**Supplementary File 2**

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| **Supplementary File 2: MWC allosteric parameters of the hemoglobin physiology**  **dataset oxygen saturation curvesa** | | | | | | |
| **Physiological dataset** | **Allosteric effector concentration** | ***bL(x105)*** | ***c*** | ***c*Calculated *n*HMWC** | ***d*Observed *n*HHill** | **Reference** |
| **pH** | **pH value** |  | | | | DiCera *et al*. (1988)  *J.Mol.Biol.* 200,  593-599 |
| 6.50 | 2.481±0.543 | 0.009±0.001 | 2.78±0.40 | 2.85±0.08 |
| 7.27 | 0.700±0.153 | 2.96±0.00 | 2.66±0.06 |
| 7.51 | 0.227±0.049 | 3.04±0.00 | 2.92±0.05 |
| 7.71 | 0.092±0.020 | 3.05±0.03 | 2.63±0.07 |
| 7.91 | 0.0485±0.010 | 3.02±0.00 | 2.72±0.06 |
| 8.50 | 0.009±0.002 | 2.85±0.29 | 2.62±0.05 |
| 9.10 | 0.005±0.001 | 2.74±0.06 | 2.24±0.06 |
| **pH** | **pH value** |  | | | | Imai, (1983)  *J.Mol.Biol*. 167,  741-749 |
| 6.70 | 14.981±3.617 | 0.007±0.001 | 2.63±0.00 | 2.77±0.08 |
| 7.20 | 1.706±0.415 | 3.02±0.12 | 2.64±0.08 |
| 7.65 | 0.148±0.036 | 3.14±0.02 | 2.58±0.06 |
| 8.00 | 0.030±0.007 | 3.05±0.19 | 2.59±0.06 |
| 8.20 | 0.007±0.002 | 2.85±0.09 | 2.56±0.05 |
| 8.80 | 0.004±0.0009 | 2.72±0.03 | 2.61±0.07 |
| **2,3-BPG** | **[2,3-BPG] (mM)** |  | | | | Benesch *et al*. (1971)  *Nat.New Biol.* 8,  174 -176 |
| 0.00 | 0.030±0.022 | 0.014±0.001 | 2.87±0.02 | 2.32±0.12 |
| 0.10 | 0.033±0.024 | 2.87±0.12 | 2.67±0.16 |
| 0.25 | 0.057±0.041 | 2.88±0.03 | 2.75±0.12 |
| 0.40 | 0.091±0.065 | 2.87±0.04 | 2.72±0.13 |
| 0.60 | 0.129±0.093 | 2.85±0.00 | 2.94±0.18 |
| 1.00 | 0.159±0.114 | 2.84±0.46 | 2.75±0.16 |
| 2.50 | 0.295±0.212 | 2.78±0.17 | 2.83±0.19 |
| **CO2** | **pCO2 (Torr)** |  | | | | Doyle *et al.* (1987)  *J.Mol.Biol.* 196,  927-934 |
| 0.00 | 0.223±0.141 | 0.007±0.001 | 2.45±0.57 | 2.47±0.14 |
| 10.60 | 0.449±0.284 | 2.69±0.00 | 2.58±0.13 |
| 27.20 | 1.120±0.712 | 2.90±0.00 | 2.63±0.13 |
| 71.60 | 3.811±2.432 | 3.06±0.12 | 2.68±0.11 |
| 192.00 | 11.539±7.371 | 3.12±0.08 | 2.62±0.10 |
| 510.00 | 30.236±19.309 | 3.14±0.28 | 2.66±0.10 |

*a*The table is adopted from Rapp and Yifrach (2017). The MWC allosteric parameters for the Hb pH, CO2 and 2,3-BPG physiological datasets were obtained using global fitting analysis, as described in Rapp and Yifrach (2017). The analysis was carried out assuming a single *c* value for each dataset curve.

*b*The values for *L* are apparent, as they were determined in the presence of varying concentrations of the same effector.

*c*Hill coefficients at half-saturation calculated based on based on **Equation 5** and using the *K*R, *K*T, and *L* MWC parameters of each physiological dataset curve.