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Review

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SARS-CoV-2, influenza virus and nanoscale particles trapping, tracking and tackling using nanoaperture optical tweezers: A recent advances review

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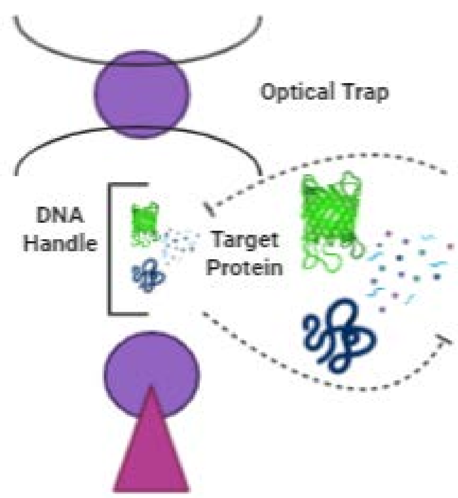
ABSTRACT

Recent advances in nanoscale technologies have provided advanced tools that can be easily used to trap, track, and tackle individual nanoscale particles and viruses such as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and influenza viruses accurately. Among the promising strategies that exist to date, optical forces based techniques are the leading tools in this task. Perfectly, focused lasers act as "optical tweezers," and can trap individual particles and viruses. These forces can be applied to study nanomaterials, viruses, the building blocks of a quantum computer, and collision processes occurring between molecules in a better way than ever before. These cutting-edge tools are capable of trapping, tracking, and tackling at the nanoscale in three dimensions. The optical tweezers have been used within biological and nanotechnological fields for trapping, tracking, and tackling nanoparticles, and viruses with high flexibility, precision, and integration. The outcomes are important breakthroughs in the field of molecular mechanics. Several scientific efforts have been prerequisites for innovation of these tools for single-molecule explorations. Here, we review the state-of-the-art optical tools employed in optical trapping, tracking, and tackling of different particles at the nanoscale. The trapping of nanoparticles down to single-digit nanometer range and individual SARS-CoV-2 are the main features discussed here. Optical tweezers are also capable of sizing and probing acoustic modes of a small virus such as SARS-CoV-2 and influenza. The optical tweezers can perform tracking of nanoparticles in three-dimensional with high-resolution by forwarding scattered light. Optical tweezers are used to grab single molecules and measure events that are occurring and employed for measuring forces and measuring distances. A miniature and modular system creates a reliable and mobile optical trap that has more potential to be applied in optical trapping technologies.



Keywords: Nanotechnologies, Manipulating Nanoparticles, Optical Tweezers, Viruses

INTRODUCTION

Arthur Ashkin and colleagues innovated optical tweezers (or traps) in 1986 and now it has become a versatile tool for developing numerous methods in cell biology and nanotechnology.[1] An optical trap i.e. a focused laser beam is capable of holding and applying forces to nanoscale and macroscale particles. Non-stop progresses in research are transforming these tools into highly versatile instruments to conduct specific experiments in molecular biophysics. Therefore, to uncover important scientific discoveries, optical traps has become a powerful tool for describing the basic theoretical concepts based on force measurement techniques that are applied widely today.[2]

Optical tweezers are implemented as an advanced tool that can enable optical trapping, tracking and tackling. The functioning of these tools is aligned on a strongly focused light. These tools can also be used for the characterization of various nanomaterials.[3] Optical tweezers separate conservative gradient force by

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generating a force that depends on the light intensity gradient. Finally, the initiated force is liable for trapping, tracking, and tackling manipulation.[4] These tools are capable of generating a non-conservative scattering force that is proportional to the incident intensity of light.[5] Conferred phenomenon have the potential to control the outmoded proof of identity of gradient and scattering force which have the concerns related to the non-spherical particles at the microscale, is more diverse. It is notified here that the shape and composition are the determinable factors compulsory in the dynamics of optically trapped particles.[6] Therefore, there is a need to understand the role of shape and composition that affects the dynamics of nanoparticles. These tactics are used to reconnoiter more claims in the field of biology, spectroscopy, nanotechnology, and stochastic thermodynamics.[7]

Optical tweezers execute accordingly to a phenomenon, where the light-employing force is applied to the matter for an optical trap.[8] These phenomena happened because of an electric field, which involved and held approximately a highly fascinated laser beam.[9]Photons existed there to have momentum and capable of collectively exert force. These bundles of energies originated from the electric field gradient and hold the dielectric particle at a place. These existent traps cannot interfere with the association of single molecules. Thus, any manipulation can be done possibly in these traps. The persistent dynamics control the interaction that depends on the force and movements.[10] These physical parameters were measured or manipulated by moving the trap, and especially for the single-molecule study, these optical tweezers were applied in the field of physics, chemistry, and biology.[11] The instigated forces and radiation pressure are the key machineries of the optical trapping technique that can be applied to do manipulations in nanoparticles and viruses.[12] Overall, these forces control the trapping events and other progressions such as accelerate, decelerate, deflect, and guide handed thereafter. The laser techniques are applied for trapping, tracking, and tackling of particles, molecules, nano-dielectric, and biological identity i.e., viruses, living cells, and cell's organelles.[10]

To control the dynamics of a nanoparticle, laser trapping, tracking, and tackling techniques may be applied for the transformation of the concerned features so that these tiny particles can execute a major role in different fields wherever it will be required.[13] These invocations considered as a breakthrough that can deliver a groundbreaking role in research concerned for the physical and biological sciences. The fundamental theory and key principles underlying optical tweezers were highlighted as key features in the present discussion and offered the consistent impost on trapping, traking and manupulating nanoscale particles and viruses such as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and influenza (figure 1).[14] As, the optical forces controlled the overall phenomenon of trapping, tracking and therefore, the transfer of motion dignified the method for trapping the particle within the beam.[15] These endeavors are titled as motions of entering and replicated or refracted rays. The angular momentum flux of the beam is the fundamental feature that need to be measured during the description of optical torques.[16] To draw a qualitative depiction of the trapping of a concerned particle that was figured as a fragile positive lens to depict the forces on the lens. Therefore, for trapping nanoparticles or small-scale materials, an inspection of the limits of trap ability is necessary in terms of the nature and size of the particles.[17] Here, the electromagnetic theory can be applied to recognize the phenomenon of optical trapping and tracking. This particular resolution imitates the identical qualitative outcome when particle is treated as a lens during the changes in the convergence or divergence occurred toward the trapping beam. It resulted as the restoring forces that are acting on the particle for answering to queries such as how climate and specific conditions affect a single virus particle at nanoscale and how nanomaterial are effective in the preventaion of spreed and useful in the tackling of viruses.[18] The double-nanohole optical tweezers can isolate single nanoparticles at the single-molecule level.[19] and detect molecular events that are going on.[20] These advanced tools can measure the space- and time-dependent rheological features and microrheology dimensions of single molecules.[21] These devices can probe the nonlinear viscoelastic response of heterogeneous, nonequilibrium materials, non-continuum mechanics, force relaxation dynamics, nonlinear strain-field heterogeneities, mechanical responses, stress propagation, and time-dependent mechanics of active nanomaterials.[22]

