Compare for Calibration Methods to Optical Trapping Force Upon Non-spherical Biological Cells*

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Abstract Both Boltzmann distribution method (BDM) and mean square displacement method (MSDM) are available for the force calibration of non-spherical biological cells in a harmonic optical trap. These two calibration methods were compared with numeric experiments. Results indicate that comparing with MSDM, BDM is not only available for the force calibration of non-spherical or anisotropic cells, but also for irregular cells in optical trap potential with inharmonic and asymmetric profiles. The results agree with the experiments reported.

Keywords Boltzman distribution; Optical tweezers; Trapping stiffness; Biological cells
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0 Introduction

"Optical Tweezers" (OT) are allowed both to measure pico-Newton forces and to manipulate transparent particles without any mechanical contact and, hence, without causing over damage. They especially turn out to be suitable for biomechanical applications. For many applications exact knowledge of the optical forces applied at the particles is important. For example, quantitative measurements of tensile strength applied to biological cells require a force calibration[1,2]. Calculations can be performed using approximate methods, but exact calculation of the optical forces acting on particles is difficult, and experimental calibration for optical trap forces is necessary. There are a number of ways to calibrate optical traps[3~10]. These ways are available for spherical isotropic particles and the harmonic potential profiles. Biological cells and crystals are usually non-spherical, and are often anisotropic. Furthermore, with unknown optical properties, the potential profiles are sometimes an-harmonic and asymmetric. In reference[11], Biological cells are assumed as Brownian particles in harmonic potentials, theoretically demonstrate that both BDM and MSDM are ways to calibrate optical traps suitable for non-spherical anisotropic cells.

In this paper, the difference between BDM and MSDM were compared by synthetic experiment data to find a predominant one.

1 Comparing for two calibration approaches

1.1 Two approaches of calibration

For small enough displacements x from the center of the trap, the optical tweezer can be modeled as a harmonic potential. The cell's potential function is $U(x)=\frac{1}{2}kx^2$, where k is the trap stiffness coefficient, and the procedure of measuring k is called trap stiffness calibration (TSC). In the case, there is

$$P(x)=C\exp\left(-\frac{x^2}{2k_B T/k}\right) \tag{1}$$

where $p(x)$ is the probability density, and C is a normalization constant ($\int P(x)\mathrm{d}x=1$).

The MSDM of TSC is the measurement of the mean square displacement $\langle x^2 \rangle$ of the cell's position fluctuations due to thermal excitations and the sample's temperature T, the trapped cell' averaged potential $\frac{1}{2}k\langle x^2\rangle=\frac{1}{2}k_B T$, thus $k=k_B T/\langle x^2\rangle$.

The Boltzmann distribution method (BDM) is the measurement of the probability density $p(x)$, the potential experienced by the cell can be calculated

$$U(x)=-k_B T\ln P(x)+k_B T\ln C \tag{2}$$

According to $U(x)=\frac{1}{2}kx^2$, k can be fitted numerically.

In principles, both MSDM and BDM are suitable for all irregular shape particles.

1.2 The method for comparing

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MSDM and BDM require the solution' s temperature and the cell' s displacement to be measured. The errors mainly come from displacement measuring. There are two important error factors: one is stochastic-error for displacement measurement, the other is system-error, i. e. the displacement offset between the centre of the trap and the origin of position coordinate.

In order to compare the two calibrating methods, and samples of synthetic data $p^{tr}(x_i)$ vs. x were generated with a prefixed set of parameters $k^{tr}=10^{-5}$ N/m、$T=300$ k, the superscript tr means true data or equivalently error-free data. Therefore, discrete values of $p^{tr}(x_i)$ in a given range of $x_i=-7,-6,\Lambda,0,\Lambda,6,7$ were obtained by the relation

$p^{tr}(x_i)=\exp\left(-k^{tr}x_i^2/(2k_B T)\right)=\exp\left(-x_i^2/8.28\right)$, here the unit of x_i is 10^{-8}m.

