



Supplemental Figure S1: Hb-O₂ saturation normalization scheme. (A) Change in the Hb-O₂ saturation output from Equation 5 for untreated samples (black) and samples incubated with 500uM Voxelotor for 1 hour (white). (B) The change in the uncorrected fractional desaturation during the transition from 160mmHg to 0mmHg was assumed to represent 100% desaturation in the untreated sample. Both the untreated and treated responses were normalized against this maximum signal change to obtain the outputs shown in Figure 3C.

Supplemental Table S1: Blood Sample Characteristics. Values labeled “N/A” were not measured.

Sample ID	Genotype	Gender	HbS	HbF	HbA	HbA2	HCT	MCV	MCHC	WBC	Transfusion	Hydroxyurea
Sample #1	HbSC	M	N/A	N/A	N/A	N/A	35.4	60	33.9	10.5	N	N
Sample #2	HbSS	M	75.9	21.4	0	2.7	23.8	91	35.3	10.5	N	Y
Sample #3	HbSS	M	33.9	8.9	54.3	2.5	28.9	86	35.6	15.6	Y	Y
Sample #4	HbS/β ⁺ Thal	M	69.7	6.1	18.9	5.3	31	69	34.5	4.8	N	N
Sample #5	HbSS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Sample #6	HbSS	F	63.5	34.4	0	2.1	26.7	85	34.5	14.8	N	Y
Sample #7	HbSS	F	80	17	0	3	15.9	92	36.5	9.8	N	Y
Sample #8	HbAA	F	0	0	97.7	2.3	41.3	91.8	32.2	6.33	N	N
Sample #9	HbAA	M	0	0	97.9	2.1	48.2	94.3	32.6	4.6	N	N
Sample #10	HbAA	M	0	0	97.4	2.6	44.6	98.2	32.5	10.43	N	N
Sample #11	HbAA	M	0	0	97.4	2.6	46.6	92.5	32.8	5.42	N	N

Supplemental Table S2: Fitting Oxygen Binding Curves.

Sample ID	Hill Equation Fitting		2 nd Order Polynomial Fitting	
	p50 (mmHg) ± 95% CI	R-Square	p50 (mmHg)	R-Square
Sample #1 (HbSC)	40.99 ± 0.8842	0.9988	41.45	0.9688
Sample #2 (HbSS)	33.71 ± 1.3354	0.9972	33.88	0.9849
Sample #3 (HbSS)	35.82 ± 2.4266	0.9917	37.38	0.9927
Sample #4 (HbS/β ⁺ Thal)	38.56 ± 2.3967	0.9915	39.14	0.9806
Sample #5 (HbSS)	28.00 ± 3.4561	0.9802	29.91	0.9852
Sample #6 (HbSS)	28.83 ± 2.5496	0.9892	30.66	0.9943
Sample #7 (HbSS)	34.02 ± 1.8693	0.9944	34.39	0.9846
Sample #8 (HbAA)	35.00 ± 1.3153	0.9974	35.42	0.9825
Sample #9 (HbAA)	31.80 ± 2.2165	0.9926	33.18	0.9884
Sample #10 (HbAA)	29.27 ± 1.5609	0.9960	30.67	0.9949
Sample #11 (HbAA)	22.57 ± 1.8805	0.9928	25.00	0.9872