

THE ACOUSTIC AND OPTICAL MANIPULATION OF ACTIVE MATTER

by

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THE ACOUSTIC AND OPTICAL MANIPULATION OF ACTIVE MATTER

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ACADEMIC ETHICS AND INTEGRITY STATEMENT

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ABSTRACT

THE ACOUSTIC AND OPTICAL MANIPULATION OF ACTIVE MATTER

This thesis explores the acoustic and optical manipulation of active matter, emphasizing both fundamental principles and biomedical applications. Active matter systems, such as flocks of sheep, schools of fish, bacterial colonies, and Janus particles in engineered media, naturally operate out of equilibrium, converting environmental energy into autonomous motion. The study begins with a theoretical foundation of Brownian and active motion in microscopic systems and progresses to experimental manipulation using a nanosecond pulsed laser. This laser system contributes to particle control and biomedical imaging through photoacoustic visualization of mouse placental tissues, enabling label-free detection of vascular structures and revealing morphological changes associated with circadian rhythm disruption. A primary experimental focus is the precise control of Janus particles, where the effects of laser energy and beam spot size on particle dynamics are systematically analyzed. Complementary simulations further examine acoustic and optical trapping mechanisms. This work advances our understanding of contactless particle manipulation and lays the groundwork for future non-invasive diagnostic and drug delivery technologies.

Keywords: Active Matter, Particle Manipulation, Pulsed Laser, Nanosecond Pulsed Laser, Photoacoustic Imaging.

ÖZET

TEZİN TÜRKÇE BAŞLIĞI

Bu tez, aktif maddenin akustik ve optik manipülasyonunu hem temel fiziksel prensipler hem de biyomedikal uygulamalar açısından ele almaktadır. Sürü halindeki koyunlar, balık sürüleri, bakteri kolonileri ve özel ortamlarda yer alan Janus parçacıkları gibi aktif madde sistemleri, doğaları gereği termodinamik dengede olmayan yapılar olup, çevresel enerjiyi kendi hareketlerini yönlendirmek için otonom biçimde kullanırlar. Çalışma, mikroskobik sistemlerde Brownian ve aktif hareketin kuramsal temelleriyle başlayarak, deneysel olarak nanosaniye darbeli lazer kullanımıyla yapılan manipülasyonlara ilerlemektedir. Bu lazer sistemi, parçacıkların kontrolünde olduğu kadar, fare plasenta dokularının fotoakustik görüntülemesi yoluyla, damarsal yapıların kontrast ajan kullanmaksızın görselleştirilmesini ve sirkadiyen ritim bozulmasına bağlı morfolojik değişimlerin ortaya konmasını da sağlamaktadır. Deneysel çalışmanın temel odağı, lazer enerjisi ve ışın nokta boyutunun Janus parçacıklarının dinamikleri üzerindeki etkilerinin sistematik olarak analiz edilmesidir. Ek olarak yapılan simülasyon çalışmaları, akustik ve optik tuzaklama mekanizmalarını detaylı biçimde incelemektedir. Bu çalışma, temassız parçacık manipülasyonuna dair bilgimizi ilerletmekte ve gelecekteki invazif olmayan tanı ve ilaç taşıma teknolojileri için sağlam bir temel sunmaktadır.

Anahtar Sözcükler: Aktif Madde, Parçacık Manipülasyonu, Darbeli Lazer, Nanosaniye Darbeli Lazer, Fotoakustik Görüntüleme.

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LIST OF SYMBOLS

X_N	Coordinate of particle on X-axis in N th time
T	Temperature
t	Time
D_T	Translational diffusion constant
D_R	Rotational diffusion constant
r, R	Radius of the particle
k_B	Boltzmann's constant
c	Speed of light constant
h	Planck's constant
R_s	S-polarized
R_p	P-polarized
V	Velocity of particle
n	Refractive index
I	Intensity of light
Q	Heat
c_p	Specific heat capacity
L_T	Thermal diffusion length
t_p, τ	Pulse duration of laser
r_i	Particle position at i -th measurement
E_0	Energy
α	Absorption coefficient
β	Compressibility paramter
ζ	Viscous friction coefficient
η	Fluid viscosity
ϕ	Orientation of the particle
$\xi_{x,y,\phi}$	White noise, with zero mean for x, y , and ϕ
Φ	Acoustic contrast factor
κ	Heat conductivity

ρ	Density
ω_0	Beam spotsizes
λ	Wavelength
Z	Partition function
h	(In heat equation) Convection heat transfer coefficient
ϵ	Emissivity
σ	Stefan-Boltzmann constant



1. INTRODUCTION

Active matter describes systems that acquire energy from the environment and spend it to move in a directed manner. As a result these systems are away from equilibrium [1, 2, 3, 4, 5]. This capability enables behaviors such as swarming, aggregation, and pattern formation, which are unattainable in systems at thermal equilibrium [6]. The realm of active matter covers a vastly different scale and complexities of both natural and synthetic entities. These systems include natural and synthetic self-propelled particles that convert energy into directed motion, demonstrating a balance between random fluctuations and active swimming. In the natural world, we encounter striking examples of active matter in the mesmerizing dance of bird flocks, the evasive motion of a school of fish, the intricate organization of cells within tissues, and the coordinated movements of bacterial colonies. Beyond the biological realm, scientists have engineered synthetic active matter systems, such as self-propelled colloids. The examples of active matter are brought in Figure 1.1. These artificial constructs provide valuable platforms for investigating the fundamental principles governing active matter behavior and hold promise for developing novel materials with unprecedented capabilities. The defining characteristic of active matter lies in the continuous energy consumption and dissipation by its individual constituents. This inherent non-equilibrium nature fuels the emergence of striking phenomena, including spontaneous pattern formation, self-organization, and unusual mechanical properties. Active matter offers valuable insights into non-equilibrium physics [1] and promises applications in areas like targeted drug delivery [7], and environmental remediation [8]. The study of these systems encompasses disciplines including biology [9], robotics [10], and biomedicine [11]. At the heart of understanding active matter lies the concept of Brownian motion, a seemingly random yet environmentally driven movement. To fully appreciate active matter, we must first understand the historical origins and principles of Brownian motion.

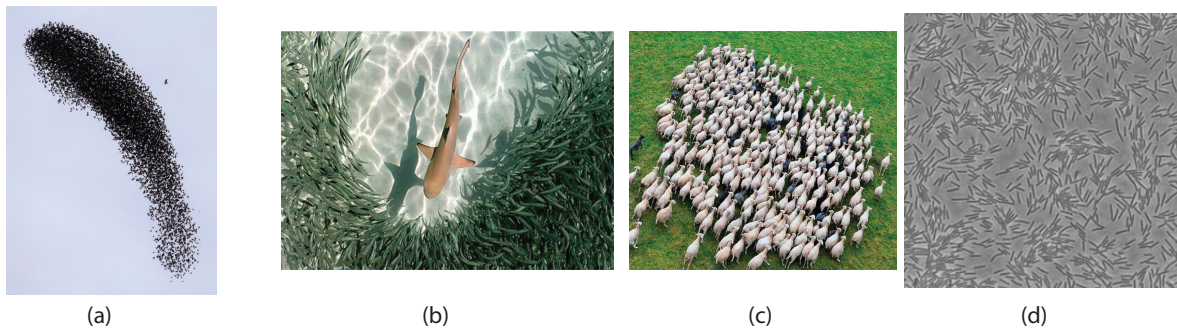


Figure 1.1 Variety of active matter examples. (a) a flock of bird, (b) school fish that is under attack by a shark, (c) flock of sheep, and (d) microorganisms.

1.1 Where it started

The story of Brownian motion began with the observations of Scottish botanist Robert Brown. In 1827, while examining pollen grains under a microscope, he noticed that they were in a state of constant motion. He initially hypothesized that this motion was due to the "life" within the pollen. Since he was a careful observer, he kept the experiment going for hours, assuming that the pollen was deprived of energy resources. However, he noticed that the motion was constant and did not stop. To test his hypothesis further, he aimed at lifeless samples. In coal-burning London, carbon dust was readily available. Upon observing this dust under his microscope, Brown witnessed the same erratic movement, disproving his initial idea [12]. Despite the intriguing nature of these observations, a full understanding of Brownian motion remained elusive until Louis Bachelier's and Einstein's groundbreaking work in 1900 and 1905, respectively.

1.2 Formulation of Brownian and active motion

At the beginning of 20th century, the atomic theory of matter was still controversial, as many scientists were reluctant to accept the idea that matter was made

of discrete particles. It was in this context that Einstein proposed his explanation of the Brownian motion, which was based on the idea that a vast number of water molecules were constantly bombarding the pollen grains. Although this idea may seem obvious today, it was a radical departure from the prevailing scientific worldview at the time. Einstein's explanation of the Brownian motion was a significant turning point in the history of science, as it provided strong evidence for the existence of atoms and molecules. Einstein further proposed that the Brownian motion of a single colloidal particle can be described by a type of random walk, where the mean-square displacement in a one-dimensional random walk increases linearly in time:

$$\langle (X_N)^2 \rangle = 2D_T t, \quad (1.1)$$

Where N is the number of steps, D_T is the translational diffusion constant, and t is time. D_T can be modeled microscopically as a sequence of discrete steps of size L , taking place at the time intervals dt , resulting in:

$$D_T = \frac{L^2}{2\Delta t}. \quad (1.2)$$

While this describes how a particle spreads, a complementary view considers how they respond to applied forces. Between the randomizing collisions, a particle of mass m is momentarily free to accelerate under an external force f . So it is subjected to Newton's law of motion; $\frac{dv}{dt} = \frac{f}{m}$. The velocity accordingly changes with time $v(t) = v_0 + \frac{f}{m}t$ where the v_0 is the starting velocity just after a collision. This leads to a motion characterized by uniform acceleration of the particle:

$$\Delta x = v_0 \Delta t + \frac{1}{2} \frac{f}{m} (\Delta t)^2. \quad (1.3)$$

Assume that each collision completely erases any memory of the previous motion. As a result, after each collision, the initial velocity v_0 is equally likely to point to the left or right, making its average value, $\langle v_0 \rangle$, equal to zero. Taking the average of 1.3, it becomes

$$\langle \Delta x \rangle = \frac{f}{2m} (\Delta t)^2. \quad (1.4)$$

In other words, although the particle experiences random collisions, it still develops an average drift velocity given by $\langle \Delta x \rangle / \Delta t$, or

$$v_{drift} = \frac{f}{\zeta}, \quad (1.5)$$

where ζ is the viscous friction coefficient and defined as

$$\zeta = \frac{2m}{\Delta t}. \quad (1.6)$$

In practice, it is not necessary to measure ζ directly, as it can be related to the particle's size through a well-established empirical expression known as the Stokes formula:

$$\zeta = 6\pi\eta r. \quad (1.7)$$

In this expression, η is the viscosity of the medium and r is the radius of the particle.

To link diffusion and friction, Einstein employed a third relation. The average velocity of the particle is linked to temperature via the equipartition theorem:

$$\frac{1}{2}m \langle v_0^2 \rangle = \frac{1}{2}k_B T, \quad (1.8)$$

where the k_B is Boltzmann's constant and T is the temperature. Eq. 1.8 can be written as $\langle v_0^2 \rangle = \frac{k_B T}{m}$ thus $(\frac{L}{2\Delta t})^2 = \frac{k_B T}{m}$. Which leads to

$$\zeta D_T = \frac{2m}{\Delta t} \frac{L^2}{2\Delta t} = \frac{mL^2}{\Delta t^2} = k_B T \quad (1.9)$$

Hence, we arrive at the famous Einstein relation:

$$\zeta D_T = k_B T. \quad (1.10)$$

This equation states that the fluctuations in the position of the particle are linked to the dissipation or frictional drag it feels. The connection is quantitative and universal: It is always given by the same quantity $k_B T$ appearing in the ideal gas law, no matter what sort of particle is studied. This foundational result, known

as the Einstein relation, is a cornerstone for understanding the connection between microscopic thermal motions and macroscopic observables like diffusion.

