This journal is © The Royal Society of Chemistry 2012

Supplementry Material: Predicting the morpholog of sickle red blood cells using coarse-granined models of intracellular aligned hemologobin polymers, by Lei and Karniadakis

Mathematical description of Sickle RBC shapes

The objective of the material presented herein is to allow interested readers to be able to repeat our results. To quantify the various types of SS-RBC discussed in the current work, we use a polynomial function $z = f(x, y)$ to fit the surface of the cell membrane for all the three types of cells, similar to the approach in Ref. [1]. The polynomial function is defined by

$$f(x, y) = \alpha_0 + \alpha_1 x^2 + \alpha_2 y^2 + \alpha_3 x^4 + \alpha_4 y^4 + \alpha_5 x^2 y^2, \tag{S1}$$

where α_0, α_1,..., α_5 are fitting coefficients determined by the specific shape of the cell. The boundary of the cell on the x-y plane is defined by $g(x, y) = 0$, which varies for different types of cell morphology as discussed below.

Moreover, to quantify the difference between the fitting surface and the discrete cell vertices, we define the L_2 error of the fitting normalized by the average thickness of SS-RBC, as

$$\varepsilon = \frac{1}{N_v}\sqrt{\sum_{i=1}^{N_v}(f(x_i, y_i) - z_i)^2 / < z >}, \tag{S2}$$

where x_i, y_i and z_i are the coordinates of a discrete cell vertex, N_v is the total number of vertices considered, and $< z >$ is the average thickness of SS-RBC.

For each cell, the membrane is divided into two parts according to the dual values in z direction; each part is fitted by Eq. (1) separately as shown in Fig. S1. The combined surfaces define the cell membrane for the classical "elongate" and "sickle" shape of cell as shown in Fig. S1 and Fig. S2. For both "elongated" and "sickle" shape of SS-RBC, the 2D projection on the x-y plane is defined by

$$(x/b_1)^p + (y/b_2)^p = 1, \tag{S3}$$

where b_1, b_2 and p vary for individual cells with different membrane distortion. The fitting parameters and the final L_2 error for the elongated and sickle shape of the cell morphology are presented from Tab. S1 to Tab. S4.

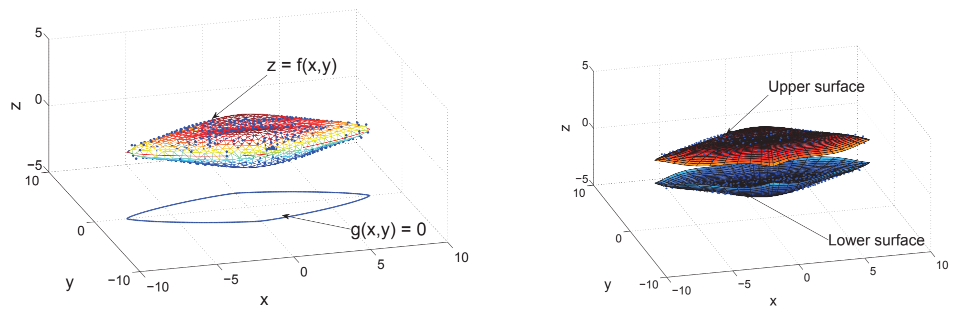

Figure S1: Left: Three-dimensional fitted surface for the simulated SS-RBC of "elongated" shape represented by Eq. (1), where the shear modulus of the cell membrane is $20\mu_0$, where μ_0

is the shear modulus of the healthy RBC. The blue dots represent the cell vertices obtained from the model described in the current work. The blue curve represents the boundary of the cell membrane on the x-y plane fitted by Eq. (3). Right: Fitted surfaces with the upper and lower part shifted by 1 and -1 in the z direction for illustration purposes.

