, first line. Should this be "?"

Page 98, last paragraph, last line, Should be "Wrenn"

Page 122, paragraph 1, line 2. "pneumology" to "pulmonology".

Page 122, paragraph 2, last line "make up their own mind".

Page 122, paragraph 3, line 5. Isn't ctH^+ the same as C_H ?

Page 122, paragraph 3, line 9. The buffer value is only invariant at constant temperature and pressure.

Page 122, paragraph 3. Final sentence. This is very important to point out.

Page 123, paragraph 1, last line. Do not need a comma.

Page 123, last paragraph, line 7. Should be "However, whatever"

Page 126, first paragraph, lines 5 and 6. SID should be in italics

Page 126, paragraph 1, line 10. "then" should be "than"

Page 126, paragraph 2, next to last line. "looses" should be "loses"

Page 128, paragraph 1. Well said! Not many people understand this.

Page 130, paragraph 2, line 6. "govern" should be "governing"

Page 136, paragraph 3, line 6, should be "than"

Should be Wooten EW in references

Guenther's textbook is referenced twice as 23 and 72 in the references.

Conclusion:

The candidate has demonstrated a very good command of the literature in this field and an excellent grasp of the theory of acid-base physiology. He has contributed to our understanding of mathematical modeling of physiological acid-base balance and to a physiological simulator for educational and clinical use.

The thesis exhibits the expectation for independent scientific work for awarding the Ph.D. I recommend that the thesis be accepted and Stanislav Matousek be awarded the Ph.D. degree.




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