Eq. 1.10 prepares the ground for deriving more equations to simulate the Brownian motion and active motion of particles. For a Brownian motion where its motion is purely diffusive, translational diffusion is defined as

$$D_T = \frac{k_B T}{6\pi\eta r}. \quad (1.11)$$

Another important parameter is defined as rotational diffusion, which is defined as [13]

$$D_R = \frac{k_B T}{8\pi\eta r^3}. \quad (1.12)$$

For the Brownian motion, in one dimension, we can write

$$m\ddot{x} = -\zeta\dot{x} + \sqrt{2k_B T\zeta}W(t), \quad (1.13)$$

which is basically Newton's second law for motion. ζ is the friction coefficient of the particle in the medium when it is moved, and $W(t)$ is $\frac{\xi_x}{\sqrt{\Delta t}}$. ξ_x is Gaussian white noise term with an average of 0 and a standard deviation of 1. One of the ways to solve this Eq. 1.13 is by incorporating the finite difference method. Solution will be [13]

$$x_i = \frac{2 + \Delta t(\zeta/m)}{1 + \Delta t(\zeta/m)}x_{i-1} - \frac{1}{1 + \Delta t\frac{\zeta}{m}}x_{i-2} + \frac{\sqrt{2k_B T\zeta}}{m[1 + \Delta t\frac{\zeta}{m}]}(\Delta t)^{3/2}\xi_x. \quad (1.14)$$

The ratio of $\frac{\zeta}{m}$ is called momentum relaxation, if we assume that $m \ll \zeta$, then we can simplify the Eq. 1.14 to

$$x_i = x_{i-1} + \sqrt{2\Delta t}\xi_x \quad (1.15)$$

In a homogeneous medium, the translational and rotational motions are independent of each other. The stochastic equations of Brownian motion in a two-dimensional space are

$$\dot{x} = \sqrt{2D_T}\xi_x, \quad \dot{y} = \sqrt{2D_T}\xi_y, \quad \dot{\phi} = \sqrt{2D_R}\xi_\phi, \quad (1.16)$$

where $[x,y]$ are particle position coordinates and ϕ is orientation of the particle, shown

in Figure 1.2(a). The stochastic terms ξ_x, ξ_y, ξ_ϕ are defined as Gaussian white noise. The equations governing each degree of freedom (x , y , and ϕ) are independent of one another. Inertial effects are disregarded, as microscopic particles generally operate in a low-Reynolds-number regime [14].

For active particles, where they are self-propelled, the direction of the motion is subject to rotational diffusion, which results to coupling between the translation and rotation. The corresponding equation are 1.16 change to

$$\dot{x} = v \cos \phi + \sqrt{2D_T}\xi_x, \quad \dot{y} = v \sin \phi + \sqrt{2D_T}\xi_y, \quad \dot{\phi} = \sqrt{2D_R}\xi_\phi, \quad (1.17)$$

where v shows the velocity of the self-propelled particle. Figure 1.2(b-e) depicts the trajectories of 5 particles undergoing Brownian motion with varying self-propulsion speeds (v). In (b), the particles exhibit pure Brownian motion with no self-propulsion. As v increases from 1 $\mu\text{m/s}$ in (c) to 2 $\mu\text{m/s}$ in (d) and finally 5 $\mu\text{m/s}$ in (e), the particles explore a larger area. This shows the interplay between random diffusion and directed self-propulsion in active motion, where increasing self-propulsion leads to greater exploration.

1.3 Manipulation of particles

The intrinsic non-equilibrium nature of active matter, coupled with the diverse mechanisms by which its constituents convert energy into motion, presents both unique challenges and exciting opportunities for manipulation and control. A variety of external stimuli have been employed to guide and control the behavior of active matter systems. Magnetic fields can be used to manipulate magnetically responsive active particles by exerting forces and torques, enabling precise control over individual particles and the creation of complex patterns in active matter assemblies [15, 16]. Similarly, electric fields can induce motion and control the orientation of electrically polarizable or charged active particles, allowing for dynamic control over particle trajectories and the creation of responsive systems [17, 18, 19]. Microfluidic devices offer precise con-

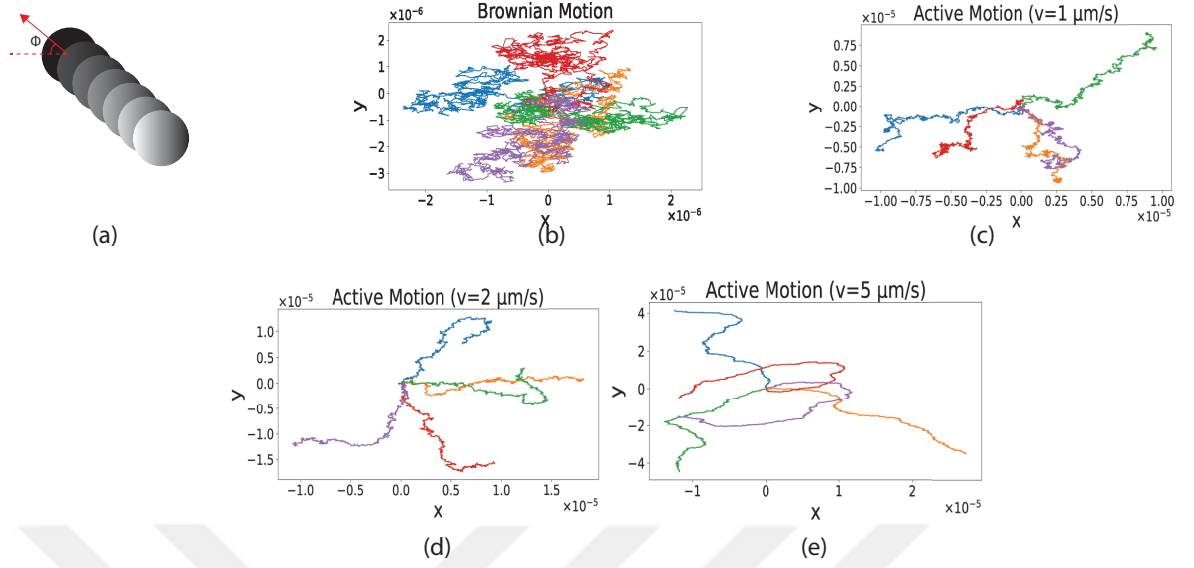


Figure 1.2 Active motion in two dimensions. (a) An active Brownian particle in water (radius $r = 1 \mu\text{m}$, viscosity $\eta = 0.001 \text{ Pa}\cdot\text{s}$) is located at position $[x, y]$. It propels itself along an orientation angle ϕ with speed v while also undergoing Brownian motion in both position and orientation. The trajectories are illustrated for various velocities: (b) $v = 0 \mu\text{m/s}$ (purely Brownian motion), (c) $v = 1 \mu\text{m/s}$, (d) $v = 2 \mu\text{m/s}$, and (e) $v = 5 \mu\text{m/s}$. As v increases, the particles travel longer distances before their direction is randomized. For each velocity, 10-second trajectories are displayed.

trol over the local environment, creating complex flow patterns and gradients that can guide and manipulate active particle motion, enabling the study of their behavior in well-defined microenvironments [20, 21, 2]. Chemical gradients can fuel and direct the motion of chemotactic active particles by creating spatially varying concentrations of chemical attractants or repellents, influencing their trajectories and collective behavior [22, 23, 24, 25, 26, 27]. Optical techniques, such as optical tweezers, provide precise and often non-invasive methods for manipulating individual active particles, facilitating the study of individual particle dynamics and collective behavior in response to external stimuli [5, 28, 29, 30, 31]. Acoustic fields can generate forces and streaming flows that manipulate and control the motion of active particles, offering a label-free method applicable to a wide range of systems, including biological cells and synthetic microparticles [32, 33, 34]. In contrast, other methods such as magnetic, electric, optical, and acoustic fields provide a non-invasive manipulation approach. These methods enable particle control through externally applied fields without altering the chemical composition or physical properties of the surrounding medium. The choice of manipulation technique depends on the specific properties of the active matter system and

the desired level of control. Acoustic and optical methods are particularly versatile, allowing for both individual particle manipulation and the manipulation of large ensembles, enabling the exploration of a wide range of collective phenomena and potential applications.

1.3.1 Acoustic manipulation

Acoustic manipulation is a rapidly evolving field that utilizes the power of mechanical waves to manipulate particles at the micro scale. This method has emerged as a promising tool for contactless manipulation of both synthetic and biological micro agents, such as blood [35], bacteria [34]. Acoustic manipulation offers several advantages. It is a low-power, biocompatible, and versatile technique that can be applied to a variety of applications in life sciences and beyond. Acoustic manipulation utilizes mechanical vibrations that do not alter cell characteristics.

For acoustic manipulation, two primary types of waves are utilized: bulk acoustic waves (BAWs) and surface acoustic waves (SAWs), each with distinct characteristics and applications. These waves are typically generated using piezoelectric materials. BAWs propagate through the volume of the medium, whereas SAWs travel along the surface of the piezoelectric material. Acoustic waves can exist in two forms: traveling waves and standing waves. Traveling waves propagate continuously through the medium until they dissipate, while standing waves remain stationary, producing a more pronounced and significant effect.

The acoustic radiation force calculation has a long history. In 1934, King [36] calculated the acoustic force on incompressible particles. In 1955, Yosioka and Kawasima [37] analyzed the acoustic force on the compressible particles. Their work was later generalized by Gorkov in 1962 [38].

The acoustic radiation force of a standing wave, in the direction of x , is [39]

$$F_x^{radiation} = 4\pi\Phi(\tilde{\beta}, \tilde{\rho})kr^3 \sin(2kx). \quad (1.18)$$

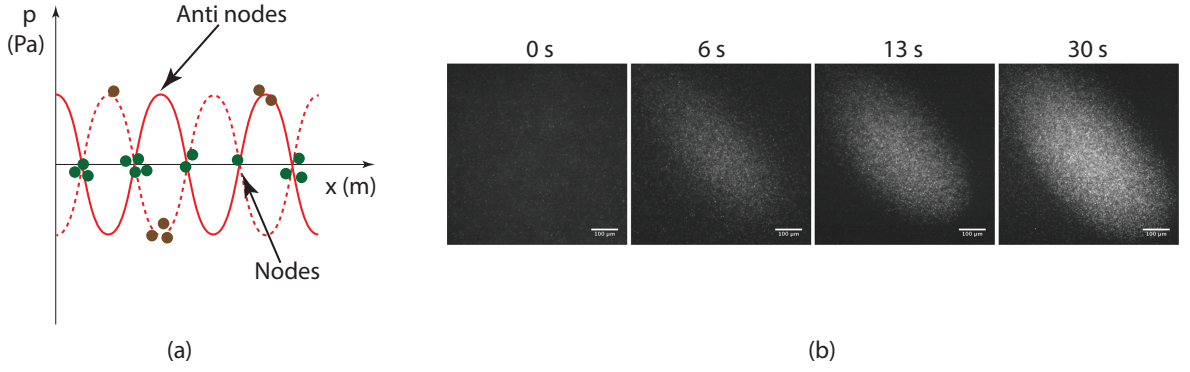


Figure 1.3 Acoustic force and its impact on particles. (a) This schematic illustrates the behavior of particles in the presence of a standing wave. Y-axis shows the pressure and the x-axis shows the location. A standing wave creates a pattern where the positions of the nodes remain constant while the peaks oscillate. Depending on the sign of the contrast factor, particles are trapped either at the nodes or at the anti-nodes. (b) This figure shows the clustering effect on a colony of *E. coli* bacteria induced by acoustic force [34].

The acoustic contrast factor, denoted as Φ , the radius of the particle, represented by r , and the wave number, indicated by k , are key parameters in understanding the behavior of particles influenced by acoustic waves. These particles exhibit fascinating behaviors depending on their acoustic contrast factor [34, 40]. Specifically, they will be trapped in either the nodes or anti-nodes of the standing wave. For instance, red blood cells are trapped into node of the acoustic waves but white blood cells are trapped into anti-nodes [35]. The acoustic contrast factor is defined as [39]

$$\Phi = \frac{5\rho_p - 2\rho_m}{2\rho_p + \rho_m} - \frac{\beta_p}{\beta_m}, \quad (1.19)$$

where the ρ_p, ρ_m, β_p and β_m are the density of the particle and medium and the compressibility of the particle and medium, respectively. Figure 1.3 (a) and (b) show the schematic of acoustic trapping and an example taken directly from [34] under CC BY license.

1.3.2 Optical manipulation

Optical manipulation leverages the unique properties of light, its intensity, wavelength, polarization, and momentum, to exert precise forces on particles. This approach

is especially advantageous for its non-invasive and highly controllable nature, making it an indispensable tool in active matter research. Optical techniques not only enable the study of individual particle dynamics but also facilitate the exploration of complex collective behaviors.

Light intensity is the most extensively employed property for actuating active matter. Using laser beams, researchers have driven the motion of microorganisms [41], synthetic micromotors [42], active droplets [43], and microrobots [44]. Microorganisms like cyanobacteria exhibit phototaxis, moving toward or away from light sources to optimize photosynthesis or avoid harmful intensities. The arrival of optogenetics has further allowed the programming of light responsiveness in otherwise non-photosensitive organisms, enabling dynamic pattern formation and applications in bioengineering.

Synthetic micromotors and particles, such as Janus particles with asymmetric coatings, have been widely studied for their ability to propel in light gradients. These particles leverage thermodynamic imbalances induced by light, resulting in self-propulsion and complex collective behaviors like dynamic clustering and the formation of photonic materials. Similarly, active droplets, which move due to light-induced surface tension gradients, have been explored for their use in microfluidics and as transport vessels [20]. Microrobots constructed from light-sensitive materials exhibit sophisticated locomotion patterns, mimicking biological systems [44].