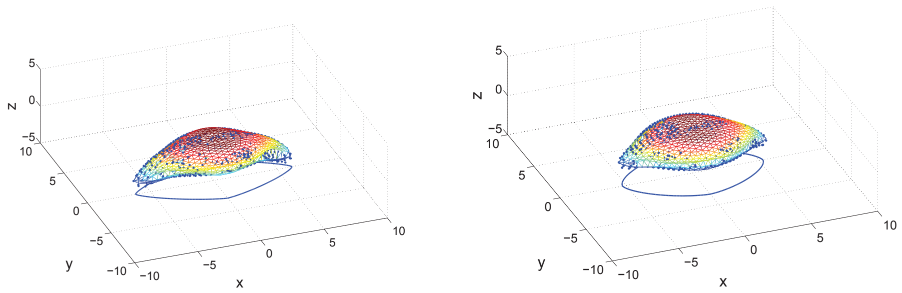

Figure S2: Three-dimensional fitted surface for the simulated SS-RBC of "sickle" shape represented by Eq. (1), where the shear modulus of the cell membrane is $20\mu_0$ (left) and $80\mu_0$ (right). The spontaneous angle θ_0 is 178.5°. The blue curve represents the boundary of the cell membrane on the x-y plane fitted by Eq. (3).

μ/μ_0	α_0	α_1	α_2	α_3	α_4	α_5	ε
20	-0.869	-2.72×10^{-3}	-0.324	2.43×10^{-4}	5.65×10^{-2}	2.11×10^{-2}	0.052
20	1.01	-1.46×10^{-3}	0.242	-2.07×10^{-4}	-4.70×10^{-2}	-1.91×10^{-2}	0.052
30	-0.678	-1.40×10^{-2}	-0.449	4.93×10^{-4}	6.10×10^{-2}	2.51×10^{-2}	0.056
30	0.83	7.13×10^{-3}	0.348	-4.03×10^{-4}	-5.15×10^{-2}	-2.27×10^{-2}	0.056
40	-0.594	-2.10×10^{-2}	-0.474	7.20×10^{-4}	5.77×10^{-2}	2.68×10^{-2}	0.061
40	0.742	-1.48×10^{-2}	0.38	-6.37×10^{-4}	-5.10×10^{-2}	-2.49×10^{-2}	0.061
50	-0.567	-2.44×10^{-2}	-0.481	8.64×10^{-4}	5.56×10^{-2}	2.75×10^{-2}	0.060
50	0.689	1.93×10^{-2}	0.405	-7.99×10^{-4}	-4.94×10^{-2}	-2.59×10^{-2}	0.060
60	-0.574	-2.85×10^{-2}	-0.455	1.09×10^{-3}	4.94×10^{-2}	2.77×10^{-2}	0.073
60	0.627	2.51×10^{-2}	0.408	-1.04×10^{-3}	-4.59×10^{-2}	-2.64×10^{-2}	0.073
70	-0.558	-3.14×10^{-2}	-0.437	1.27×10^{-3}	4.56×10^{-2}	2.77×10^{-2}	0.064
70	0.612	2.90×10^{-2}	0.4084	-1.22×10^{-3}	-4.37×10^{-2}	-2.67×10^{-2}	0.064
80	-0.570	-3.16×10^{-2}	-0.437	1.30×10^{-3}	4.56×10^{-2}	2.79×10^{-2}	0.058
80	0.589	2.98×10^{-2}	0.416	-1.26×10^{-3}	-4.43×10^{-2}	-2.71×10^{-2}	0.058

Table S1: Fitting parameters for the "elongated" shape of SS-RBCs obtained from the simulation with different cell rigidity; μ_0 and μ represent the shear modulus of the healthy cells and SS-RBCs, respectively. For each case of cell rigidity, the two rows of parameters represent the lower and upper part of the fitted cell membrane surface respectively. The unit of x, y and z in Eq. (1) is in micrometers.

μ/μ_0	b_1	b_2	p
20	7.9	2.8	1.33
30	7.15	2.95	1.40
40	6.7	3.05	1.45
50	6.4	3.1	1.5
60	6.1	3.19	1.55
70	5.85	3.25	1.58
80	5.8	3.29	1.60

Table S2: Parameters of Eq. (3) for the range of "elongated" shape of SS-RBC on the x-y plane, where the boundary of the cell membrane is defined by a pseudo-elliptical curve.