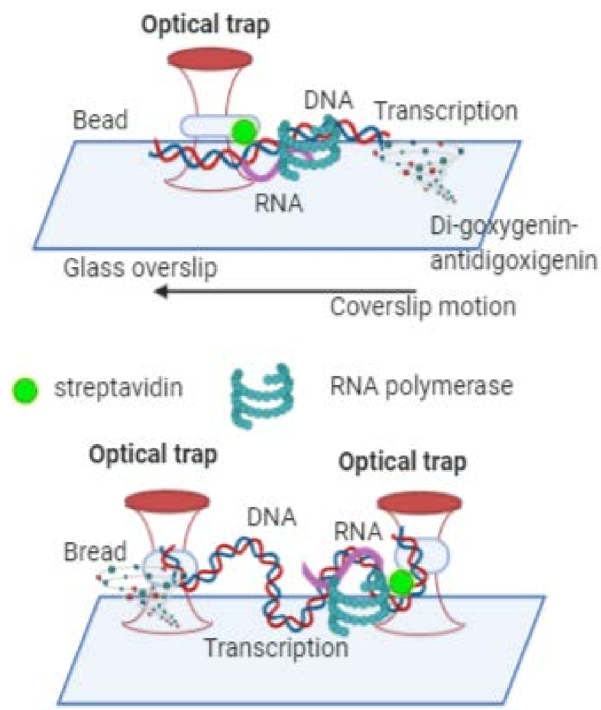

Figure 1. Schematic illustration of dynamics controls the interaction that depends on the force and movements. "Acknowledged [biorender.com] as per instructions"

During the coronavirus pandemic, researchers are trapping and tracking SARS-CoV-2 and influenza viruses required for further investigation of SARS-CoV-2 and how it was the spread on an epidemiological level.[23] Scientist specialty is applying optical tweezers to probe individual SARS-CoV-2, influenza virus and nanoscale particles for further investigaton just a few atoms across.[22] The double-nanohole optical tweezers can isolate single nanoparticles at the single-molecule level.[19] Optical tweezers are used to grab single molecules and detect molecular events that are going on.[20] In this review article, authors describe the basic principles underlying optical tweezers microrheology, and key applications to consider in trapping, tracking, and tackling of nanoscale particles and viruses such as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and influenza.[24] In this review article, such importanct facts werealso discussed that covered the basic principles underlying optical tweezers microrheology, and their key applications to be considered in trapping, tracking, and tacklingnanoparticles, corona, and influenza viruses.

Bubble and Convection Assisted Trapping: Nanotweezers

A bubble-and convection-assisted technique is developed for trapping to overcome the limitations of techniques of diffusion applied for trapping in nanoaperture tweezers to increase their throughput.[25] These nanotweezers enable us to reduce the particle-trapping time compared to convection-assisted traps. This novel technique is capable of transporting particles from 'far-off' expanses and trap one particle at a time using a single nanoaperture that is purely based on an optical way.[26] Opto-thermal-induced flow generated according to bubble-induced Marangoni and Rayleigh-Bénard convection to quickly transport particles from huge spaces to the nanoaperture tweezers without depending on regular diffusion.[27] Nanoaperture tweezers can trap, make sense, and with help the spectroscopic study of nanoscale materials[28,29] as required for single-molecule sensitivity with enhanced sensitivity and throughput.[30] Nanotweezers can provide a breakthrough in the conventional diffraction analysis.[31] These tools enable precise manipulation at the nanoscale and can generate new opportunities by doing optical manipulation in the field of biomedicine (figure 2).

To perform controlled tackling of nanoscale materials, fundamental pieces of training, and technological advances in nanotechnology are necessary.[32] The need to develop the technique of nanomanipulation is there because the techniques of optical and plasmonic tweezers cannot trap real-time and transport of nanoscale payload. The magnetically controlled nanorobots with optical illumination can do the needful. Therefore, the nanotweezers can execute the trapping of nanoscale objects with great proficiency in a confined electromagnetic field.[33] Subsequently, nanotweezers can simultaneously perform selectively trap, transport, and release colloidal cargo in the presence of a magnetic field.[34] Throughout optical trapping, the gripping particles may be heated up in a liquid medium in the existence of an optical trapping beam and as a result, bubble formation may happen. At nano and microscale, the surface tension can be affected powerfully, while regular thermal convection is insignificant.[35] Similar impacts initiate bubble formations, and after that, these happenings can be transpired in the regions where the high temperature may persist. These circumstances provide a powerful means that are necessary for trapping bubbles. The process of temperature measurements is necessary to bubble formation, which befalls above the boiling point of the surrounding liquid. These conditions are acting as a reasonable agreement along with the nucleation concepts.[36]

Basic Principles of Optical Tweezers and its Scattering Phenomena

The optical tweezers rely upon the extremely high gradient in the electric field produced near the beam waist of a tightly focused laser beam, which creates a force sufficient to trap micron-sized dielectric particles in three dimensions. Commercial tweezers systems are now available (Cell Robotics International Inc., Albuquerque, New Mexico, USA; PLAM GmbH, Bernried, Germany), and although originally devised by physicists, but it is mainly biologists who have put optical tweezers to use. In 1970, Ashkin[37]initiated experiment with optical traps and realized that

