Table 1- Compatibility of the various models in Figure 10 to accumulated experimental data.

	Model A $k_{on}=\frac{[H^+]^2k_{on(EH_2)}+[H^+]K_{a_1}k_{on(EH)}+K_{a_1}K_{a_2}k_{on(E)}}{K_{a_1}K_{a_2}+[H^+]K_{a_1}+[H^+]^2}$	**Model B** $k_{on}=\frac{[H^+]^2k_{on(EH_2)}+[H^+]K_ak_{on(EH)}+(K_a)^2k_{on(E)}}{(K_a)^2+[H^+]K_a+[H^+]^2}$	**Model C** $k_{on}=\frac{(K_a)^2k_{on(E)}}{(K_a)^2+[H^+]K_a+[H^+]^2}$	**Model D** $k_{on}=\frac{k_{on(EH_2)}[H^+]+k_{on(E)}K_a}{K_a+[H^+]}$
R^2	0.982	0.957	0.935	0.973
Stoichiometry of $2H^+$/ 1 Dimer	Yes	Yes	Yes	No
pK_a well above 7.0	pK_{a_1} =6.80 pK_{a_2} = 8.16	pK_a =7.70	pK_a =7.28	pK_a =7.72
Single pK_a	No	Yes	Yes	Yes
Single exponential binding reaction (No intermediate)	No	No	Yes	Yes

Model A assumes two different pK_a's and three different rates for fully protonanted protein ($k_{on(EH_2)}$), protein that released one proton ($k_{on(EH)}$) and deprotonated protein ($k_{on(E)}$). Model B is similar to A, but assumes that the pK_a's of the two groups are identical. Model C is similar to B but under the assumption that binding to protonated protein is impossible, therefore $k_{on(EH_2)}$ and $k_{on(EH)}$ are both zero. Model D is a model for protonation of a single group, under the assumption that the two protons leave the protein practically at the same time due to high cooperativity. The validity of the models is challenged with four different accumulated experimental results.