θ_0	μ/μ_0	α_0	α_1	α_2	α_3	α_4	α_5	ε
179°	20	-0.840	-0.104	-0.586	1.41×10^{-3}	6.85×10^{-2}	4.65×10^{-2}	0.067
179°	20	0.674	-0.0273	0.176	-7.75×10^{-4}	-3.78×10^{-2}	-3.58×10^{-2}	0.067
179°	40	-0.811	-0.110	-0.651	1.79×10^{-3}	7.16×10^{-2}	4.78×10^{-2}	0.071
179°	40	0.665	-0.0292	0.126	-7.44×10^{-4}	-3.12×10^{-2}	-3.11×10^{-2}	0.071
179°	60	-0.684	-0.122	-0.533	2.87×10^{-3}	4.69×10^{-2}	4.09×10^{-2}	0.063
179°	60	0.645	-0.0153	0.138	-1.38×10^{-3}	-2.3×10^{-2}	-2.59×10^{-2}	0.063
179°	80	-0.652	-0.127	-0.506	3.30×10^{-3}	4.22×10^{-2}	3.93×10^{-2}	0.072
179°	80	0.628	-0.00953	0.139	-1.67×10^{-3}	-2.15×10^{-2}	-2.49×10^{-2}	0.072
178.5°	20	-0.910	-0.201	-0.702	3.59×10^{-3}	8.22×10^{-2}	7.32×10^{-2}	0.062
178.5°	20	0.658	-0.0382	0.0756	-1.15×10^{-3}	-3.18×10^{-2}	-4.35×10^{-2}	0.062
178.5°	40	-0.825	-0.181	-0.688	3.57×10^{-3}	7.05×10^{-2}	5.96×10^{-2}	0.091
178.5°	40	0.686	-0.0443	0.0275	-1.42×10^{-3}	-2.11×10^{-2}	-3.16×10^{-2}	0.091
178.5°	60	-0.709	-0.176	-0.613	4.16×10^{-3}	5.38×10^{-2}	5.02×10^{-2}	0.083
178.5°	60	0.659	-0.0353	0.0705	-1.75×10^{-3}	-1.98×10^{-2}	-2.69×10^{-2}	0.083
178.5°	80	-0.685	-0.178	-0.597	4.44×10^{-3}	5.06×10^{-2}	4.87×10^{-2}	0.063
178.5°	80	0.647	-0.0304	0.0731	-2.01×10^{-3}	-1.90×10^{-2}	-2.58×10^{-2}	0.063

Table S3: Fitting parameters for the "sickle" shape of SS-RBCs obtained from the simulation with different cell rigidity. θ_0 represents the spontaneous deflection angle for the AHP domain of the current model.

θ_0	μ/μ_0	b_1	b_2	p
179.0°	20	7.0	2.9	1.22
179.0°	40	6.55	3.03	1.29
179.0°	60	5.8	3.32	1.38
179.0°	80	5.5	3.4	1.48
178.5°	20	6.2	2.95	1.37
178.5°	40	5.8	3.1	1.38
178.5°	60	5.4	3.25	1.51
178.5°	80	5.3	3.35	1.54

Table S4: Parameters of Eq. (3) for the range of "sickle" shape of SS-RBC on the x-y plane, where the boundary of the cell membrane is defined by the pseudo-elliptical curve.

Similarly, the surfaces of the cell membranes with "holly leaf" are fitted by Eq. (1). Fig. S3 shows the fitted surface of the SS-RBCs with cell membrane shear modulus $\mu = 40\mu_0$ and $100\mu_0$, respectively. In addition, we note that multiple spicules appear on the cell membrane. Correspondingly, the 2D projection of the cell membrane on the x-y plane is represented $g(x, y) = 0$ defined by

$$g(x,y) = \begin{cases} \left(\dfrac{x}{a}\right)^p + (-1)^s \left(\dfrac{y}{b}\right)^p = 1 \\ \left(\dfrac{x}{c}\right)^q + (-1)^t \left(\dfrac{y}{d}\right)^q = 1, \end{cases} \tag{S4}$$

where the parameter a, b, c and d defines the length and width of the cell on the 2D projection. Here, s and t are chosen as 0 or 1, which determines the hyperbolic ($s,t = 1$) or elliptic properties ($s,t = 0$) of the cell boundary curves; p and q define the generalized power for the hyperbolic or elliptical properties. The fitting parameter and L_2 error for the cell membrane are presented in Tab. S5 and Tab. S6.