Beyond intensity, other properties of light have shown great promise for active matter manipulation. The wavelength of light enables selective control by exploiting material-specific absorption, such as plasmon resonances in metallic coatings [45]. Polarization introduces new avenues for control, with natural examples like *Euglena* algae aligning their motion to polarized light [46]. Man-made systems, including nanomotors with dichroic materials, demonstrate navigation capabilities based on light polarization. Lastly, the momentum of light, both linear and angular, has been harnessed to propel micro motors and influence particle trajectories, opening pathways to programmable collective behaviors.

So far it is shown that active matter systems are uniquely characterized by their capability to acquire energy from environment and spend the energy into a directed motion (in oppose to Brownian motion), exhibiting complex collective behaviors that cannot emerge in passive, in-equilibrium systems. This chapter has laid the foundation by reviewing historical and theoretical aspects of Brownian motion and the active motion of particles, along with discussing various manipulation strategies such as acoustic and optical techniques. The exploration of these manipulation methods provides the basis for the subsequent chapters including precise particle manipulation and biomedical imaging.



2. LASERS TO MANIPULATE ACTIVE MATTER

The mid-20th century witnessed a revolution in our understanding and manipulation of light, a revolution sparked by the invention of MASER. This device is an acronym for Microwave Amplification by Stimulated Emission of Radiation. The MASER was an exceptionally low-noise microwave amplifier, but it was its operational principle that truly set it apart. It harnessed the subtle interaction between matter and electromagnetic radiation. This interaction is governed by the field of quantum mechanics. It was a departure from the conventional and classical formulas into a future where quantum mechanics was used to harness practical and device applications. The invention of MASER suggested another possibility: could this revolutionary technique, the "stimulated emission," go beyond the microwave domain and into the visible light range?

In 1958, Townes and Arthur L. Schawlow took up this very challenge. In a collaborative work, they meticulously outlined the physical prerequisites for achieving what they named Light Amplification by Stimulated Emission of Radiation (or LASER). Their work was more than just theoretical speculation; it was a roadmap, a blueprint for a device that would fundamentally alter our understanding of traditional light sources at the time. Just two years later, in July of 1960, Theodore H. Maiman revealed the first operational optical MASER, or as it would come to be known, the LASER. This was a paradigm shift, a giant leap for science that would influence through the decades. This achievement was a significant moment in scientific history, so much so that it won the Nobel Prize in 1964. Since then, lasers are inseparable parts of many major fields like microscopy imaging, astronomical imaging, material processing, etc.

The laser is a representation of quantum mechanics in action. It is a device that produces light by orchestrating the complex interactions between atoms and elec-

tromagnetic radiation. To understand the LASER, we must first understand some basic physical concepts leading to the discovery, such as blackbody radiation, discrete energy levels, population inversion, stimulated emission, and Einstein A and B coefficients. Blackbody radiation provides the framework for describing the relationship between an object's temperature and the spectrum of electromagnetic radiation it emits. This foundational knowledge is not only crucial for understanding thermal light sources but is also indispensable for any treatment of the interaction between electromagnetic radiation and matter on a fundamental level. In the sections that follow, we will examine those discrete energy levels in detail and, critically, the creation of a population inversion, the non-equilibrium condition in which more atoms reside in excited states than in the ground state—that enables stimulated emission to dominate. Finally, we turn to stimulated emission itself, facilitated through Einstein's A and B coefficients, mathematical constructs that quantify the probabilities of absorption, spontaneous emission, and, above all, stimulated emission. These coefficients, derived by Einstein in his groundbreaking work on the quantum theory of radiation, are the key to unlocking the secrets of the laser.

2.1 Thermal Radiation and the Quantum Hypothesis

Our exploration begins, as many scientific inquiries do, by examining a seemingly simple phenomenon: the glow of a heated object. As an object's temperature rises, it transitions from emitting invisible infrared radiation to glowing red, then orange, yellow, and eventually white-hot. This relationship between temperature and the color of emitted light has intrigued scientists for centuries and has even helped to estimate the temperature of stars. However, it was the quantitative study of this phenomenon, known as blackbody radiation, that provided some of the first compelling evidence for the quantum nature of light.

2.1.1 Blackbody Radiation

In the late 19th century, physicists, led by Gustav Kirchhoff, introduced the concept of an idealized object known as a "blackbody." A blackbody is defined as a perfect absorber of electromagnetic radiation; it absorbs all incident radiation, regardless of wavelength or angle. While a perfect blackbody is a theoretical construct, it serves as a remarkably useful approximation for many real-world objects, such as the filament of an incandescent lightbulb or the surface of a star. In 1879, Josef Stefan found experimentally that the total power per unit surface area emitted by a heated body is proportional to T^4 : $P = \epsilon\sigma T^4$, where $\sigma = 5.670 \times 10^{-8} \text{ W/m}^2 \text{ K}^4$ is the Stefan-Boltzmann constant. Ludwig Boltzmann theoretically derived this relationship in 1884 using thermodynamic arguments. Kirchhoff postulated the existence of a distribution function, $I_\lambda(T)$, that would provide the spectral flux density within a thermal enclosure. He reasoned that the total energy absorbed by the chamber's walls must precisely balance the total energy emitted to maintain thermal equilibrium at temperature T . Despite the success of the Stefan-Boltzmann Law, the exact form of $I_\lambda(T)$ remained elusive. Classical physics predicted that the energy density should increase indefinitely as the wavelength decreased, leading to the ultraviolet catastrophe. This prediction contradicted experimental observations, which showed that the energy density reached a peak and then decreased at shorter wavelengths. The resolution came in 1900 when Max Planck made the radical assumption that energy was quantized in discrete packets: $E = hf$, where h is Planck's constant ($6.626 \times 10^{-34} \text{ J.s}$). This revolutionary idea marked the birth of quantum theory and led to Planck's Law:

$$I_\lambda(T) = \frac{2\pi hc^2}{\lambda^5} \frac{1}{e^{hc/\lambda k_B T} - 1} \quad (2.1)$$

Planck's work demonstrated energy quantization, but the distribution of particles among energy levels is described by the Boltzmann distribution. For a system in thermal equilibrium at temperature T , the probability of finding a particle in energy

state E_i is:

$$P(E_i) = \frac{e^{-E_i/k_B T}}{Z} \quad (2.2)$$

where $Z = \sum_i e^{-E_i/k_B T}$ is the partition function. The Boltzmann distribution reveals that lower energy states are more likely to be occupied, with the probability decreasing exponentially with increasing energy. As temperature increases, the distribution broadens, and higher energy states become more populated. This statistical framework is essential for understanding how atoms populate different energy levels in laser systems.

2.1.2 Einstein A and B Coefficients

Building upon the foundation laid by Planck's Law and the Boltzmann distribution, which successfully described the characteristics of blackbody radiation, Einstein, in 1916, introduced his A and B coefficients, providing crucial insight into the fundamental processes of light absorption and emission by atoms.

Einstein considered a collection of atoms interacting with electromagnetic radiation. He proposed three fundamental processes:

- **Absorption:** An atom in the ground state that has an energy of E_1 can absorb a photon and transition to a higher energy state E_2 , where the photon energy is exactly equal to $hf = E_2 - E_1$. The absorption rate is proportional to the number of atoms in the ground state N_1 and the energy density of the radiation at the resonant frequency $\rho(f)$. Einstein denoted the proportionality constant as B_{12} , known as the Einstein B coefficient for absorption (Figure 2.1(a)).
- **Spontaneous Emission:** An atom in an excited state E_2 can spontaneously decay to the ground state E_1 , emitting a photon of energy $hf = E_2 - E_1$. The rate of spontaneous emission is proportional to the number of atoms in the excited state N_2 . Einstein denoted the proportionality constant as A_{21} , known as the Einstein

A coefficient for spontaneous emission (Figure 2.1(b)).

- **Stimulated Emission:** An atom in an excited state E_2 can be stimulated to emit a photon by the presence of radiation at the resonant frequency. This emitted photon has the same frequency, phase, and direction as the stimulating radiation. The rate of stimulated emission is proportional to the number of atoms in the excited state N_2 and the energy density of the radiation at the resonant frequency $\rho(f)$. Einstein denoted the proportionality constant as B_{21} , known as the Einstein B coefficient for stimulated emission (Figure 2.1(c)).

Einstein showed that in order to maintain thermal equilibrium and reproduce Planck's Law, the following relationships must hold between the coefficients:

$$B_{12} = B_{21} \quad (2.3)$$

and

$$\frac{A_{21}}{B_{21}} = \frac{8\pi h f^3}{c^3} \quad (2.4)$$

These relationships reveal profound connections between the processes of absorption, spontaneous emission, and stimulated emission. The equality of B_{12} and B_{21} (Eq. 2.3) indicates that the probability of absorption is equal to the probability of stimulated emission. Eq. 2.4 shows that the ratio of spontaneous emission to stimulated emission is proportional to the cube of the frequency, implying that spontaneous emission dominates at higher frequencies (like visible light), while stimulated emission becomes more significant at lower frequencies (such as microwaves).

The concept of stimulated emission is the cornerstone of laser operation. It is the

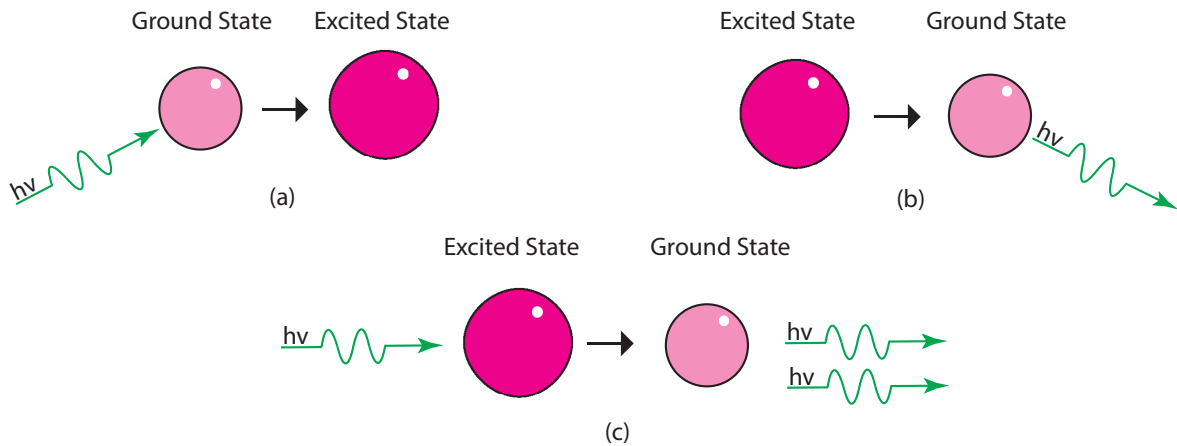


Figure 2.1 Schematic representation of possible transitions in an atom. (a) Absorption, (b) spontaneous emission, and (c) stimulated emission.

process that allows for the amplification of light, leading to the intense, coherent beam characteristic of lasers. In the next section, we will see how these fundamental principles are harnessed to create a population inversion and achieve laser action.

The concept of stimulated emission, as quantified by Einstein's B coefficient, is the foundation of laser operation and provides a pathway for the amplification of light. However, in ordinary circumstances, absorption dominates over stimulated emission because the majority of atoms reside in the ground state. To achieve the coherent, intense beam characteristic of a laser, this natural order must be overturned, creating a situation known as population inversion, see Figure 2.2.