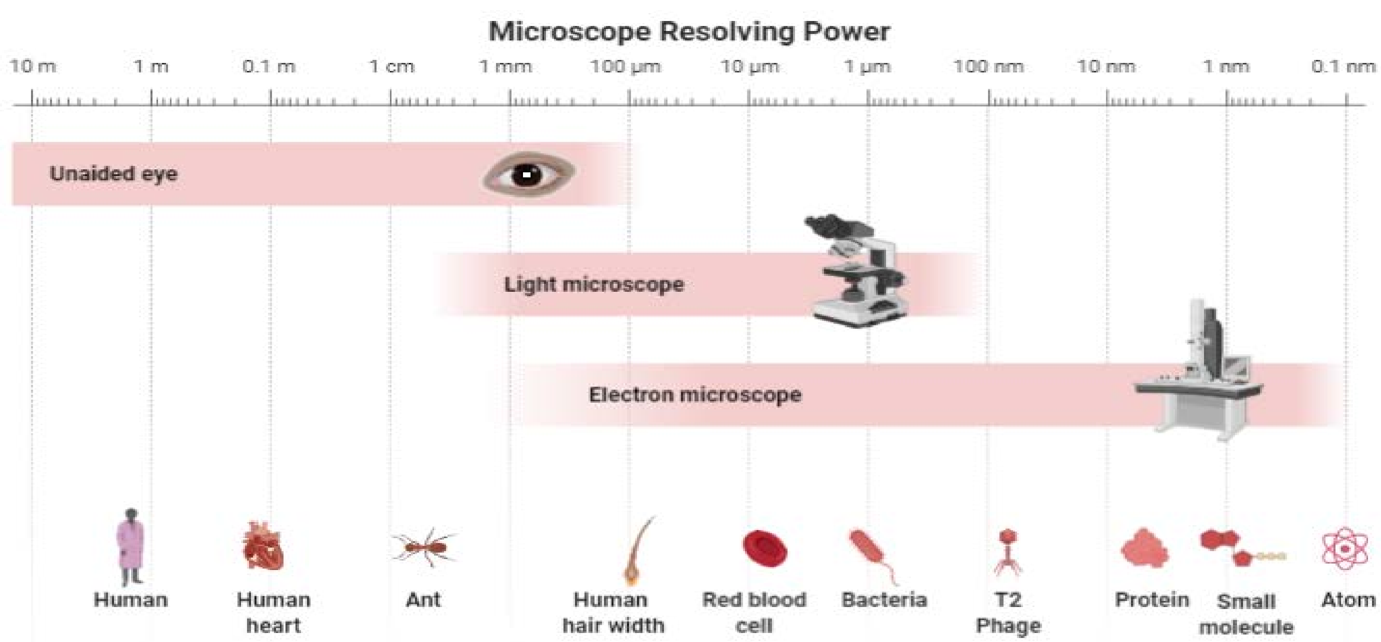

Figure 2. Schematic representation of nano, micro, and macroscale objects. "Acknowledged [biorender.com] as per instructions".

an unfocused laser beam would draw objects of high refractive index towards the centre of the beam; and propel them in the direction of propagation.[38] An arrangement of two counter-propagating beams allowed objects to be trapped in three dimensions. In these experiments, the effects of radiation pressure was observed and to overcome the usually much larger heating (radiometric) effects of light by using relatively transparent objects in a relatively transparent medium. It was discovered later that a single, tightly focused laser beam could be used to capture small dielectric particles in three dimensions.[39] This technique enables small particles to be picked up and moved at will using a beam of visible light and hence was christened optical tweezers. When anyone is trying to understand the origin of the forces acting within optical tweezers, two distinct approaches may be adopted, either based upon ray optics or on the electric field associated with the light. In optical tweezers, the electric field gradient of a tightly focused laser beam is used to trap small particles.[40]

In this interaction, momentum is imparted to the trapped object when it scatters photons from the incident optical field. The particle position can then be determined by measuring these scattered photons at the back-focal plane of a condenser lens, typically with a quadrant detector.[41] The particles in optical tweezers are tracked by measuring their perturbing influence on the electric field as they scatter photons. The scattered light is collected with a high numerical aperture lens, providing an image of the particle. The motion of the particle is responsible for displacements of the image, which typically measured by a resulting power imbalance on a quadrant detector.

A useful constraint on momentum uncertainty Δp_i is must be within the total photon momentum $P_{ph} = \frac{2\pi h}{\lambda}$, where λ is the vacuum wavelength, because;

$$\Delta p_i^2 = \langle p_i^2\rangle - \langle p_i\rangle^2 \leq \sum_{i=x,y,z}\langle p_i^2\rangle - \langle p_i\rangle^2 = p_{ph}^2 - \sum_{i=x,y,z}\langle p_i^2\rangle \quad (1)$$

Where, all symbols and notations are having their usual meanings. We introduce parameters fi to characterize Δp_i along each axis, such as; $\Delta p_i = \mathrm{f_i}\Delta_{\mathrm{ph}}$ (2)

Where, $f_x^2 + f_y^2 + f_z^2 \ll 1$, this relation becomes an equality for a photon, which is scattered with no preferred direction (i.e. (pi) = 0). Using this, a position measurement is limited to an uncertainty and given by following expression;

$\Delta q_i \gg \frac{\lambda}{4\pi f_i}$ (3) Above condition has a similar form to the Rayleigh criterion. In the events of optical tweezers, Rayleigh and Mie scattering are having valuable roles. Both the scattering rate κ and momentum distribution parameter f can be calculated analytically in the Rayleigh scattering regime, in which the particle diameter d<<λ. If an objective with numerical aperture of NA focuses an incident TEM00 mode on the particle, the scattering rate is give as follows;

$$\kappa = \frac{2}{3}\pi^5 (\mathrm{NA})^2 \left(\frac{d}{\lambda}\right)^6 \left(\frac{n_p^2 - n_m^2}{n_p^2 + 2n_m^2}\right)^2, \quad (4)$$

Where, np and nm are the refractive index of the particle and surrounding medium respectively.[42] The Rayleigh scatterers polarized along the x-axis, the scattered photons enter the mode ψ, with amplitude given as follows;

$$|\psi|2 = \frac{3}{8\pi}\frac{1-\left(\frac{x}{r}\right)^2}{r^2}, \quad (5)$$

Where, r is known as the radial distance. The measurement then only includes the light present in the area A of this aperture, and the parameter f is calculated as;

$$f_x^2 = \int |\psi|^2 x^2 dA - \left(\int |\psi|^2 x dA\right)^2, \quad (6)$$

The value of $\left(\int |\psi|^2 x dA\right)^2$ is zero for all the cases, due to photons scattered from cantered particles have no preferred transverse direction. The optical tweezers experiments usually operate with particles, which are too large to be accurately approximated as Rayleigh scatterers. For such particles, the scattering profile is complicated by such effects as multiple internal reflections and the interference between optical paths of different length. The particles in spherical shapes are focused optical fields, this scattering regime is described mathematically by extended Mie theory.[42] Evaluations of the scattering profiles were done numerically with the Optical Tweezers Toolbox.[43] These profiles are integrated as described in equation (6) to find the quantum sensitivity limit for particle track.