$p^{ex}(x_i)$ was used to express the experimental data which involves experimental errors, different levels of the pseudo experimental error δ which were introduced in the probability. Therefore, discrete values of $p^{ex}(x_i)$ in the range of $x_i=-7,-6,\Lambda,0,\Lambda,6,7$ were obtained as follows

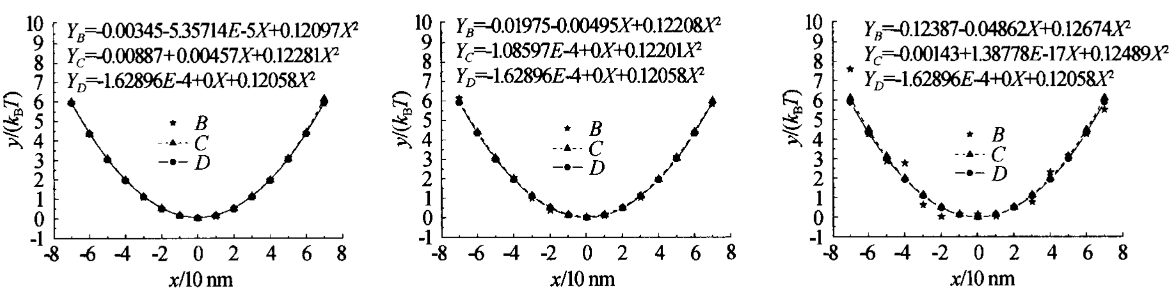
$$p^{ex}(x_i)=p^{tr}(x_i-x_0)(1+\delta G) \quad (3)$$

in Eq. (3), G is a Gaussian random number with zero mean and unit variance which is included to simulate the experimental noise, and x_0 is the displacement offset between the centre of the trap and the origin of position coordinate. Therefore, according to Eq. (3), experiment data with different levels of error ($\delta=0.02, 0.1, 0.5$, $x_0=0, 10, 20$ nm) were produced to which the two calibrating procedures were applied, and the potential energy can be obtained, then k^{ex} can be fitted by using a harmonic potential model. In comparing k^{ex} obtained above with $k^{tr}=10^{-5}$ N/m, the error is measured as it is defined to express the fit goodness as follow

$$\text{err}=\frac{|k^{ex}-k^{tr}|}{k^{tr}}\times 100\% \quad (4)$$

2 Comparative results and discussion

Results are shown in Fig. 1(a)、(b)、(c), where the potential energy $y(x)$ as function of displacement x for different levels of the experiment error δ ($\delta=0.02, 0.1, 0.5$) at the same displacement offset x_0 ($x_0=0$) is plotted. In the same Fig., the predictions of the MSDM and the BDM are included for comparison with the same level of the experiment error δ and the binomial equations fitted by the data accordingly are also included for the stiffness coefficient errors comparison, where "D" represents the predictions of the true data, "B" refers to the BDM and "C" to MSDM. It is observed that the numerical predictions of the stiffness coefficient error obtained with BDM and MSDM procedure are not significantly difference for different levels of the experiment error δ. The resulting of the stiffness coefficient errors are presented in Table 1.



(a)The experiment error δ=0.02 (b)The experiment error δ=0.1 (c)The experiment error δ=0.5