In this non-equilibrium condition, a substantial percentage of atoms are excited to a higher energy level, leaving the ground level relatively unpopulated. This can be visualized as if the Boltzmann distribution were flipped (Figure 2.2), with the higher energy state (E_2 in our two-level model) now being more populated than the ground state (E_1). When a photon with energy matching the transition energy ($h\nu = E_2 - E_1$) encounters this inverted population, it triggers an avalanche of stimulated emission. Each emitted photon is in phase with, has the same polarization, and propagates in the same direction as the stimulating radiation. This cascade of identical photons, all adding constructively to the initial wave, results in the amplification of light. To

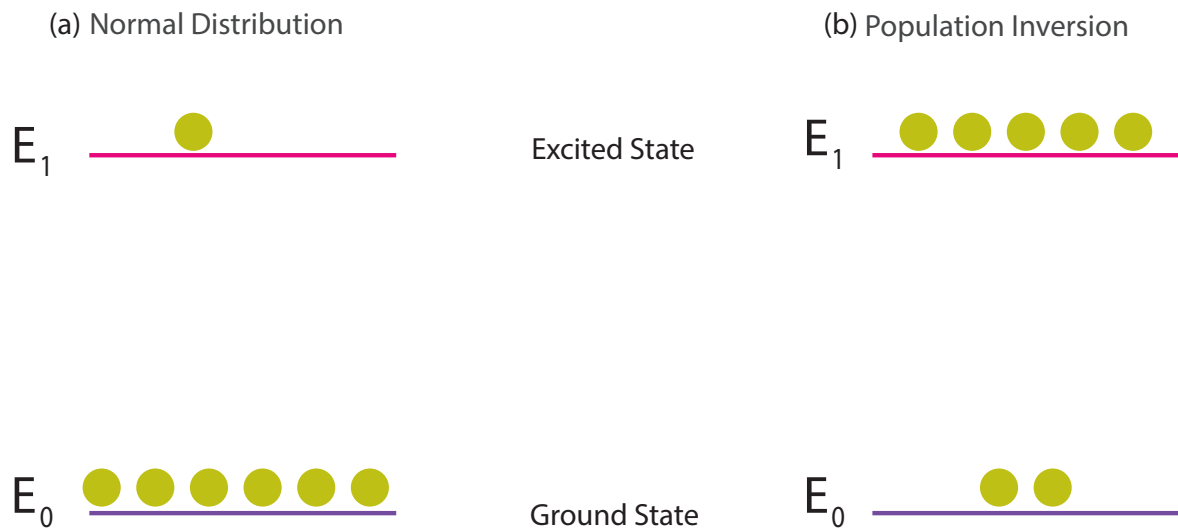


Figure 2.2 Representation of population inversion. (a) In ordinary conditions, most atoms occupy the ground state, and only a small fraction populate higher energy levels. (b) In population inversion, the most atoms are found at higher energy state rather than ground state.

sustain laser operation, energy must be continuously supplied to the system via a process called "pumping" (which can be electrical, chemical, optical) to maintain the population inversion and overcome any loss mechanisms within the system.

To summarize all these abstracts and theorems and to give it some visibility in practice, let's have a look at the first functioning laser device first demonstrated in 1960. In this laser, Maiman used a pale pink synthetic ruby rod (Al_2O_3 doped with approximately 0.05 wt % Cr_2O_3) as its gain medium. Both ends of the cylindrical crystal were polished flat, kept strictly parallel to the optical axis, and coated with silver: one side nearly 100 % reflective, the other partially transmissive to serve as the output. A helical xenon flashtube wrapped around the rod delivered a broadband, millisecond-scale light pulse that optically pumped the chromium ions. Because Cr^{3+} absorbs strongly in the blue-green, ruby's red appearance conveniently lets most pump light be absorbed where it is useful.

After absorption, excited Cr^{3+} ions drop non-radiatively within ~ 100 ns to a pair of closely spaced metastable states. With a lifetime of roughly 3 ms at room temperature, these metastable states store energy long enough for a population inversion

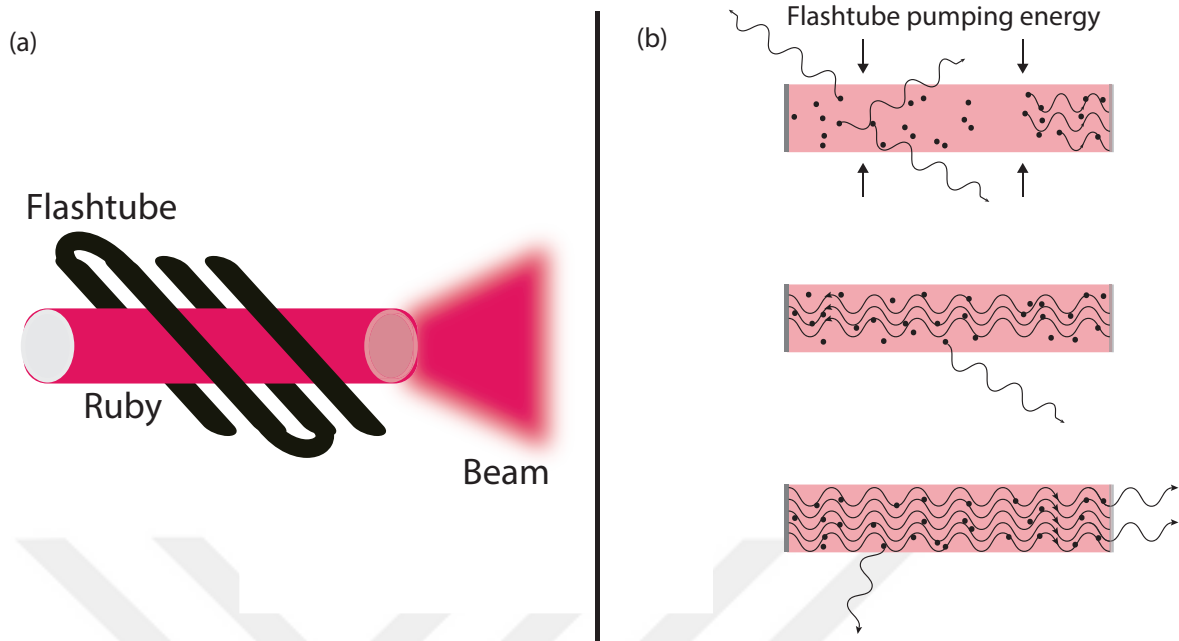


Figure 2.3 Pulsed (Ruby) laser configuration. (a) the Ruby medium and flashtube around it. (b) schematic of laser generation inside Ruby.

to develop relative to the ground state. Hence, the ruby laser is classically categorized as a three-level system: (1) the broad pump bands, (2) the long-lived metastable level, and (3) the ground state. The existence of this metastable state enables the creation of population inversion, which is essential for laser operation. The choice of material and its spectroscopic characterization are also critical in determining whether it is suitable for use as a laser medium.

Once inversion is achieved, the first few spontaneous photons at 694.3 nm stimulate coherent emission from neighboring ions. Each stimulated photon is phase-locked to the incident wave and propagates along the resonator axis; repeated round trips through the mirrored cavity rapidly amplify the light. When the optical gain surpasses losses at the partially reflective mirror, a short, intense burst of red laser radiation emerges. Maiman's original device produced ~ 0.5 ms pulses with a spectral width near 0.01 nm and pulse energies on the order of joules [47].

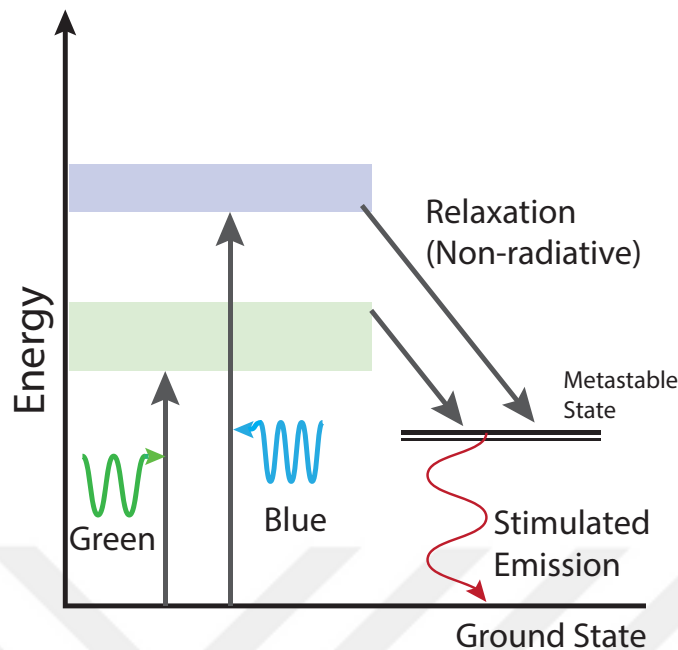


Figure 2.4 Ruby laser energy levels. After absorption of the light produced by flashtube, the Cr^{3+} ions are excited and going to higher energy states. Through a non-radiative relaxation, ions drop to long-lived metastable state. Ions remain here several milliseconds (approximately 3 ms) then they randomly and spontaneously drop down to ground state.

2.2 Lasers

Lasers can be broadly categorized based on their temporal emission profile, which describes how the laser power is distributed over time. In continuous-wave (CW) lasers, the optical output is constant, delivering a steady power level. This mode is advantageous for applications requiring stable emission over extended periods.

In contrast, pulsed lasers emit light in a short time. Because the energy is concentrated in brief time intervals, pulsed lasers can achieve significantly higher peak powers than CW lasers, even when their average powers are similar.

Three key parameters often used to characterize pulsed lasers are:

- **Peak Power:** The maximum instantaneous power during a pulse, typically calculated by dividing the pulse energy by the pulse duration.
- **Pulse Energy:** A measure of one pulse's total emission, which is the only light

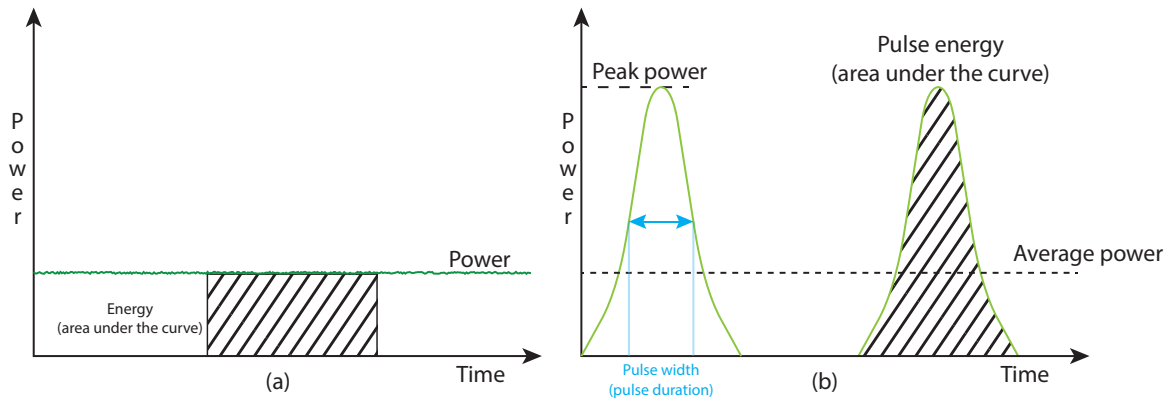


Figure 2.5 Schematic representation of Laser. (a) CW laser system, (b) Pulsed laser system.

emitted by the laser over the entire period.

- **Average Power:** The product of pulse energy and pulse repetition rate.

Pulsed operation is achieved by incorporating additional physical mechanisms. Pulsed lasers are classified according to their pulse durations: nanosecond, picosecond, femtosecond, and even attosecond regimes, each suitable for different applications. Notably, breakthroughs in attosecond pulse generation were recognized with the Nobel Prize in 2023, underscoring the importance of ultrafast laser science.

The focus of this thesis will be on nanosecond pulsed lasers, which strike a balance between high peak power and relatively straightforward operational requirements, making them especially useful for a wide range of practical applications. To generate nanosecond pulses, typically an electro-optic switch is added into the laser cavity. It modulates the Q parameter of the resonator (high loss/low loss), resulting in short pulses of laser output.

Figure 2.5 depicts the difference between power delivered through CW and pulsed system.

Having distinguished CW from pulsed operation on temporal properties, we now

focus on a second fundamental basis of laser classification: the gain medium. Depending on application requirements, several laser configurations have emerged throughout the advancement of laser technology. Below, I highlight three of the most popular laser types—solid-state, gas, and semiconductor lasers—and provide a brief historical overview of each.

2.2.1 Solid-State Lasers

Solid-state lasers employ glass or crystalline rods doped with ions that provide the necessary energy levels for laser action. Output wavelengths typically span from around 170 nm to 3900 nm. The pioneering ruby laser exemplifies this category. Among the most important solid-state lasers are neodymium-doped systems: Nd:Glass and Nd:YAG, both operating around 1060 nm. Nd:YAG lasers can generate continuous power exceeding a kilowatt and find extensive use in surgery, material processing, and frequency doubling. More recent developments include Nd:YLF and Nd:YVO₄ lasers operating around 1064 nm. Ytterbium-doped media (Yb:YAG, Yb:KGW) provide substantial power in the 1020-1050 nm range. Medical applications include Ho:YAG lasers (2100 nm) for gallstone and kidney stone procedures, and Er:YAG lasers (2940 nm) for dentistry. For high-power pulsed systems, multiple lasers operate in tandem, typically with a Q-switched oscillator feeding amplifier stages. Ruby systems delivering gigawatts in nanosecond pulses are commercially available. Notable examples include the Nova laser at Lawrence Livermore (18 kJ in 1 ns) and the National Ignition Facility with 192 beams designed for 500-TW output.