PARTICLE TRACKING MEASUREMENTS WITH OPTICAL TWEEZERS: A COMPUTATIONAL TOOL

The computational tool, a piece of Matlab code, was employed to do calculations for measuring the signal persisted in the particle tracking route with a sensor engaged for optical tweezers.[44] The shot-noise is applied to limit the position resolution. Such a theoretically categorized approach permits the measurements patented during optical tweezers experiments in a fast and easy manner. This Matlab code backs particles and executes a vector calculation of pertinent fields.[45] These calculations have displayed the path of the tracking signals observed for different particles and considered a shot-noise limit for highlighting the position of the sensitivity as a function. A set-up is offered to improve tracking of nanoscale particles using optical tweezers embedded[46] within a Sagnac interferometer and counter-propagating trap beams. Measurement of displacement of particles from the trap center can also measure that found to be proportional to the applied force.[47]

Quantum enriched sensitivity is designed for upgrading the phenomenon of optical tweezers for originating better particle tracking and the same was revealed in recent times.[48] Overall, the significance of sub-shot noise displayed inadequate sensitivity to applied experiments. Specifically, the biophysical experiments are interrelated with the optical power limitations, which, therefore, edge the out-and-out sensitivity, is characteristically feasible. Quantum enhanced particle tracking was done to overcome the fixed limit and therefore likely to play a key role in these biophysical tryouts.[49] It is a reported, finding that an optical arrangement is proficient for engendering stereoscopic imaginings to trap nanoscale particles in three dimensions. The three-dimensional nanoscale particle tracking phenomenon of each image produces a three-dimensional view.[50] By changing the proportion of the horizontal to the axial trap toughness, it is possible to change the intensity of the beam at the back aperture of the microscope objective.[51] These beams can concentrate on their optical power at the extremes of the back aperture produce, and are much more efficient for axial trapping.[52] The flexibility of using nanotweezers promotes is creating multiple traps with different shapes.

Force Detection in Optical Tweezers

By applying a calibrated force, simple manipulation can be done to achieve nanometer-level displacements for improving application in an optically trapped object.[53] The ability to generate piconewton range force to nanoscale particles and instantaneously assessing displacement in nanometers with high accuracy is possible after using these developed tools.[54] Further, it is practically possible to determine applied force consistently for the analysis of molecular motors at the single-molecule level, dynamics of the colloids, nanoscale and microscale systems (figure 3).[55] Theoretical and experimental research experiments were going on the essential features of optical trapping which approved the principles of trapping and detection; different calibration methods, the influence of surfaces, viscosity, and the evident widespread use of optical trapping.[56]

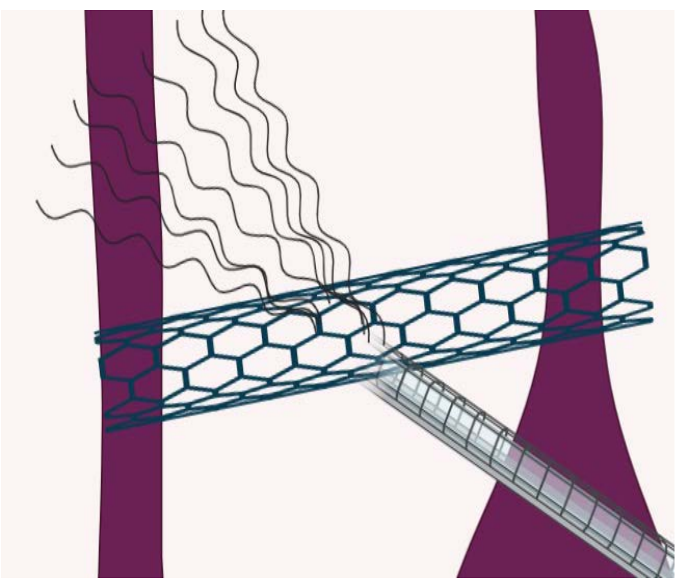

Figure 3. Schematic representation of holding and manipulating the nanoscale materials in a nano optical tweezers. "Acknowledged [biorender.com] as per instructions".

This review provides deep insight into the application of optical tweezers to the various fields of nanotechnology and trapping the viruses.[57] Therefore, the need to develop methods that can determine the force-position curve with and without synchronous force and position measurements of the trap is there.[58] The force-position curve is related to the nature of the particle and the trapping beam, and the same was observed during the implementation of the single-molecule trapping techniques and solid-state nanopores.[59] The optical tweezers were also applied to determine the position of a trapped particle with high accuracy in the presence of the nanopore by reflecting light from the bead.[60] Recent developments transformed the optical tweezers into more sensitive single-molecule tackling techniques which is capable of determining the motions of nanoscale material and viruses at the subnanometer level.[61] These interpretations are approaching quite nearer to the fundamental limit set by Brownian fluctuations.