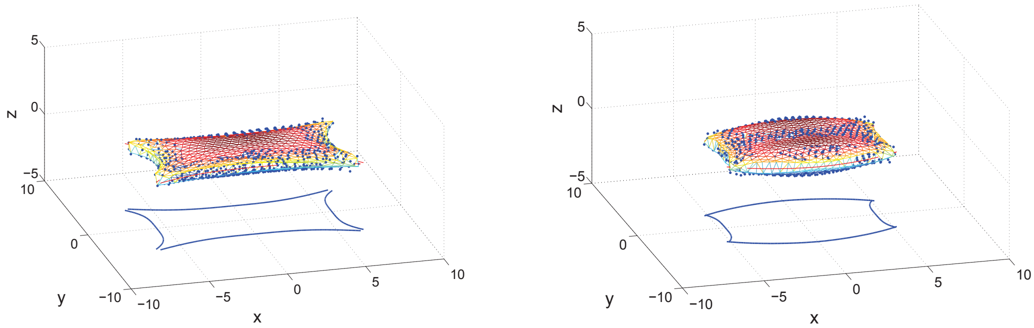

Figure S3: Three-dimensional fitted surface for the simulated SS-RBC of "holly leaf" shape represented by Eq. (1), where the shear modulus of the cell membrane is $40\mu_0$ (left) and $120\mu_0$ (right). The angular width of the AHP domain w is 60°. The blue curve represents the boundary of the cell membrane on the x-y plane fitted by Eq. (4).

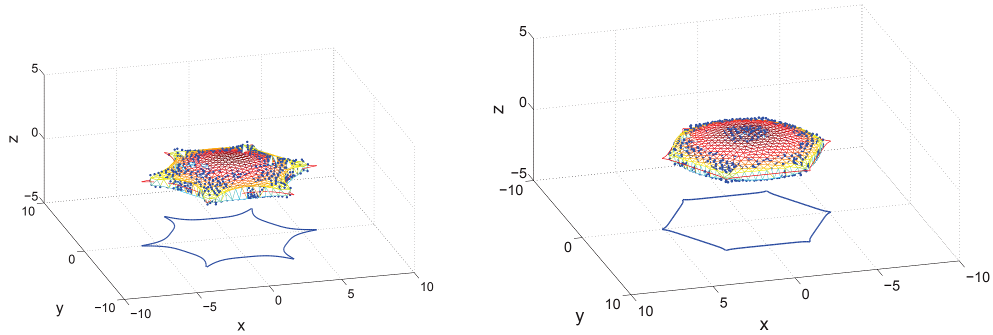

Figure S4: Three-dimensional fitted surface for the simulated SS-RBC of "granular" shape represented by Eq. (1), where the shear modulus of the cell membrane is $40\mu_0$ (left) and $2000\mu_0$ (right). The blue curve represents the boundary of the cell membrane on the x-y plane fitted by Eq. (5).

μ/μ_0	α_0	α_1	α_2	α_3	α_4	α_5	ε
30	-0.957	9.30×10^{-3}	5.63×10^{-2}	4.86×10^{-4}	6.70×10^{-3}	-4.49×10^{-3}	0.092
30	-0.982	-6.32×10^{-3}	$6.95\times10-2$	-6.97×10^{-4}	-8.75×10^{-3}	-5.77×10^{-3}	0.092
50	-0.856	1.69×10^{-2}	-2.77×10^{-2}	2.42×10^{-4}	8.03×10^{-3}	-1.93×10^{-3}	0.077
50	0.862	-1.64×10^{-2}	$2.69\times10-2$	-3.12×10^{-4}	-8.4×10^{-3}	2.12×10^{-3}	0.077
90	-0.808	1.50×10^{-2}	5.39×10^{-2}	2.53×10^{-4}	6.98×10^{-3}	8.2×10^{-4}	0.073
90	-0.826	-1.43×10^{-2}	$5.71\times10-2$	-3.67×10^{-4}	-7.59×10^{-3}	-7.12×10^{-4}	0.073
120	-0.803	1.11×10^{-2}	-6.22×10^{-2}	4.67×10^{-4}	6.80×10^{-3}	2.28×10^{-3}	0.087
120	0.823	-1.02×10^{-2}	$6.70\times10-2$	-6.02×10^{-4}	-7.45×10^{-3}	2.28×10^{-3}	0.087

Table S5: Fitting parameters for the "holly leaf" shape of SS-RBCs obtained from the simulation with different cell rigidity.

μ/μ_0	a	b	c	d	s	t	p	q
30	5.6	3.7	4.9	2.6	1	1	4.0	3.3
50	5.1	3.44	6.11	3.3	1	0	4.0	8.0
90	4.8	3.17	6.8	3.7	1	0	4.0	2.0
120	4.6	3.05	7.15	3.9	1	0	4.0	1.8

Table S6: Parameters of Eq. (4) for the range of "holly leaf" shape of SS-RBC on the x-y plane, where the surface of the cell membrane is defined by a combination of pseudo-hyperbolic and pseudo-elliptical curves.