2.2.2 Gas Lasers

Gas lasers represent a versatile group with operational wavelengths from far-infrared to ultraviolet (around 150 nm). Key examples include helium-neon, argon, and molecular systems like CO₂. The argon ion laser emits in violet, blue-green, and green regions (457.9 nm, 488.0 nm, 514.5 nm), offering several watts CW with some

systems achieving 150 W. Compared to He-Ne lasers, argon systems provide greater power and shorter wavelengths but at higher cost. CO₂ lasers, operating at 10.6 μm through vibrational transitions, achieve unusually high efficiencies ($\sim 15\%$) with N₂ and He additions, offering CW power from watts to kilowatts. Nitrogen lasers operate in UV at 337.1 nm, while helium-cadmium systems provide CW UV at 325 nm and blue at 441.6 nm.

2.2.3 Semiconductor Lasers

Invented in 1962, semiconductor (diode) lasers have become pivotal in electro-optics due to their spectral purity, high efficiency (approaching 100%), ruggedness, rapid modulation capability, long lifetimes, and moderate power output (up to 200 mW) from compact packages. They're extensively used in fiber optics, CD/DVD systems, and laser pointers. Early homo-structure lasers (single materials like GaAs) had high thresholds, limiting them to pulsed cryogenic operation. Modern hetero-structure designs enable CW room-temperature operation. Lasing occurs between conduction and valence bands near the p-n junction, where forward current causes electron-hole recombination and photon emission. Modern semiconductor lasers cover wavelengths from ~ 400 nm to 30 μm . GaAs/GaAlAs systems operate at 750-900 nm, while GaInAsP/InP lasers (1.2-1.6 μm) are optimized for fiber optics. GaN diode lasers (405 nm) enable Blu-ray technology, and quantum cascade lasers provide mid- to far-IR radiation.

This survey also acknowledges the existence of other laser types such as free electron lasers (operating from 600 nm to 3 mm), X-ray lasers, doped glass fiber lasers, and color center lasers. Some lasers are designed for very specific properties, like generating extremely short pulses or possessing extraordinary frequency stability, which are crucial for fields like high-resolution spectroscopy and emerging research areas such as the interferometric detection of gravity waves. Such sources are out of the scope of this thesis.

2.3 Laser-Matter Interaction

Lasers provide a precise and controllable means of delivering energy to a material, leading to various transformations at microscopic and nanoscopic scales. When laser radiation interacts with a material, its energy can be absorbed, transmitted, or reflected, producing different physical, thermal, and structural modifications.

The field of laser-matter interaction is vast, and a comprehensive description is beyond the scope of this thesis. Consequently, the following discussion is narrowed to the specific context of this work: low-fluence interactions (The maximum fluence used in the published work is 1.75 J/cm^2) with gold. Given that the research investigates thin metal coatings on particles, this section is structured to first introduce the primary optical phenomena: surface reflection and light absorption, as described by the Beer-Lambert law. Following this, the focus shifts to the thermal processes, as metals like gold, with their free electrons, are particularly susceptible to photothermal activation in this regime.

2.3.1 Light Propagation and Absorption in Materials

When the light hits the surface of a material, some of the light reflects because there is a change in the refractive index, and the rest goes into the material. The amount of light that is reflected depends on polarization, the angle at which the light arrives (angle of incidence, θ_i), and also the refractive indices of both the atmosphere (n_1) and the material (n_2). We can calculate how much reflection happens for the two polarization types (s-polarized and p-polarized) by using the Fresnel equations [48].

$$R_s = \left[\frac{n_1 \cos(\theta_i) - n_2 \cos(\theta_t)}{n_1 \cos(\theta_i) + n_2 \cos(\theta_t)} \right]^2, \quad (2.5)$$

$$R_p = \left[\frac{n_1 \cos(\theta_t) - n_2 \cos(\theta_i)}{n_1 \cos(\theta_t) + n_2 \cos(\theta_i)} \right]^2. \quad (2.6)$$

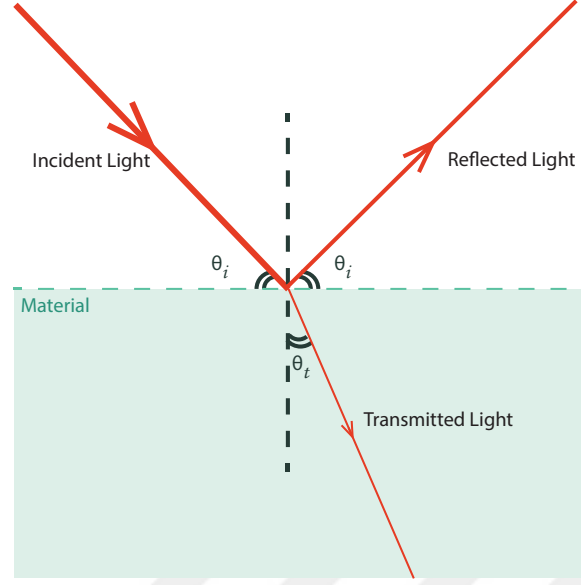


Figure 2.6 Schematic of when an incident light hits the surface of a material.

If the incident light is perpendicular to the surface of the material, the above equations can be written as

$$R = R_s = R_p = \left(\frac{n_1 - n_2}{n_1 + n_2} \right)^2. \quad (2.7)$$

The Figure 2.6 depicts an incident, reflected, and transmitted light, and the angles they form.

When the light enters the material, the absorption makes its intensity decrease as it goes deeper. How quickly this intensity decreases depends on something called the absorption coefficient (α). Typically, this α changes with the wavelength and temperature. But if α is constant, the intensity $I(z)$ will reduce exponentially with increasing depth z , as described by the Beer-Lambert law,

$$I(z) = I_0 e^{-\alpha z} \quad (2.8)$$

where I_0 is the initial intensity after accounting for reflection losses. The optical penetration depth, defined as $\delta = 1/\alpha$, characterizes the depth at which light intensity drops to $1/e$ of its initial value. For metals, absorption is highly localized within a few

nanometers, whereas semiconductors and dielectrics exhibit varying absorption depths based on their bandgap and defect states. In the following sections, the Beer-Lambert law will be explained thoroughly.

2.3.2 Energy Absorption Mechanisms

The absorption coefficient (α) determines how the intensity of light decreases when it enters a material. This coefficient can be calculated from the material's dielectric function and conductivity. However, the exact way absorption happens depends strongly on what kind of material is involved.

For insulators and semiconductors, the main way laser light is absorbed is through resonant excitations. This usually means electrons jump from the valence band to the conduction band (called interband transitions), or move within the same band (intersubband transitions). After electrons absorb this energy, they transfer it to the material's atoms, causing vibrations called phonons. If the photon energy is lower than the bandgap (the minimum energy needed for electron transitions), the material usually will not absorb the photons. This means photons with energy below ultraviolet in insulators or below visible and infrared in semiconductors are not easily absorbed unless special states or multiphoton processes are available [49].

For metals, the main absorption mechanism is due to free electrons, often through a process called inverse bremsstrahlung, where free electrons absorb photon energy. After absorbing energy, electrons collide with atoms, transferring energy and creating lattice vibrations (phonons) [50]. A critical parameter for understanding absorption in metals is the plasma frequency (ω_p), which depends on the electron density (N_e). Below this plasma frequency, metals strongly reflect and absorb because electrons quickly respond and shield the material [51]. But above this frequency, electrons cannot respond quickly enough, and the metal's reflectivity and absorption significantly decrease. Additionally, electrons or atoms associated with defects, impurities, or surface states can also be excited, causing other forms of energy absorption (e.g., plasmons,

polaritons) [52].

After energy is absorbed, electrons eventually transfer their energy to phonons (atoms vibrating). How quickly this happens varies greatly between materials:

Metals: Thermalization (energy transfer) is very fast, usually about 10^{-12} to 10^{-10} seconds [49]. **Non-metals:** This transfer is slower and can take up to 10^{-6} seconds. Special states (like defects or quantum confinement) can slow it down even more [49].

If the laser excitation happens slowly compared to thermalization, the absorbed energy directly turns into heat. This kind of interaction is called photothermal (or pyrolytic). Typical examples include metals and semiconductors irradiated by lasers with longer pulses (nanoseconds or more).

If the laser excitation happens quickly compared to thermalization, energy can accumulate in the excited states and directly break chemical bonds without heating the material significantly. This kind of interaction is called photochemical (or photolytic). Examples include polymer irradiation with short-wavelength lasers or metals and semiconductors processed with very short laser pulses (femtosecond pulses).

In many real cases, both thermal and non-thermal mechanisms happen simultaneously, and these combined effects are called photophysical interactions.

2.3.3 Thermal Effects and Heat Diffusion

The calculation of temperature distributions in gases, liquids, and solids resulting from the absorption of laser radiation is based on the heat equation. In the most comprehensive scenario, the temperature, denoted as $T = T(x, t)$, is dependent on both spatial coordinates (x) and time (t). When laser parameters are kept constant, the temperature distribution is influenced by the optical absorption within the illuminated area, the transfer of heat away from this area, and potentially by the energy changes associated with processes like crystallization, melting, vaporization, or chemi-

cal reactions (whether exothermal or endothermal). If heat transfer through convection and thermal radiation is negligible, the heat equation can be expressed in a coordinate system that remains stationary relative to the laser beam.

$$\rho(T)c_p(T)\frac{\partial T(\vec{r},t)}{\partial t} - \nabla \cdot (k(T)\nabla T(\vec{r},t)) = Q(\vec{r},t). \quad (2.9)$$

Where $\rho(T)$ is the material density, $c_p(T)$ is the specific heat capacity, $k(T)$ is the thermal conductivity, v_s is the substrate relative to the heat source, and $Q(\vec{r},t)$ is volumetric heating rate. If all the temperature dependencies of the substrate is ignored, the heat equation becomes linear.

The first term in Eq. 2.9, $\rho(T)c_p(T)\frac{\partial T(\vec{r},t)}{\partial t}$, shows the rate of thermal energy stored per unit volume and describes the ability of the material to store heat. Second term, $\nabla \cdot (k(T)\nabla T(\vec{r},t))$, represents the net rate of heat transfer by conduction, how heat spreads through a material from hotter region to a cooler region.

$Q(\vec{r},t)$ depends on the laser and material paroperties. For instance, in a pulsed laser with pulse duration τ , and with Gaussian spatial distribution with beam waist ω_0 , if the absorption coefficient of the material is α , $Q(\vec{r},t)$ can be written as:

$$Q(\vec{r},t) = A \exp\left(-\frac{2r^2}{\omega_0^2}\right) \exp\left(-\frac{t^2}{2\tau^2}\right) \exp(-\alpha z), \quad (2.10)$$

where A is a constant and z is the axial distance into the material measured from the surface ($z=0$), and r is radial distance from the center of the beam.

The behavior of light propagation in the medium is governed by its dielectric permittivity and magnetic permeability, expressed as complex quantities $\epsilon = \epsilon' + i\epsilon''$ and $\mu = \mu' + i\mu''$ respectively.

For most practical purposes, it is assumed that $\mu' = 1$ and $\mu'' = 0$. This assumption means the material is treated as non-magnetic and does not absorb any energy from the magnetic component of the light. Under this approximation, the

complex refractive index becomes:

$$\tilde{n} = \sqrt{\epsilon} = n + i\kappa_a, \quad (2.11)$$

which n is refractive index and κ_a is absorption index. In the case of weak absorption ($\epsilon' \gg \epsilon''$), we will have $n \approx \sqrt{\epsilon'}$ and $\kappa_a = \frac{\epsilon''}{2\sqrt{\epsilon'}}$. Assuming the laser beam propagates in the z direction, the attenuation of the intensity leads to the Beer-Lambert law:

$$\frac{dI(z)}{dz} = -\alpha I(z) \quad (2.12)$$

with the absorption coefficient α given by:

$$\alpha = \frac{4\pi\kappa_a}{\lambda} = \frac{2\omega\kappa_a}{c} \quad (2.13)$$

Here, λ denotes the wavelength in vacuum. The quantity α characterizes how strongly light is absorbed as it penetrates through the material, and its reciprocal defines the optical penetration depth:

$$l_\alpha = \alpha^{-1} \quad (2.14)$$

In cases where light attenuation is due to both absorption and scattering, the effective attenuation is described by the extinction coefficient:

$$\beta = \alpha + \alpha_s \quad (2.15)$$

where α_s is the scattering coefficient.