Optical Tweezers to Trap Molecules and Nanoparticles at Nanoscale

In optical tweezers, a high streak laser beam electric field gradient is employed to entrap smaller particles. In the process, the scattered photons impart momentum of the incident optical field to the entrapped particle.[62] The position of the particle caged can be ascertained by a quadrant detector while dotting the measurements at the back-focal plane. This feed enhances particle detection sensitivity significantly to the order of sub-nano dimensions as forces ranging from sub-piconewton to nano-newton are controllably applied.[63] This technique fructifies into wider applicability in the study of Brownian motion in optomechanics, besides which it also has a solid and a significant footing in sub-cellular biology. The biophysics, which has been revealed through optical tweezers includes both the dynamics and magnitude of the forces applied by biological motors, flexible properties of DNA and RNA, are important for their biological functions, the dynamics of virus-host coupling by studying the intrinsic mechanical activity directly, the strain on an enzyme during catalysis brought about on the association of enzyme and substrate and the rheological properties i.e., a study in which materials deform to applied stresses, of cellular cytoplasm.[64] While exploiting processes that lead to smaller and faster movements, it becomes imperative to devise a mechanism sustainable enough to attain high sensitivity. A range of factors like laser noise, electronic noise in the detector, or drifts of mirror in the experiment constrain the position sensitivity, which is curiously mitigated through substantial efforts.[65] However, the sensitivity per photon must eventually be limited by noise due to the quantization of light, at this point reseachers have control over two prerogatives only to improve the sensitivity; augmenting the number of photons that can damage biological samples, or using photons with quantum correlations allowing the breach of fundamental limit, as reported in optical tweezers.[66]

Optical Tweezers: Manipulation, Assembly, and Patterning of Nano- and Microscale Particles

Combining nanoapertures onto the plane of an optical fiber can open up new aspects for chemical and biological sensing studies. Therefore, the optical trapping of a single polystyrene sphere was demonstrated at the cleaved end of a fiber with a double nanoaperture in a gold layer and with low optical trapping power.[67] The integration of the nanohole on the tip of the fiber was developed by depositing 5-nm titanium and 80 nm of gold followed by a 20 nm angled sputter deposition of gold/palladium to the fiber tips.[68] Photons that carry change in momentum consequently led to optical force. Abraham-Minkowski problem is a fixed debate on momentum carried by electromagnetic fields. This leads to consequences that in a viscous medium embedded with particle, the optical force is calculated with different approaches, thereby derived by combining momentum flux on a closed surface for covering the particle.[69] A strong research impetus backs the trapping techniques as researchers tackle matter at the nanoscale for chip-scale devices. This way we have been able to generate energy-efficient nano-tweezers compared to the contemporary microscope-based optical tweezers.[70] There has been researching laid that covers able devices enough to entrap particles in the micron scale (i.e., bacteria and cells). The onus is now to work on sub-micron and nanoscale objects such as nanobeads and DNA strands, which require tethering them to larger beads and high values of input power, can damage the surface properties and the activity of the trapped objects.[71] Research is, therefore focused on trapping devices that can overcome these limitations and achieve living matter manipulation with high efficiency and low power levels to enable trapping of nanoparticles smaller than 100 nm, and it is essential for life science applications. There are several approaches that have been proposed in the literature for confinement and tackling of living matter at the nanoscale.[72] Of them, optical phenomena have demonstrated the highest productivity in terms of the size of the trapped objects and low energy consumption.

A number of routes have been proposed to allow trapping of very small particles like hydrodynamic trapping where particles are studied by isolating them using hydrodynamic force. Tanyeri et al. applied two contra directional laminar flows to craft an inertia point having a null flow, at this point, nanoparticles up to 100 nm can be trapped for a while.[73] However, techniques other than the optical approach provide large displacements for trapped particles corresponding to lower values of trapping stagnation.[74] For trapping of particles, magnetic fields are also used. Magnetic trapping sites can be realized using a desired spatial distribution of magnetic fields, which depends on the position and distance between the magnets and coils. Magnetic beads having functioned exteriors utilized for binding the objective. Efficient sorting, as well as its manipulation at the nanoscale, has been reported.[75] However, magnetic trapping at the nanoscale is challenging because large magnetic fields are required to trap insignificant particles, which induce dangerously high heating effects for the biological matter.[76] Under the auspices of quantum mechanics, the quantum noise limit is an established maxim, however, its increasing relevance in experimental physics poses a new dimension altogether.[77] Numerical interpretations of quantum limit are so far paltry derived only in the paraxial optical regime with Rayleigh scattering, narrowing its applicability in most experiments while also making it intuitive comprehension vague.[78] Simple treatment based on the principles of the Heisenberg's Microscope helps to derive a quantum sensitivity limit for optical tweezers while also engaging with particles of arbitrary shape and size. This technique easily deciphered analytically in the Rayleigh scattering parlance besides allowing the analysis of several optical setups.[79] The technique opens relevant gates to other measurements like fluorescent particle microscopy.

TRAPPING OF NANOPARTICLES AND INFLUENZA VIRUS

The trapping of an individual nanoscale particles and viruses such as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and influenza for the analysis has significantly enhanced the possibilities for understanding fundamental biological components and such molecular diagnostic is rapidly becoming relevant to various applications in the emerging field of biological and chemical characterization.[80] Optical and electrical trapping techniques have existed for tracking, trapping, analyzing, manipulating single biomolecules and nanoscale material. These methods are suitably assimilated form to apply for multimodal exploration with high throughput. Therefore, a dual-mode electrical and optical single-nanoparticle sensing device that has the capabilities and techniques applied individually for trapping nanoparticles and influenza virus is applied.[81] These tools inbuilt with an optofluidic chip that has an assimilated nanopore provides space for entry to control the delivery of individual nanoparticles and a virus in an optical excitation region for ensemble-free optical analysis rapidly. Electro-optofluidic was applied for an electro-optical detection of single influenza viruses that have a mixture of fluorescent nanobeads. These devices can identify single viruses within a mixture of equal sized fluorescent nanoparticles with high accuracy.[82]

The process of biomolecular interactions that is crucial for antibody-antigen binding, is an important component in various biological processes. This analysis depends on the various stages of immobilizing processes ensued within the interacting molecules one by one on a sensor surface.[81] Any deviation in the measurement of natural binding affinity and capacity of the molecules can create a division in natural free-solution behavior. Therefore, a label-free method is helpful for investigating the free-solution interactions that existed between a single influenza virus and specific antibodies at the nanoscale.[83] This analysis is possible using near-field optical trapping and light-scattering techniques. By examining the Brownian variations, the key component of features of virus, there is a need to track numerous specific antibody binding prospects that occur in an optically trapped influenza virus. These analytical models can be applied in determining the enlarged size of viral consequential occurred because of the antibodies binding to the viral membrane. Nanophotonic tweezers can be applied to various molecular interactions because it can handle molecules from tens to thousands of nanometers in diameter.[84]