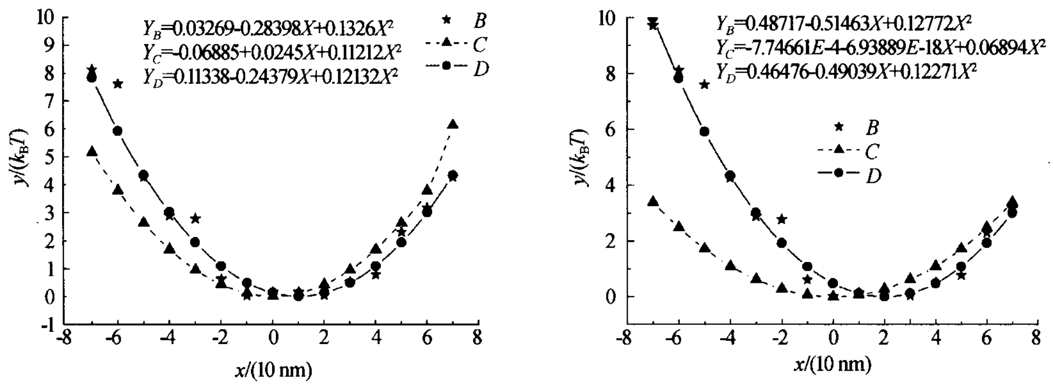
Fig. 1 Potential energy y as function of displacement x obtained from synthetic data for different values of the experiment error δ at the same displacement offset $x_0=0$

Table. 1 Stiffness coefficient errors from the two calibration methods in various cases

methods	$\delta=0.02$	$\delta=0.1$	$\delta=0.5$	$\delta=0.5$	$\delta=0.5$
	$x_0=0$	$x_0=0$	$x_0=0$	$x_0=10$ nm	$x_0=20$ nm
BDM	1%	2%	5%	6%	7%
MSDM	2%	2%	4%	13%	42%

In Fig. 2(a)、(b), the predictions of the MSDM and the BDM are shown, where "D" represents the predictions of the true data, "B" refers to the BDM and "C" to MSDM, in this case, the displacement offset x_0 is 10 nm and 20 nm with the same level of the experiment error $\delta=0.5$, respectively. The results of the stiffness coefficient errors are presented in Table 1.

Results above indicate: when there is no offset between the origin of the coordinate and the center of the trap, errors of the stiffness coefficient from the two methods have no obviously difference at different levels of the experiment error, which is



(a) Potential offset x_0=10 nm (b) Potential offset x_0=20 nm

Fig. 2 Potential energy y as function of displacement x obtained from the synthetic data for different potential offset at the same experiment error $\delta=0.5$

agreement with the experiment reported in reference[4]; with the offset increasing, errors from MSDM increase prominence, while from BDM almost unchanged, this show that BDM is uneasy disturbed by external field and can be used to measure potential profiles which are allowed to be inharmonic and asymmetric[12~14], but MSDM only applicable for a harmonic potential.

3 Conclusions

Both MSDM and BDM are available for the force calibration of non-spherical or anisotropic biological cells in optical tweezers which can be modeled as a harmonic and symmetric potential. In contrast to MSDM, BDM enables us to measure potential profiles which are allowed to be inharmonic and asymmetric, we expected it to become a universal method for trapping force calibration of biological cells.

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两种非球形细胞光镊阱力标定方法的比较

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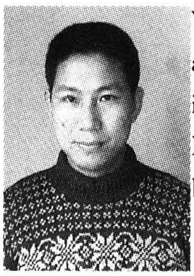
摘 要 玻尔兹曼统计法和均方位移法是两种可用于对非球型生物细胞在简谐光势阱中光阱力的标定方法. 用数字实验对这两种标定方法进行了比较, 结果表明: 与均方位移法相比,玻尔兹曼统计法不仅适用于各向异性非球性细胞,也适用于非简谐、非对称光势阱中任意形状的生物细胞光阱力的标定,结论与已有直接实验相符.

关键词 玻尔兹曼分布;光镊;光阱刚度; 生物细胞



Yu Youli was born in 1966. He received his Bachelor's degree and M. S. degree from Xi'an Jiaotong University PRC in 1989 and 1998, respectively. Now he is a Ph. D. candidate in School of Life Science and Technology, Xi'an Jiaotong University and works as a lecturer in school of science, Xi'an Jiaotong University. His research subject is on biophotonics and biomechanics.