Given the nature of the problem at hand, choosing an appropriate coordinate system simplifies the calculations significantly. Depending on the symmetry and characteristics of each system, certain coordinate systems can be more convenient. In the case of the problem addressed in my thesis, the cylindrical coordinate system proved to be the most suitable, as it greatly simplified the mathematical formulation. In cylindrical coordinates, the heat equation takes the following form:

$$\frac{1}{r} \frac{\partial}{\partial r} \left(kr \frac{\partial T}{\partial r} \right) + \frac{1}{r^2} \frac{\partial T}{\partial \phi} \left(k \frac{\partial T}{\partial \phi} \right) + \frac{\partial}{\partial z} \left(k \frac{\partial T}{\partial z} \right) + Q(\vec{r}, t) = \rho c \frac{\partial T}{\partial t}, \quad (2.16)$$

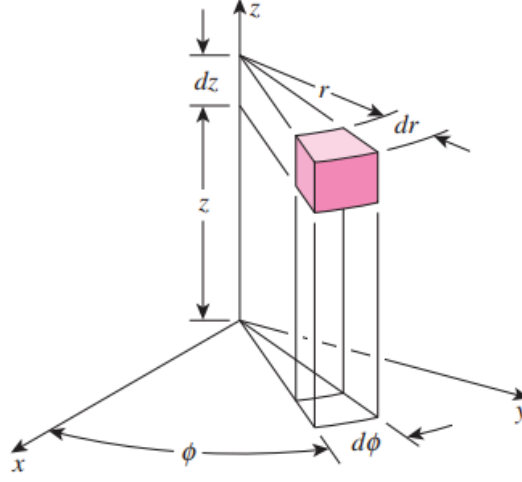


Figure 2.7 A differential volume element in cylindrical coordinates.

where r is the radius, z is the length of the cylinder and ϕ is the angular coordinate [53]. The Figure 2.7 shows the differential element in cylindrical coordinates.

To solve a differential equation, in addition to initial conditions, appropriate boundary conditions are also required. These boundary conditions are

- Specified temperature boundary condition: The temperature of boundaries are set to specific amount. Like $T(\vec{r}_1, t) = T_1$ and $T(\vec{r}_2, t) = T_2$.
- Specified heat flux boundary condition: The rate of heat transfer per unit area is set to a specific value on the surface. For a plane wall, this is expressed as $-k \frac{dT(\vec{r}_0, t)}{dx} = Q(\vec{r}_0, t)$ and $-k \frac{dT(\vec{r}_1, t)}{dx} = Q(\vec{r}_1, t)$.
- Insulated boundary condition: A well-insulated surface is modeled with a specified heat flux of zero. This means the temperature gradient normal to the surface is zero, like $\frac{dT(\vec{r}_0, t)}{dx} = 0$.
- Thermal symmetry: At a center plane of symmetry, there is no heat flow, which is mathematically expressed like an insulated boundary. For a plane wall of thickness L , the condition is $\frac{dT(\vec{r}/2, t)}{dx} = 0$.
- Convection boundary condition: Heat conducted to the surface of a body is equal to the heat convected from that surface to the surrounding fluid. For a surface

at $x=0$, this is written as $-k \frac{dT(\vec{r}_0, t)}{dx} = h[T - T(r_0, t)]$, which h is convection heat transfer coefficient.

- Radiation boundary condition: Heat conducted to a surface is equal to the heat exchanged by radiation between that surface and its surroundings. For a surface at $x=0$, this is expressed as $-k \frac{dT(\vec{r}_0, t)}{dx} = \epsilon \sigma [T_{Surr}^4 - T(r_0, t)^4]$ where ϵ is emissivity of the surface and σ is Stefan-Boltzmann constant.

2.3.4 Material Responses to Laser Irradiation

The response of a material to laser irradiation depends on the specific material properties and laser parameters. When the laser excitation rate is slow compared to the thermalization time, the process is termed photothermal, where absorbed energy is converted into heat. The heating rates can reach up to 10^9 K/s for nanosecond pulses and even higher for femtosecond lasers, leading to significant material modifications. The thermal response is governed by the heat equation, determining temperature gradients, maximum temperatures, and cooling rates.

2.3.5 Thermally Activated Processes

For fluences below the melting threshold, laser heating can trigger temperature-dependent processes such as diffusion enhancement, impurity doping, and phase transformations. Rapid laser-induced heating can lead to self-quenching, trapping materials in non-equilibrium structures. Thermal stresses generated due to large temperature gradients can induce mechanical changes like work hardening [54], cracking [55], and the excitation of acoustic waves [56].

2.3.6 Surface Melting

When the laser fluence exceeds the melting threshold, transient molten layers form on the surface, enhancing atomic mobility and material homogenization. Rapid cooling rates, sometimes exceeding several m/s [57, 58], can trap defects and create metastable phases. Convective flows, influenced by temperature gradients ($10^2 - 10^4 \text{ K/mm}$) [58], contribute to material redistribution through the Marangoni effect [59], where liquid moves from hotter to cooler regions due to surface tension variations. These flows result in various morphological changes such as rimmed indentations, crater formations, and nanostructures [60, 61].

2.3.7 Ablation

Laser ablation is a process where material is removed from a surface through the direct absorption of laser energy. This removal only begins once the laser's energy density, or fluence, surpasses a specific threshold. This threshold varies depending on the material: for metals, it is typically between 1 and 10 J/cm², for inorganic insulators it's 0.5 to 2 J/cm², and for organic materials, it is between 0.1 and 1 J/cm² [48]. Above this threshold, the volume of material removed per pulse generally increases logarithmically with the applied fluence, which is related to how the material absorbs light exponentially with depth.

The specific method of material removal depends on the fluence level. At lower fluences, photothermal mechanisms like evaporation and sublimation are dominant. As the fluence increases, the process can intensify to include normal boiling and even explosive boiling, where the material is heated so rapidly that it approaches its thermodynamic critical temperature. In situations where the laser excitation happens faster than the material can thermalize, such as with ultrashort pulses, non-thermal photochemical ablation can occur. This may involve direct ionization and the formation of dense electron-hole plasmas, which can lead to phenomena like Coulomb explosions where the lattice disintegrates due to electronic repulsion [62].

In all cases, the process ejects a highly directed plume of material from the irradiated area. This vapor plume can interact with the incoming laser light, especially with pulses longer than a picosecond, by absorbing and scattering it, altering the actual energy reaching the material's surface. The duration of the laser pulse significantly affects the ablation dynamics. Shorter pulses, in the picosecond and femtosecond range, deposit energy more rapidly, leading to a faster ejection of material. Because the excited material is removed before it can transfer significant heat to the surrounding area, the ablation is more precise and confined, resulting in a much smaller heat-affected zone (HAZ) [63]. This precision is particularly noticeable in metals, which have high thermal diffusivity and tend to develop large molten regions and HAZs when processed with longer, nanosecond pulses.

Ultimately, the material's response to laser irradiation is often a complex interplay of ablation, surface melting, and other thermally activated processes. These combined effects can produce intricate, multiscale modifications to the surface's texture, morphology, and chemistry, which are harnessed in a wide range of laser processing applications.

3. PHOTOACOUSTICS

Having discussed lasers and their fundamental interactions with materials, this chapter now introduces the photoacoustic phenomenon. Consistent with the structure employed previously, a historical perspective highlighting key events and foundational milestones will first be presented to provide context and depth for subsequent discussions.

After the invention of the telephone in 1876, Alexander Graham Bell focused on a brave and ingenious idea. The idea was to transmit speech using light rather than wires [64]. The photosensitivity of Selenium was discovered in 1873 [65], and in 1878, Bell began experiments with Selenium to turn his idea into reality. Although Bell credited A. C. Brown of London with the first demonstration of reproducing speech using selenium and a battery-operated telephone circuit, Bell and his assistant, Charles Sumner Tainter accomplished the first well-documented transmission of voice via light. In June 1880, they successfully transmitted wireless voice messages over a distance of approximately 213 meters [66, 67].

On August 27, 1880, Bell presented his invention, the Photophone, to the American Association for the Advancement of Science in Boston [66]. The photophone functioned by modulating light intensity through a silvered glass disk that vibrated in response to sound waves. Sunlight was focused onto this mirror, and the fluctuations in reflected light were collected by a distant receiver, which consisted of a parabolic mirror focusing the light onto a selenium cell. The selenium cell, integrated into a telephone circuit, converted the modulated light intensity into a modulated electrical current, thereby reproducing sound at the receiving end [66, 67]. This innovation marked the first practical use of wireless telephony and was a pioneering optical communication system.

Beyond wireless speech transmission, Bell's research led to another important

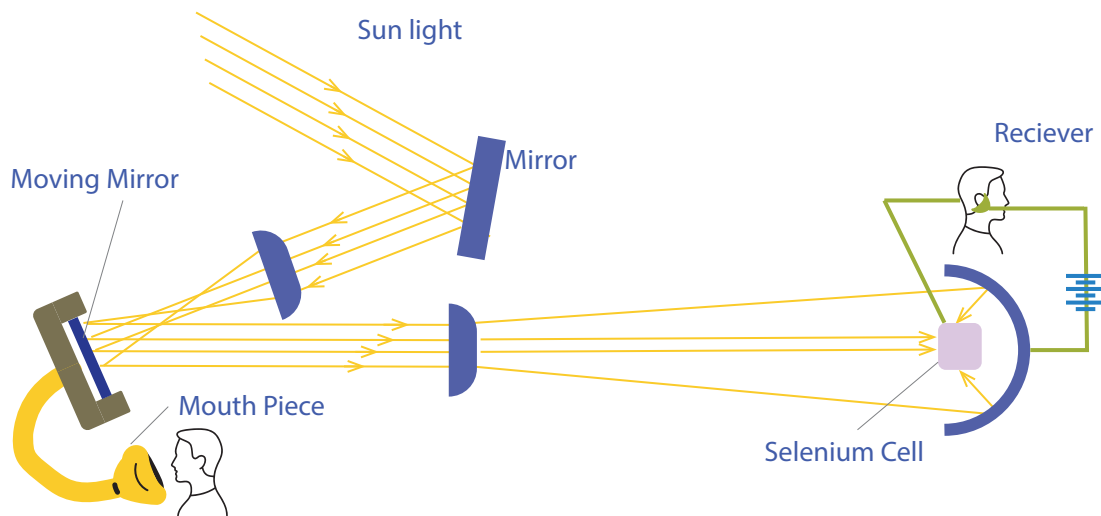


Figure 3.1 Schematic of Bell's wireless communication.

discovery, the photoacoustic effect. He found that when various solid substances were exposed to a rapidly interrupted beam of light, they emitted acoustic energy corresponding to the modulation frequency of the light [66]. In a letter to his father on February 26, 1880, Bell expressed his excitement, stating, "I have heard articulate speech by sunlight! I have heard a ray of the sun laugh and cough and sing!" [64]. This effect was further investigated and formally introduced in a paper Bell presented to the National Academy of Arts and Sciences on April 21, 1881 [34]. In this paper, he envisioned an alternative version of the photophone that used a lamp-black receiver, directly converting light modulations into sound. His experiments demonstrated speech transmission over distances up to 40 meters, a remarkable feat at the time [67].

The discovery of light-induced sound generation sparked significant interest among scientists of the late 19th century. Lord Rayleigh proposed in 1881 that the sounds were produced by vibrations due to unequal heating of illuminated surfaces, a hypothesis that Bell strongly supported [68, 69]. Other scientists, including Mercadier [70] and Preece [71], explored the effect in different materials and suggested that the phenomenon resulted from the expansion and contraction of air in contact with the heated surface. Independently, Röntgen [72] and Tyndall [73] expanded these studies to gases and vapors, demonstrating that sound production was not restricted to solid bodies. Tyndall even proposed using this method for detecting small amounts of

flammable gases in mines [73].

Bell realized that this phenomenon could be used for spectroscopic analysis, leading to his development of the spectrophone [68]. This device allowed scientists to analyze the absorption spectra of different substances by measuring the photoacoustic response when light passed through a sample. Bell noted that the sounds produced by various materials depended on the specific wavelengths they absorbed, laying the foundation for modern photoacoustic spectroscopy [66].

Although Bell initially referred to his discovery as "photophonic phenomena" or the "production of sound by radiant energy," Mercadier introduced the term "radiophony" in 1881 [70], which quickly gained acceptance in the scientific community as a general term describing sound production by radiant energy of any form, not just visible light [74].

Despite the excitement surrounding these discoveries, interest in radiophony diminished over time, mainly because experiments relied on human hearing for signal detection, making quantification difficult. The Bell Telephone Company, which had acquired Bell's photophone invention, did not pursue its development for practical applications. During World War I, military organizations- including the German Navy, the British Admiralty, and U.S. research institutions- attempted to use the photophone for secure optical communications, achieving transmission distances between 8 and 11 kilometers. However, these systems remained inferior to Marconi's radio transmissions, which had already demonstrated superior range by the early 20th century [75, 76]. As a result, the photophone was largely forgotten as a serious technological contender.

Nevertheless, Bell's vision of light-based communication indicated the modern era of optical fiber telecommunications. Today, almost all high-bandwidth voice and video data transmission is conducted using light signals in fiber-optic networks rather than copper-based electrical communication. This advancement has revolutionized global communication. In 2009, Bell Labs researchers in France set a new record for optical data transmission, achieving a staggering 100 petabit-per-second-kilometer

capacity using 155 lasers, each transmitting 100 gigabits per second at different frequencies [77]. Bell's early work with the photophone and radiophony, though initially underappreciated, ultimately contributed to the foundation of today's optical communication technologies.