The tactic of trapping and tacklingmanipulation of individual nanoscale particles and viruses such as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and influenza is in demand and can also be applied for the architecting varieties of materials and geometries. The other important aspects of the trapping conditions are that displace or release a particle which can be controlled and be governed according to the needs.[85,86] These advanced techniques can control the initiation of the forces and diffusion processes associated with biological objects. Therefore, these methods are highlighted to be applied in the field of optonanofluidics and plasmonics. More, the optical tweezers allow that contains double nanohole, can be applied to the trapping of nanoscale objects such as DNA fragments, individual proteins, viruses, and quantum dots.[87] These devices can apply magnetic force/optical force for the depiction of magnetic nanoparticles by applying magnetic gradient force. The most important aspects of these devices are that they are capable of isolating single nanoparticles and observing their size, determining their permeability, remanence, and permittivity.[88] Various optical transmission processes such as trapping, transmission intensity, transmission values, and variations in magnetic field amplitude were intercepted separated to expose the characteristics of magnetic nanoparticles. Recently, gold nanoparticles were trapped with a minimum of turbulence by applying a single laser beam.[89]

Optical Trapping of Severe Acute Respiratory Syndrome Coronavirus-2 (Sars-Cov-2)

It is a well-known fact that optical tweezers determine the force, twisting, and strain generated by molecular motors, as a function of time at the single-molecule level. These powerful nanomachines detect force in the piconewton range. Optical tweezers can easily detect the elasticity and condensation behavior of nucleic acids that naturally attach to the viral packaging.[90] These procedures may apply to tracking the viruses and viral molecules. A virus propagates by channeling genetic material that may vary from cell to cell at the nanoscale in thermal excitement. Viruses displayed resourceful passive and active approaches during the release of nucleic acids and affect the dynamic behavior of viruses. Various biochemical and physical techniques are that to be applied to study the structural, morphological, and dynamics. Therefore, the intrinsic mechanical activity can be dignified openly.[91] By producing laser radiation pressure, a virus can be trapped optically and tackled via single-beam gradient traps. Nano optical tweezers can detect different types of biostructures such as viruses and bacteria.[92] These targeted detection methodologies can also be applied for detecting biostructures, nanoscale objects, chemical surface modification of nanoplatforms, and tuning of nano optical properties. Moreover, the nano-optical tweezers can be used to discover biological variability. These applications will help determine the variable related to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) generated by a virus at the nanoscale (figure 4).[93]

The obtained variable genetic information of the biomembrane constitution could be detected in different manners depending on

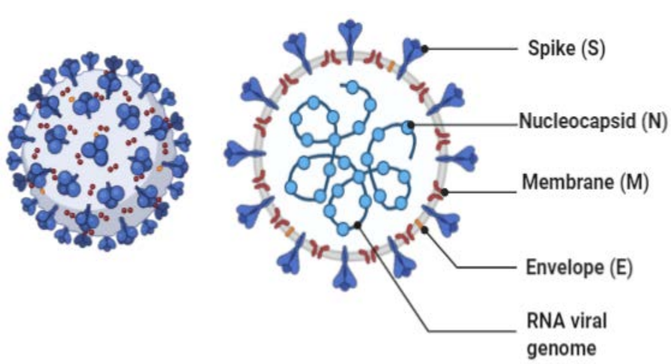

Figure 4. Illustration of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)..

the genetic codes. Similarly, these advanced tools can be helpful to determine a large variability of biostructures responsible for various illnesses.[94] The refractive index is the parameter that is observed during the optical trapping of the virus and its value varied according to size.[95] The obtained parameter represents a single virus interconnected with the toughness of an optical trap. An analytic expression, as a result, can be used to define the phenomenon that occurred during the optical trapping of used particles quantitatively.[96] The technology is developed that enables sensitive detection of virus-specific RNA sequences by attaching the virus' RNA to a fluorescent molecule.[97] The detection was performed at the time of emitting light when illuminated by a laser beam. For trapping a virus, or any nanoscale particles, two laser beams are generated at opposite ends of a channel.[98] At the juncture, where the forces exerted by the two beams are equal, the concerned particle gets trapped. Nano-optics innovations were applied to accomplish targeted biodetections. Antibodies-antigen interactions involucrated for coronavirus (COVID-19) detection were also testified.[99] Simultaneously, a scientific approach for detecting non-covalent interactions for higher-sized biostructure detection was performed, and that was based on bioimaging generation and optical signaling modifications. The detection and traping of corona virus is emergency requirement in current pandemic, particurly due to unavailability of suitable therapeutic drug for COVID-19.[100–102]

Lab-on-particles and functional nanoparticles were revealed.[99] These techniques can be tuned for biodetection. These innovative tactics may be applied to develop the targeted nanoplatforms that can be applied for light delivery applications. These aforementioned techniques highlighted the importance of the process of controlling nanoscale trapping and tackling and having tunable optical properties for variable sizes of biostructures.[103] The generation of nanolasers, biolasers, and living lasers is a key source that can be applied in different fields such as biosciences, and biodetection.[104] These tools will enhance the possibilities of innovation of new nano-photo-thermal therapeutics and theranostics. Nano-optics may be transformed into nano-bio-optics and can be applied for detecting different diseases caused by the viruses.[105]

Optical Tweezers: Self-Assembly process of a Virus

Optical tweezers were also utilized for detecting the viral genome assembly and having the transient nature of intermediate structures which become elusive during the reaction.[106] These technologies make such complicated procedure to be a reality by optimizing the packaging of therapeutic agents in these particles. A fine analysis of the assembly pathways of the viruses will lead to the success of the theme. The undiscovered pathways and processes of particle nucleation, particle growth, and the mode of genome compaction will expose by the use of optical tweezers.[107] Recently, it was reported that DNA is highly suitable for the packaging of drugs during helical wrapping into a nucleocapsid.[98] The discovery of real-time assembly through optical tweezers by tracking the processes of elucidation of viral nucleation and growth principles will open new ventures for a fundamental understanding of assembly pathways naturally evolved in viruses.