Finally, the membrane surface of the "granular" cell is also fitted by Eq. (1). Fig. S4 shows the fitted surface of the SS-RBCs with cell membrane shear modulus $\mu = 40\mu_0$ and $100\mu_0$, respectively. The 2D projection on the x-y plane is represented by a combination of the pseudo-hyperbolic curves $g(x,y)=0$ defined by

$$g(x,y)=\begin{cases}\dfrac{(-\sin(\phi_1)x+\cos(\phi_1)y)^p}{b^p}-\dfrac{(\cos(\phi_1)x+\sin(\phi_1)y)^p}{a^p}=1\\ \dfrac{(-\sin(\phi_2)x+\cos(\phi_2)y)^p}{b^p}-\dfrac{(\cos(\phi_2)x+\sin(\phi_2)y)^p}{a^p}=1\\ \dfrac{(-\sin(\phi_3)x+\cos(\phi_3)y)^p}{b^p}-\dfrac{(\cos(\phi_3)x+\sin(\phi_3)y)^p}{a^p}=1,\end{cases} \tag{S5}$$

where a and b defines the size of the 2D projection and the p defines the generalized power of the hyperbolic curves. The fitting parameters of the 3D surface and 2D curve are presented in Tab. S7 and Tab. S8.

Electronic Supplementary Material (ESI) for Soft Matter
This journal is © The Royal Society of Chemistry 2012

μ/μ_0	α_0	α_1	α_2	α_3	α_4	α_5	ε
40	-1.42	9.44×10^{-2}	0.101	1.86×10^{-3}	-2.23×10^{-3}	-3.54×10^{-3}	0.084
40	1.33	-9.52×10^{-2}	$-8.91\times10-2$	-1.95×10^{-3}	1.65×10^{-3}	3.45×10^{-3}	0.084
80	-1.25	6.90×10^{-2}	6.79×10^{-2}	-1.19×10^{-3}	-1.15×10^{-3}	-2.05×10^{-3}	0.097
80	1.21	-6.78×10^{-2}	$-6.40\times10-2$	1.09×10^{-3}	1.03×10^{-3}	1.64×10^{-3}	0.097
160	-1.13	4.23×10^{-2}	4.18×10^{-2}	-1.68×10^{-4}	-9.50×10^{-5}	-1.61×10^{-4}	0.074
160	1.11	-4.22×10^{-2}	$-3.97\times10-2$	8.8×10^{-5}	1.10×10^{-6}	-8.74×10^{-5}	0.074
320	-1.12	3.04×10^{-2}	3.07×10^{-2}	5.07×10^{-4}	5.51×10^{-4}	1.33×10^{-3}	0.071
320	1.08	-2.75×10^{-2}	-2.76×10^{-2}	-6.78×10^{-4}	7.29×10^{-4}	1.71×10^{-3}	0.071
200 0	-1.16	3.39×10^{-2}	3.33×10^{-2}	6.08×10^{-4}	6.06×10^{-4}	1.19×10^{-3}	0.089
200 0	1.13	-3.06×10^{-2}	$-3.02\times10-2$	-8.32×10^{-4}	7.83×10^{-4}	1.66×10^{-3}	0.089

Table S7: Fitting parameters for the "granular" shape of SS-RBCs obtained from the simulation with different cell rigidity.

μ/μ_0	a	b	p	ϕ_1	ϕ_2	ϕ_3
40	2.5	3.8	2.8	0	$\pi/3$	$-\pi/3$
80	2.6	4.0	3.6	0	$\pi/3$	$-\pi/3$
160	2.7	4.2	5.5	0	$\pi/3$	$-\pi/3$
320	2.7	4.3	6.0	0	$\pi/3$	$-\pi/3$
2000	2.8	4.4	10.0	0	$\pi/3$	$-\pi/3$

Table S8: Parameters of Eq. (5) for the range of SS-RBCs with "granular shape" on the x-yplane, where the boundary of the cell membrane is defined by the combination of pseudo-hyperbolic curves.

References

[1] Evans, E. A. and Skalak, R. *Mechanics and thermodynamics of biomembranes*. CRC Press, Inc., Boca Raton, Florida, 1980.