Photoacoustic hibernated until 50 years later, when Veingerov wanted to detect small concentrations of gases. Veingerov was a researcher at the State Optical Institute in Leningrad, and had studied the works of Röntgen and Tyndall, and paid attention to Tyndall's earlier prediction that the method could be used for gas detection. In 1938, he published a paper in the Proceedings of the USSR Academy of Sciences (Doklady Akademii Nauk SSSR), titled "A method of gas analysis based on the optico-acoustic Tyndall-Röntgen effect." With this, Veingerov is credited for reviving interest in the photoacoustic effect. He used advanced equipment for the time, including charged capacitive microphone diaphragms and a Nernst glower as a powerful infrared source. This setup allowed him to detect CO₂ concentrations in N₂ down to about 0.2% by volume [78].

Following Veingerov's revival of photoacoustic gas detection, further advancements quickly emerged. In 1939, Pfund [79] introduced a similar system at Johns Hopkins Hospital for detecting CO and CO₂ gases, where instead of measuring pressure variations, a thermopile shielded from direct radiation was used to detect temperature changes induced by gas absorption, thus eliminating the need for acoustic noise shielding. Around the same time, Luft developed a commercial infrared gas analyzer called URAS (Ultrarotabsorptionsschreiber), which was widely applied in the chemical industry as early as 1938 [80]. The 1943 version of the analyzer [81] utilized a double-cell design, one with reference gas and the other with the target species, connected to a shared acoustic chamber equipped with a membrane capacitor microphone. Periodically interrupted infrared radiation, created by a rotating disk with two sectors, generated differential acoustic signals that enabled sensitive detection. A theoretical basis for the optico-acoustic effect was established, and its applications extended beyond gas detection to include studies on vibrational relaxation rates and molecular energy transfer in gases [82, 83, 84, 85, 86, 87]. These instruments were often referred

to as "spectrophones," in homage to Bell's early absorption spectrometer based on the effect [88, 89]. Interest in the technique eventually waned as optico-acoustic gas analysis was superseded by more sensitive and versatile methods like gas chromatography and infrared spectrophotometry. However, the invention of the laser in 1960 revived interest once again. Lasers brought significant advantages, such as high power, spectral purity, stability, and reproducibility, making them ideal for photoacoustic detection. Kerr and Atwood were the first to develop laser-illuminated absorptivity spectrophones in 1968, using a pulsed ruby laser and a chopped CW CO₂ laser with acoustic detection by a capacitance microphone [90]. This was further advanced by Kreuzer in 1971, who used chopped He-Ne laser excitation and an electret microphone, demonstrating ultra-trace gas detection at parts-per-billion levels [91]. This work also arguably marked the first use of the term "optoacoustic" in the context of gas analysis.

Following this revival of photoacoustic technology in the 1960s, the technique underwent significant evolution over subsequent decades. The combination of improved laser technology, advanced detection methods, and sophisticated signal processing algorithms gradually transformed photoacoustic sensing from a specialized gas detection method into a powerful biomedical imaging modality. Researchers recognized that the fundamental principles of photoacoustic generation, where absorbed light energy converts to acoustic signals, could be leveraged to visualize biological tissues with unique contrast mechanisms. This transformation represented a remarkable expansion of Bell's original discovery, applying the photoacoustic effect to create non-invasive images of living systems with capabilities that complemented existing biomedical imaging technologies. The journey from gas analysis to clinical imaging illustrates how this century-old phenomenon found new purpose in addressing modern healthcare challenges, particularly in areas where conventional imaging modalities faced limitations [92, 93, 94].

The development of photoacoustic technology, particularly under the thermoelectric regime, represents a pivotal chapter in biomedical imaging. In this regime, short optical pulses are absorbed by biological tissues, and the resulting heat is converted almost instantaneously into vibrational energy, acoustic pressure waves, without signif-

icant thermal diffusion. This mechanism, highly efficient and largely non-dissipative, offers distinct advantages over the traditional thermal wave propagation dominant in lower frequency regimes of photoacoustics [95].

The first step into the biomedical exploration of this phenomenon came in 1964, when Amar et al. conducted groundbreaking experiments using a ruby laser on live rabbit eyes. They detected elastic ultrasonic waves, induced by laser pulses, through the occipital bone. These pulses, although modest in energy (about 50 mJ, 1 μ s duration), successfully propagated from the retina through the skull and were captured by a barium titanate ultrasound detector. The findings, supported by oscillographic evidence, confirmed that the waves were elastic in nature, not shock waves, and maintained a consistent frequency of around 40 kHz [96]. Interestingly, signal strength diminished significantly when the laser struck less optically transparent tissues, such as the iris or sclera, and was absent when directed to other facial structures like the nose.

Amar’s team extended their studies to ex-vivo human eye samples and even theorized, albeit speculatively, that coherent laser-like processes in the retina might underlie human vision itself [97]. While this idea didn’t gain traction, it underscored early curiosity about photoacoustic mechanisms in sensory systems.

As the scientific community’s interest deepened, subsequent investigations through the 1970s and 1980s shifted focus toward potential retinal damage from laser pulses. Confirmatory experiments, employing nanosecond-duration pulses and advanced detection methods like piezoelectric sensors and schlieren visualization, validated that laser absorption did indeed induce ultrasonic pressure waves-offering both diagnostic potential and caution for clinical applications [98]. Researchers such as Rosencwaig recognized that photoacoustics provided a unique advantage in studying highly scattering biological samples. The traditional Bell method, relying on intensity-modulated light, was largely insensitive to scattered radiation. By contrast, photoacoustic techniques opened new doors, enabling analysis of drug absorption in skin or the optical characteristics of cataractous lenses [99, 100, 101]. These studies showed distinct absorption

differences linked to tryptophan and tyrosine residues, proteins implicated in cataract formation [100]. The field made a major leap toward imaging in 1982, when Olsen captured the first 2D thermoacoustic projection images using microwave pulses and a detector array. This was soon followed by improved imaging of a human hand model in 1983. These crude but promising results demonstrated the potential of thermoacoustic imaging for structural visualization [102].

Light-based methods also progressed rapidly. Researchers in Hiroshima developed a laser photoacoustic microscope to analyze tissue microstructure, while Cross et al. investigated the acoustic effects of UV and visible laser radiation on human aortic tissue. These studies, aimed at supporting laser angioplasty, identified two distinct acoustic regimes: a sub-threshold thermoelastic response and a higher-energy regime characterized by material ablation and recoil momentum. Through careful analysis of acoustic signal profiles, researchers could infer absorption coefficients and even differentiate between diseased and healthy vascular tissue [103].

The first true in vivo pulsed photoacoustic imaging occurred in 1993, when Chen et al. created a compact probe that could capture photoacoustic A-scans from a human finger. Their setup (a piezoelectric detector with a central optical fiber connected to a nanosecond, pulsed Nd laser) enabled backward mode imaging, detecting reflections from structures like bone and fingernail layers. These scans mirrored the results of conventional ultrasound, marking a breakthrough in non-invasive imaging [104].

That same year, Oraevsky et al. advanced theoretical understanding by introducing the concept of time-resolved stress detection (TRSD). Their experiments, using multiple laser wavelengths and a lithium niobate detector, demonstrated accurate estimations of tissue absorption coefficients in biological samples including human aorta and bovine liver [105]. The subsequent year, they introduced the term optoacoustic to describe the laser-based imaging method. This technique demonstrated promise for visualizing absorbed optical energy in turbid and layered biological media [106].

In parallel, Kruger and colleagues used short pulses from a xenon flashlamp to

demonstrate absorption contrast imaging in a tissue-mimicking lipid medium. Their work further validated that photoacoustic imaging could accurately capture spatial distributions of optical absorption, even in highly scattering environments [107].

From this fertile period of innovation, the promise of photoacoustics as a hybrid imaging modality became evident. It combined the molecular contrast of optical imaging with the deep tissue penetration of ultrasound. By the early 2000s, the technique had matured significantly, ushering in a new era of biomedical imaging, with critical reviews and further advancements following rapidly [108].

Physics and Formulation of Photoacoustics

In photoacoustics, signals originate from optical absorption, and the mechanism of signal generation unfolds in three primary steps: (1) optical absorption by the target tissue or object, (2) conversion of the absorbed optical energy into heat leading to a localized temperature rise, and (3) thermoelastic expansion takes place, causing the generation of acoustic waves. This process only leads to efficient acoustic wave generation if the thermal expansion occurs in a time-varying manner. Such rapid expansion is typically achieved using a pulsed laser source or, alternatively, a continuous-wave (CW) laser with intensity modulation at a constant or variable frequency.

Following a short laser pulse excitation, the induced local fractional volume expansion $\frac{dV}{V}$ can be written as [109]:

$$\frac{dV}{V} = -\kappa p(\vec{r}) + \beta T(\vec{r}), \quad (3.1)$$

where κ is the isothermal compressibility, β is the thermal coefficient of volume expansion and $p(\vec{r})$ and $T(\vec{r})$ are the difference in the pressure and temperature respectively.

To ensure the effective generation of a photoacoustic wave, the laser excitation must satisfy two essential conditions, thermal confinement and stress confinement.

The thermal confinement condition ensures that the heat generated by optical absorption remains within the illuminated region during the laser pulse, without diffusing into the surrounding tissue. This occurs when the laser pulse duration τ is shorter than the characteristic thermal diffusion time $\tau_{thermal}$, given by [110]:

$$\tau < \tau_{thermal} = \frac{d_c^2}{4D_T} \quad (3.2)$$

Here, d_c is the desired spatial resolution to be achieved, and D_T is the thermal diffusivity.

The stress confinement condition ensures that the mechanical expansion of the absorber does not occur significantly during the laser illumination. In this regime, the laser pulse duration is shorter than the time it takes for stress (sound) to propagate out of the heated region. This is expressed as:

$$\tau < \tau_{stress} = \frac{d_c}{v_s}, \quad (3.3)$$

where v_s is the speed of sound.

These confinement conditions are typically satisfied when using nanosecond-duration laser pulses, which are standard in biomedical photoacoustic imaging systems. Their fulfillment is critical for generating high-resolution, high-contrast photoacoustic signals with minimal distortion due to heat or stress dissipation.

When both thermal and stress confinement are simultaneously satisfied, the fractional volume expansion (Eq. 3.1) ($\Delta V/V$) becomes negligible:

$$\frac{dV}{V} = -\kappa p(\vec{r}) + \beta T(\vec{r}) \approx 0 \quad (3.4)$$

leading to an initial pressure rise described by:



Figure 3.2 Photoacoustic of palm at 795 nm with photoacoustic imaging modality.

$$p_0(\vec{r}) = \frac{\beta T(\vec{r})}{\kappa}. \quad (3.5)$$

The temperature rise ($T(\vec{r})$) can be further defined as a function of optical absorption:

$$T(\vec{r}) = \frac{A_e}{\rho C_V}. \quad (3.6)$$

Here A_e is absorbed energy density which is the product of the absorption coefficient (μ_a) and the local optical fluence ($F(\vec{r})$). ρ is density of the absorber and C_V is the specific heat capacity at constant volume.

Based on Eqs. 3.5 and 3.6, the initial photoacoustic pressure wave can be shown as:

$$p(\vec{r}) = \frac{\beta A_e}{\rho C_V \kappa} = \Gamma \mu_a F(\vec{r}). \quad (3.7)$$

Here, $\Gamma = \frac{\beta}{\rho C_V \kappa}$, the Grüneisen coefficient, which increases as the temperature rise and combines thermal and acoustic properties [111]. With the historical background and theoretical framework now established, the discussion moves from past discoveries to contemporary practice. Modern photoacoustic systems utilizes the same light to sound conversion that Bell first observed but pair it with nanosecond lasers, broadband ultrasound detectors, and advanced reconstruction algorithms to produce images shown in Figure 3.2.

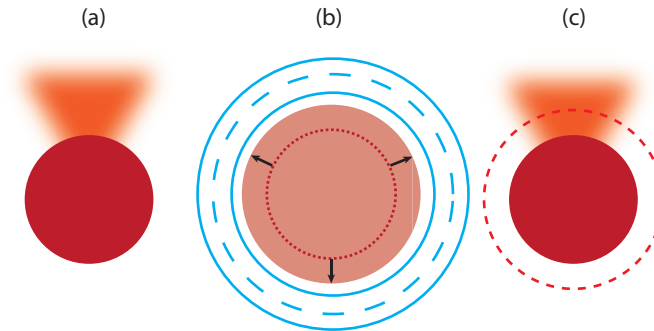


Figure 3.3 Photoacoustic generation in a single red blood cell (illustration only, not to scale). (a) A nanosecond, 795 nm laser pulse (red cone on top of red blood cell) is illuminating a red blood cell; hemoglobin strongly absorbs the light. (b) Once the pulse has passed, hemoglobin absorption produces a rapid (~ 10 ns) thermoelastic expansion, the dashed red outline, inside the cell, marks the cell's original diameter (expansion exaggerated for clarity). This volumetric change generates pressure waves into the surrounding medium, shown as blue rings. (c) During the time interval of two pulses, the cell cools and relaxes back to its initial size in time for the next laser incident.

