

How I Finally Came to Terms with pK_a

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I sat on the desk in my office. Ten unhappy faces looked at me. Silence reigned, and an atmosphere of gloom and despair pervaded the room. Outside, the sky had darkened and the birds had ceased to sing. It was my annual revision tutorial on acid-base balance.

I had courageously led the party through the steaming jungles of buffer theory and together we had negotiated the reptile-infested swamps of the Henderson-Hasselbalch equation. Many were the traps that awaited the unwary, but we had emerged unscathed. It would soon be over now; our basecamp was in sight. All we had to do was to cross the calm-looking lake of the carbonic acid/bicarbonate buffer and we would be safely home. Everything was going according to plan – when suddenly a girl who up to now had said nothing, quivered into wakefulness and asked me to explain pK_a .

I had been dreading this. Let me tell you why. To be honest, I had never been particularly impressed by pK_a . In my school chemistry days he had always been surrounded by an impenetrable mist. I had tried to escape him by fleeing to the refuge of a university course, only to find him lurking in stories. By then, though, I had found a way to deal with him: whenever he appeared I would close my eyes and hope that he'd go away. By carefully avoiding any examination questions that bore even so much as a hint of him, I had passed my student days without a major confrontation. But now here I was with ten first-year medical students sitting at my feet waiting for me to explain pK_a to clothe him in *meaningful* terms for them.

I closed my eyes and hoped that he'd go away. He didn't. Neither did the ten faces. They had suddenly started to eye me with interest. The atmosphere had changed subtly. There was still silence in the air, but it was the kind that usually precedes a thunderstorm. It was as if they sensed that I was being backed into a corner, and they were waiting to see what would happen.

It was to be a fight to the finish between me and pK_a – David and Goliath. David, I remembered, had gone into battle with only five smooth stones¹ but had slain the giant Goliath with the first one.² I too had five smooth stones, five definitions of pK_a gathered over more than a decade of teaching biochemistry, and with these I hoped to bring some meaning to this elusive character.

I girded my loins for battle. In the opposite corner I saw the pK_a stretch to his full height: how tall and menacing he looked! The ten faces looked on, and the pK_a prowled around the office like a lion circling its prey. Every now and then he growled at me, as if to say, "Just you dare reveal me for what I really am".

I picked up my first stone, *the negative log of the acid dissociation constant*, and threw it at the pK_a . The stone just bounced off harmlessly. I wasn't altogether surprised: true as the definition undoubtedly was, it was too slippery: it meant little to me, and nothing at all to the ten faces who were now looking puzzled. The pK_a growled and began to edge towards me.

My second stone, *the inverse indication of acid strength*, and my third, *the mid-point of the acid-base titration curve*, both hit the pK_a but did nothing to halt his advance. He merely laughed in my face, and moved still closer.

In desperation I threw my last two stones together: *that pH below which the ionisable group is protonated*, and *that pH at which there are equal proportions of protonated and unprotonated forms*. They stopped the pK_a momentarily, and I could see that he was wounded – but only slightly. He was almost upon me now.

I stood defenseless, my weapons gone. With a growl of triumph the pK_a sprang through the air and knocked me to the floor. He was on top of me now, trying to seize me by the throat. I could see his sharp fangs and feel his hot breath. Saliva dripped from his mouth and mingled with the sweat on my brow. I struggled, of course, but he was far far stronger than me.

The pK_a was now sitting on my chest squeezing the breath out of me. I gasped, and the world began to mist over. I saw an acid give up a proton to form its conjugate base; this dissociation was mathematically described by K_a . Then the base turned into an enzyme, the proton turned into a substrate and the two bound together. The binding was mathematically described by K_m ... and under certain circumstances K_m was an inverse measure of the strength of binding between enzyme and substrate.³ It gave an upside down view of the affinity of the enzyme for its substrate.

That was it! All these years I had feared pK_a because I had been looking at the *dissociation* of acids: his very name had fooled me into doing that. But the key to unmasking pK_a did not lie there, as I now saw. No; the key lay in the *binding* of protons to bases.

'The pK_a was now an inch from my throat. I could not hold him off for much longer. If I did not

act now all would be lost. As his jaws closed about my throat I made one last supreme effort.

“Binding affinity”, I croaked.

The pK_a turned pale and relaxed his grip on my throat. I was able to push him off my chest.

“Proton-binding affinity!” I shouted, sitting up shakily. The pK_a turned a deadly white and began to cower away from me. I rose weakly to my feet, leaning heavily against my desk, and tried to think of some way to push home my advantage. Perhaps the ten faces could help me here.

“Think of a buffer”, I said to them, “what does it do?”

“Mops up protons,” came the answer.

“How?” I asked.

“By binding them.”

“That’s right”, I said. “Well, you can think of pK_a as giving an indication of the proton-binding affinity. If a group has a low pK_a then it has a low affinity for protons. It binds protons weakly; gives them up readily – it’s a strong acid. See.

They did see. And so did the pK_a . It was whimpering in a corner. Strange how different he looked: small and insignificant now that his fog was lifting. I continued.

“If a group has a high pK_a then it has a high affinity for protons; it binds them strongly; it releases them reluctantly – it’s a weak acid.”

The pK_a was writhing about on the floor. I ignored it and proceeded. I wanted there to be no doubt at all about my victory over this pestilence.

“All right,” I said, “the pK_a of deoxyhaemoglobin is 7.71 while the pK_a of oxyhaemoglobin is 7.16. What does that mean?”

The girl who had originally asked me to explain pK_a answered, “Why”, she said, “it means that oxyhaemoglobin has a lower affinity for protons, therefore it gives up protons more readily than does deoxyhaemoglobin.”

“So what?” I asked.

“So – er – so – when oxyhaemoglobin gives up oxygen, its pK_a increases so that it will bind protons more readily.” She looked shocked at her own understanding of the subject. “Why, it’s simple!” she said.

At this the pK_a uttered a blood-curdling scream, and collapsed on the floor. I scraped up the remains with a nickel spatula and put them into a bottle of preserving fluid. Later on I would have him stuffed and mounted so that he could take his place on my office wall alongside the kilojoule⁴ and the kilopascal⁵ – But meanwhile I had a tutorial to finish.

“Are there any more questions?” I asked, hoping that there wouldn’t be. There was one question, however. But it caused me little trouble. It came from a Keen student who, during the whole of

my skirmish with pK_a had been making notes in a bulging ring-file. He had noticed that I had escaped by noting the similarity between base-proton binding and enzyme – substrate interaction. He wanted to know, reasonably enough, whether acid-base dissociation could be subjected to the Michaelis-Menten treatment. “Leave it with me”, I said, “and I’ll see if it can be done.”⁶

Outside the sun was shining and the birds were singing once more. The tutorial ended and the ten faces filed out of the room. On her way out, the girl paused to thank me for explaining pK_a “It’s the first time that I’ve really understood it”, she said.

I didn’t tell her, but it was the first time that I’d really understood it, too!

¹ I Samuel 17:40

² I Samuel 17:49- 50

³ Stryer L (1981) “Biochemistry”, 2nd edition, WH Freeman and Co, San Francisco, p 114

⁴ Brown BS (1979) *Biochem Educ* 7, 88

⁵ Brown BS (1981) *Biochem Educ* 9, 109

⁶ The Keen student was on the right track. A Lineweaver-Burk treatment of acid-base dissociation is given by Solomons CC (1965) *J Chem Educ* 42 225