The optical trapping of single viral particles guided for a proper characterization of single particles with high molecule sensitivity.[108] Optical tweezers can be used for manipulation indirectly to expose virus-cell interactions. This analysis offered insight into the fundamental features of protein-mediated receptor activation. The structural exploration of various viruses performed by optical trapping which resolved several features in atomistic detail, exposed the processes of the assembly and interconnected pathways.

Unresolved issues are also existent there and are the key features of the assembly process.[109]Such routes and topographies belong to particle growth of the critical nucleus, the successive self-assembly reaction, and complications of the viral genome.[110] Supramolecular complex viruses propagated by commandeering host cells.[111] Therefore, the features of research on the fundamental viral mechanisms will be a key discovery to be applied in the fieds of biomedicine and (bio) nanotechnology.[112]

OPTICAL NANOTWEEZERS: MANIPULATE VIRUSES

Optical nanotweezers can do manipulations in the virus by applying laser light that can generate a single-beam gradient force for trapping.[113] A precise optical wavelength can tackle the individual viruses and the same was witnessed by observing the changes in volumes of a few cubic micrometers. Nanotweezers can be oriented arrays of viruses optically by restricting noticeable damages.[114] These manipulations were performed with a high grade of precision.[115] The techniques of optical trapping and tackling displayed a high impact which played a crucial role in the innovation required for physical and biological systems. Not only, these techniques were applied for trapping a single vision, but also the received outputs further used to calculate the refractive index of the virion. The obtained results have a high grade of precision. For example, optical nanotweezers quantitate the heterogeneity in virion through single-molecule resolution.[116] Therefore, the techniques of optical trapping and tackling can easily expose the molecular machinery of virion infectivity. The routes of dissociation and their concerned events of individual virion followed at the time of manipulation and these processes had impacts on the host cell surface that can be exposed.[117] These analyses and obtained outcomes play a key role to define the process of diffusion during the handling of viral attachment to host cells (figure 5).

Optical tweezers are also applied for isolating the tiny particles of the same scale as viruses easily. A special class of plasmonic nanotweezers was discovered that can trap nanoscale particles using laser light.[29,118] These tools are the modern outfits that can create strong forces more efficiently comparatively optical tweezers. These setups do not allow overheating and by doing so, these machines reduce any possibility that may cause hurdles in the setup.[119] Tacklingof colloidal objects with light is promising and these findings are crucial in the allied fields. The nanotweezers can also easily transport nanoscale material at the surface where it's required.[120] They applied optical force having lower side intensities without damaging the living micro-organisms.[121]

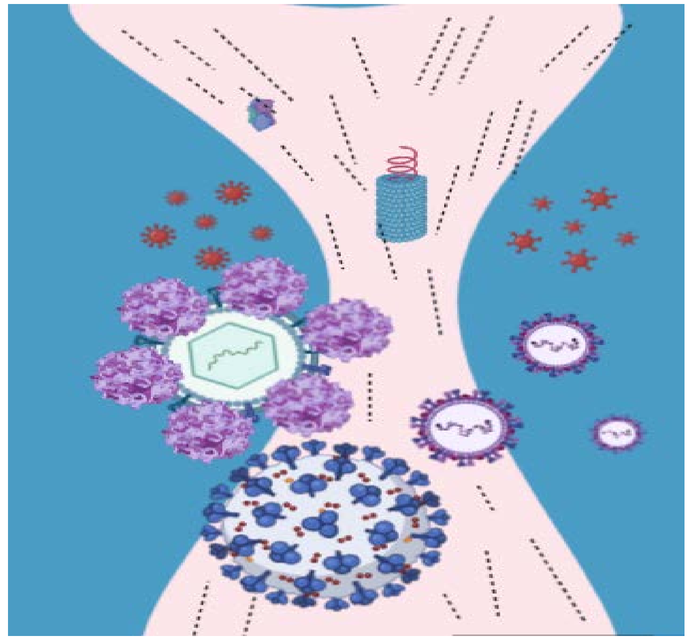

Figure 5. Schematic illustration of optical nanotweezers quantitate the heterogeneity in virion through single-molecule resolution. "Acknowledged [biorender.com] as per instructions".

These tweezers allow parallel and independently controlled manipulation of different types of nanomaterials and nanoparticles.[122] Optical tweezers can detect viruses, cancer, and neurodegenerative damages. Recently, tweezers that can trap and manipulate 10 nm objects such as biomolecules have been reported in the journal of nature nanotechnology.[123] The development of these tools was based on the concept in which a tightly focused laser beam is applied to isolate nano micro-scale objects, that are having sized up to the size of erythrocytes.[124] It is challenging aspects to detect these tiny objects, besides this, the nano-optical tweezers were very useful during the instigation and detection of pathogens, manipulating viruses for researching proteins that caused illnesses and neurodegenerative diseases. Earlier detection of disease is considered as an advanced application of these tools, which can effectively capture low levels of molecules responsible for causing disease. Such investigations will help in detecting earlier phases of the diseases by identifying disease-causing molecules during the sate of pathogenesis.

Additionally, these nano-optical tweezers can be combined with other research techniques to do manipulation at nanoscale. In the field of bio/microfluidics, various procedures such as positioning, sorting, transporting and the collection of single particles cannot be possible before the development of these tools. With the help of the nano-optical tweezers, a virus can be transported on a surface without any damage, and trapping of it is always possible practically. With the help of these tools, the process of hybrid nanoscale assembly can be performed easily.[125] Because of these advanced tools and devices, it is now possible to place nanoscale materials and objects in specific positions. These innovations will be key resources and can be applied as an impactful tool in next-generation quantum computing and sensing devices.[126] The most important aspects of these findings will be fruitful in the development of biomedicine. The other significant features of these nano-optical tweezers are their abilities to tackle biological objects, which make these tools and devices compatible with biomedical applications.[127] Thus, the biological entities can be trapped, detected, and transported according to the need of the biological systems, is a new innoation that can be applied in different innovations.

Plasmonic Optical Tweezers: Three-Dimensional Tracking

Earlier, optical tweezers displayed a one-dimensional approach, therefore, it is difficult to have a three-dimensional interpretation of biological systems.[54] Optical tweezers generate high-intensity trapping laser, which can destruct biological models.[128–130] These hurdles restrict their applicability and feasibility for vivo applications. Therefore, trapping of biological matter at the nanometer scale does not look possible by using general tweezers. But, nowadays, the updated version of optical tweezers, is based on innovations of laser technology and advances which can trap and manipulate nanoscopic biological objects. These plasmonic optical tweezers used localized surface plasmons to generate optical traps with enhanced trapping potential.[131] With the help of the aforementioned tools, the three-dimensional optical tracking method generates a multiple-beam optical trap to facilitate advanced trapping geometries. These new innovative technologies overruled exciting discoveries.[132] Thus, these enhanced tackling capabilities are capable of doing more challenging tasks by applying force detection. These tactics are highlighted as an efficient method that is capable of doing multiple traps and enabling fast and accurate 3D force.[113] The plasmonic optical tweezers can tackle microscopic objects without tempting undesired changes in the assembly.[133] Therefore, three-dimensional (3D) micro/nano-manipulation is a significant innovation and has recently been applied in biology and nanotechnology.[115] These advanced tools are also applied for distance revealing of multiple objects simultaneously and have the technology that can manipulate objects like multiple-beam optical tweezers. These innovative methods are implemented in many filed of physics and biology for manipulation of the structure and dynamics of nano- and mesoscale objects by exerting micro-scale force on biological samples in three-dimensional.[134] The role of micromachines in biological research explores possible feed-forward applications, and extensions into two- and three-dimensional optical force clamps.[135] The three-dimensional scattering and interferometric imaging was used in measuring of the spatial interaction potentials for nano-objects. These tools can trap gold particles by reflecting interface, do imaging, high-speed and accurate 3D tracking, and do probing to detect weak and long-range interaction.

Optical Nanotweezers: Three-Dimensional Manipulation

To full fill the current needs of nanotechnologies, which can be accurately addressed by manipulating the individual nanoscale particles and viruses such as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and influenza by making efforts, will further explore new horizons. The combination of weak optical forces and photothermal techniques[136] improved the impact of nanotechnology and its experimental success.[137] For example, advanced nanotweezers can do three-dimensional optical manipulation of single dielectric nano-objects. These tools and devices can do manipulations, observe, and modify the "building blocks" at the nanoscale.[138] Optical tweezers can directly trap objects nanoscale particles, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and influenza without overheating and damaging the specimen that is why it is very useful in biology and quantum optics. This proof of concept demonstrates the mechanism and empower to do 3D manipulation according to the applications.[113] Therefore, by applying the plasmonic nano-tweezers, the trapping and 3D manipulation can be done using an extremely small, non-invasive laser intensity. The trapping, tracking , tacklingand monitoring of the trapped specimen is possibly using optical fiber. These advanced tools manipulate colloidal particles in three-dimensional with various materials, sizes, and shapes and can perform in low-power and high-resolution fashion.[139] These devices can trap parallel particles and can be applied in particle filtration and biological studies. Their ability to manipulate tiny bio-object efficiently can be applied to find a wide range of applications in fields of life sciences, nanomedicine, colloidal sciences, photonics, and materials sciences.[140] Thus, a 3D manipulation can release of a single nano-object with positive impact without exerting any mechanical contact or other invasive action.

Optical tweezers are innovative tools in the field of biology and quantum optics because it can be directly trapped objects having nanometers sizes. Therefore, this technique opens new avenues to do tackling of entities at the single-molecule/virus level and as a tool that can be displayed many benefits in the field of medicine to expose the biological mechanisms of the diseases and can innovate new methodology for their treatment.[141] Optical tweezers have proved their worth in nanotechnologies and enhanced it, as a potentail devices and tools for developing miniature effeciency that will have upgraded and potential applications.

Future Prospects and Conclusion

Optical tweezers were applied in the field of biology, nanotechnology, chemistry, biochemistry, and physics for various investigations and played an important role in innovation. Optical trapping and tackling of large numbers of nanoscale particles and viruses such as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and influenza and these discoveries are leaving an impact on bioengineering and nanoscience, for example, to do attempts to control the organization of cells during organ and tissue growth. These advanced tools are capable of trapping, tackling and tracking severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and influenza virus by providing unprecedented access at the nanoscale, and thus open new avenues for fundamental and applied research. Moreover, the techniques is used for trapping and tackling of large numbers of particles, holding of particles, atoms, molecules, and even bacteria and other living cells. Optical laser deals with these complicated task without damaging the nanoscale objects and thus it can be recommanded in pharmaceutical research. These advanced tools are useful in biological applications for measuring extremely small forces. Therefore, optical tweezers utilized to perform single-molecule force spectroscopy characterizations and investigations from an experimental perspective of the studied onanoscale particles, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and influenza.[142] The experimental configurations and derived physical parameters concerned with optical tweezers were employed nowadays while dealings with the single-molecule. Such efforts are applied for detecting unparalleled precision for enhancing the understanding of the vital enzyme and help nourish the methodologies applied for better cancer treatments.

The phenomenon of the optical tweezers is based on the powerful lasers that can generate small forces that are pulling and holding nano/microscale objects such as strands of DNA, virus, and enzyme at the time of investigations.[143] Therefore, optical tweezers can deal with the machinaries of the cell and can hold and tackle them on the surface. On the other side, a stronger force is required for trapping nanoscale and microscopic particles and that can be achieved only using a high-powered laser to trap the tiniest targets. Therefore, it can able to tackle, manipulate and probe objects of the same scale. These tacklings nourish the phenomenon that to be applied for the exploration and tackling of a virus and nanomaterials to explore their significance in the fields of nanotechnology, biophysical and biomechanical. Further, the 3D printing techniques and electronic controllers were also developed by applying the motorized beam blockers and optical attenuators. Therefore, the authors present recent advances in the field of biodetection by the use of nano-optical tweezers to expose bioconjugation strategies within this communication.

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AUTHOR CONTRIBUTIONS

RK, and KG supervised and wrote this review article. MPC wrote section (basic principles of optical tweezers and its scattering phenomena) and MPS wrote section (optical tweezers to trap molecules and nanoparticles at nanoscale and optical tweezers: characterization of nano- and microscale particles). All authors read and approved the manuscript.

COMPETING INTERESTS

The authors have declared that no competing interest exists.

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