To explain the mechanism step by step, it helps to zoom in on a single absorber, in this case, the red blood cells (erythrocyte). When a nanosecond, 795 nm laser pulse irradiates an red blood cells, hemoglobin absorbs the incident photons and converts their energy to heat almost instantaneously. Because the pulse duration (~ 5 -10 ns) is far shorter than both the thermal diffusion and acoustic transit times across an 8 μm cell, the interaction satisfies thermal and stress confinement. The resulting, highly localized temperature rise triggers a brief thermoelastic expansion of the cell, launching a pressure wave into the tissue. By the time the next laser pulse arrives (for example, if the repetition rate of the laser is 10000 pulses per second, the time interval between two pulses is 100 μs), the cell has cooled back, preventing cumulative heating. Figure 3.3 depicts the generation of photoacoustic in red blood cells. Ultrasonic transducers capture these time of flight pressure signals, and tomographic back projection algorithms convert the data into quantitative maps of optical absorption thereby revealing physiological metrics such as hemoglobin concentration and oxygen saturation with ultrasonic spatial resolution and centimeter scale penetration depth.

Having established the foundational theory, historical context, and physical mechanisms underlying photoacoustics, the next chapter will illustrate how this powerful imaging technique can be practically applied in biomedical research. Specifically, I will present my own experimental work, employing photoacoustic imaging to non-

invasively investigate the placenta in mice. This study exemplifies the potential of photoacoustic methods, bridging the theoretical insights covered thus far with tangible biomedical applications, demonstrating both the versatility and sensitivity of this modality.



4. PHOTOACOUSTIC IMAGING OF RAT PLACENTAL TISSUE

In this chapter, I present original research conducted on the application of photoacoustic imaging to study placental structures in rats. The motivation behind this study lies in the inherent advantages of photoacoustic techniques-combining optical contrast with ultrasound penetration to visualize placental vascularization and oxygenation without invasive methods. This research is published in the journal *Placenta* and was featured as the cover art for the December 2024 issue. The full article can be found in the following publication: Cizmeciyan, M. N., Bektas, N. I., Derin, N., Denizaltı, T., Khoshzaban, A., Unlu, M. B., & Celik-Ozenci, C. (2024). Unveiling placental development in circadian rhythm-disrupted mice: A photo-acoustic imaging study on unstained tissue. *Placenta*, 158, 57-61. doi:10.1016/j.placenta.2024.10.001.

4.1 Introduction

Photoacoustic imaging (PAI) enables the acquisition of highly sensitive images of tissue vasculature, leveraging the strong optical absorption of red blood cells (RBCs) [112]. Due to the linear relationship between RBC-mediated laser absorption and the amplitude of the resulting photoacoustic waves, this technique allows for label-free, concentration-dependent visualization of blood vessels [113]. This fundamental advantage sets PAI apart from traditional imaging approaches, offering precise identification of hypoxic regions, often a hallmark of various pathological conditions [114]. Despite its proven value in applications related to oncology and vascular pathologies, the clinical potential of PAI remains underutilized in one crucial area: placental health monitoring. The placenta serves as the principal interface responsible for nutrient and oxygen exchange between mother and fetus, and disruptions in this vital communication have been linked to a wide array of adverse fetal outcomes [115, 116, 117, 118].

Although a few initial investigations into placental photoacoustic imaging have demonstrated the technique’s promise and identified its limitations, they have fallen short of fully elucidating placental physiology. Research began in 2015 with studies on ex vivo placental tissues [119], followed by advancements in 2016 that enabled accurate assessments of umbilical cord oxygenation [120, 121]. By 2017, pathological case studies began to shed light on the placenta’s protective response to reduced ambient oxygen exposure [122]. Collectively, these studies have illustrated PAI’s potential to explore placental blood flow and enrich our understanding of this essential organ [123, 124]. Motivated by these insights, we employed photoacoustic microscopy (PAM) to examine the physiological state of placental tissue slices subjected to maternal circadian rhythm disruption. Our findings indicate that PAM can sensitively detect even subtle developmental abnormalities in placental growth.

The connection between circadian rhythm and placental development was first established in a landmark 2008 study, which reported that pregnant rats exposed to constant illumination developed lighter and smaller placentas [125]. This finding drew substantial interest due to its possible long-term consequences across generations. Since then, a wide range of investigations has been carried out to examine the causes, prevention, detection, and broader significance of this phenomenon [126]. Several studies have demonstrated that circadian rhythm disturbances during gestation can alter hormonal regulation, hinder fetal development [127, 128], and raise the likelihood of non-communicable diseases (NCDs) such as diabetes, obesity, cardiovascular disorders, and certain cancers [129, 130]. Additional research has explored the relationship between gestational chrono-disruption (GCD), intrauterine growth restriction (IUGR), and increased NCD susceptibility later in life.

Nonetheless, the cellular and molecular mechanisms underlying these effects remain incompletely understood [131, 132], largely due to the complex and multifaceted role of the placenta. This transient organ not only governs metabolic gas exchange and fetal waste elimination, but also modulates maternal physiology through hormone production and acts as an immune barrier between maternal and fetal systems [133]. Its function relies on intricate hormonal signaling and multiple parallel mechanisms

designed to optimize resource delivery for fetal growth. In this study, we focused on the mature murine placenta, which is composed of three main regions: the labyrinth zone (LZ), the spongiotrophoblast or junctional zone (ST), and the decidua. The decidua, representing the maternal side of the placenta, plays a key role in vascular development and includes migrating glycogen cells (GCs) originating from the junctional zone [134, 135]. The ST zone contains the placenta's primary endocrine cells, trophoblast giant cells, as well as clusters of GCs essential for fetal growth [136, 137]. Notably, only maternal vasculature is present in this zone [138]. The fetal side, comprised of the labyrinth zone, includes maternal sinusoids, fetal vasculature, and trophoblast cells, making it the central site for nutrient and gas exchange between mother and fetus [139].

In addition to cellular structure, the relative sizes of these three placental zones carry critical physiological implications. The dimensions of each region directly affect the placenta's capacity for nutrient transfer, thereby influencing fetal development outcomes. An appropriately sized labyrinth zone, for instance, ensures optimal oxygen and nutrient exchange. Conversely, size deviations can impair placental efficiency and lead to fetal growth deficits. Thus, understanding both the composition and proportion of placental regions in the murine model is essential for advancing reproductive biology and for developing strategies to mitigate placental dysfunction and poor pregnancy outcomes.

Even today, the impact of circadian rhythm disturbances on fetal development remains an active area of research, particularly concerning their role in placental insufficiency. While existing fetal monitoring technologies, such as Doppler ultrasound and serum biomarker testing, are reliable for detecting major abnormalities, they often fail to identify more subtle developmental deficiencies during gestation. The present study seeks to: (1) evaluate photoacoustic imaging and microscopy as an alternative to traditional hematoxylin and eosin (HE) staining for analyzing placental morphology and (2) investigate the relationship between placental zone proportions and circadian rhythm disruption.

4.2 Materials and Methods

Ethics statement: Female BALB/c mice, six weeks of age, were obtained from the Animal Research Unit of Akdeniz University, Antalya, Turkey. The experimental procedures were carried out with the explicit approval of the Animal Care and Use Committee of the Faculty of Medicine at Akdeniz University, and they were strictly adherent to the ethical approval protocol (Ethical Approval No. 2023.07.002). Upon the commencement of the experiments, all mice were housed in a controlled environment with a regulated 12-hour light/dark cycle and provided unrestricted access to food. At the end of the experiments; the euthanization of mice was performed through cervical dislocation after receiving anesthesia with a mixture of ketamine and xylazine (0.1 ml/10g body weight, intraperitoneal injection to collect fetus and placenta. Additionally, the weight of the placenta and fetus samples were noted.

Preparation of Mouse: Pregnancy in female mice was induced by mating them with fertile males of the same strain. Each cage was allocated one male mouse to mate with two female mice. The appearance of a copulatory plug was considered as day one of pregnancy, resulting in the formation of two distinct groups. In the control group (C), female mice were exposed to a standard 12L-12D light-dark cycle (lights on at 06:00, lights off at 18:00) throughout the gestation period. Placentas and fetuses were collected from this group on the 16th and 18th days of pregnancy. In contrast, the maternal circadian rhythm disrupted group (MCRD) underwent a manipulated light-dark cycle. Starting from the day of vaginal plug detection, the standard 12L-12D cycle was advanced by 6 hours every five days, to mimic the shift work model, deliberately disrupting the circadian rhythm [140]. Similar to the control group, fetuses and placentas were retrieved from the MCRD group on the 16th and 18th days of gestation.

Preparation of Tissue Sections: Placentas and fetuses were collected from all experimental groups on the 16th and 18th days of gestation. Initially, each fetus and placenta were weighed using precision scales, and their respective weights were documented. The placentas were then processed for subsequent histological analyses to

discriminate the placental zones. For these analyses, the placental tissues were fixed in 10% formaldehyde (Merck, Germany) for 24 hours to preserve their structure. Subsequently, they were dehydrated using a graded ethanol series and embedded in paraffin to facilitate sectioning. Sections, five micrometers in thickness, were prepared from each placenta. To maintain standardization, only sections derived from areas passing through the umbilical cord were collected. Prepared tissue sections were scanned under the photoacoustic microscope.

Following the photo-acoustic microscope (PAM) scans, the paraffin was removed from each tissue section, and they were rehydrated. The sections were then stained with hematoxylineosin to highlight cellular and structural details. All stained sections were imaged using a Zeiss (Oberkochen, Germany) light microscope for further evaluation.

Photo-acoustic Microscope: The photoacoustic microscopy images were collected with a homemade optically resolved PAM. The samples on glass slides were immersed in water. A laser (SpectraPhysics, Explorer One) operating at 532 nm with a repetition rate of 20 kHz and an average power of 10 mW was focused on the samples with a 50 mm lens. Emitted acoustic waves from remaining blood content were received through a 5 MHz single-element ultrasonic transducer and amplified (50dB) with a two-stage amplification scheme in all experiments. To record the photo-acoustic signals coming from the tissue slices, a custom MATLAB (SN: 1076960) code simultaneously translated the motorized stages and recorded the emitted signals through a DAQ card (Gage Compuscope). Later, recorded signals were constructed to the scanned position values to form the photo-acoustic images.

4.3 Results and Discussion

This study evaluated the effectiveness of photoacoustic microscopy (PAM) for assessing placental tissue, particularly under conditions of maternal circadian rhythm disruption (MCRD). Our primary objective was to demonstrate PAM's sensitivity in detecting subtle abnormalities in placental development. To achieve this, we conducted

a comparative analysis of placental slices collected from both MCRD-exposed and control (non-disrupted) rats. These samples were imaged using PAM and then examined via traditional hematoxylin and eosin (HE) staining under a light microscope.

In rodents, the gestational period spans approximately 19-20 days. The initiation of the first placental circulation occurs around embryonic day 9. From this point forward, the placenta undergoes active development until about day 15, reaching a mature state by day 16. Based on this timeline, we selected gestational days 16 and 18 as key observation points to evaluate vascular changes in the placenta both immediately post-maturation and shortly before birth [132].

To highlight PAM's ability to detect physiological changes, we quantified the total placental area and labyrinth zone (LZ) area based on PAM signal intensity, and compared these results with those from HE-stained samples. The setup we used for photoacoustic imaging is shown in Figure 4.1. The measurements, detailed in Table ??, revealed a modest increase (less than 1.65%) in mean placental size between days 16 and 18 in the control group. However, the LZ area increased significantly, by 29% in HE and 21% in PAM images, corresponding with the increasing nutritional needs of the fetus. In other words, the LZ-to-total-placenta area ratio increased from 63% (HE) and 54% (PAM) on day 16 to 80% (HE) and 64% (PAM) on day 18 in control animals. Figure 4.2 depicts the acquired images.

In contrast, the MCRD-exposed animals showed a 21% increase in total placental area from day 16 to 18, a compensatory response to developmental insufficiencies. However, this did not coincide with a proportional growth in the LZ. The LZ-to-placenta ratio remained static, 66% (HE) and 49% (PAM) on day 16, and 66% (HE) and 47% (PAM) on day 18. Furthermore, in both days examined, the absolute LZ and placenta areas in MCRD animals were consistently 20-32% smaller than those in the control group. These findings underscore the potential impact of circadian disruption on LZ development and overall placental growth, suggesting impaired vascular formation and nutrient exchange capacity.

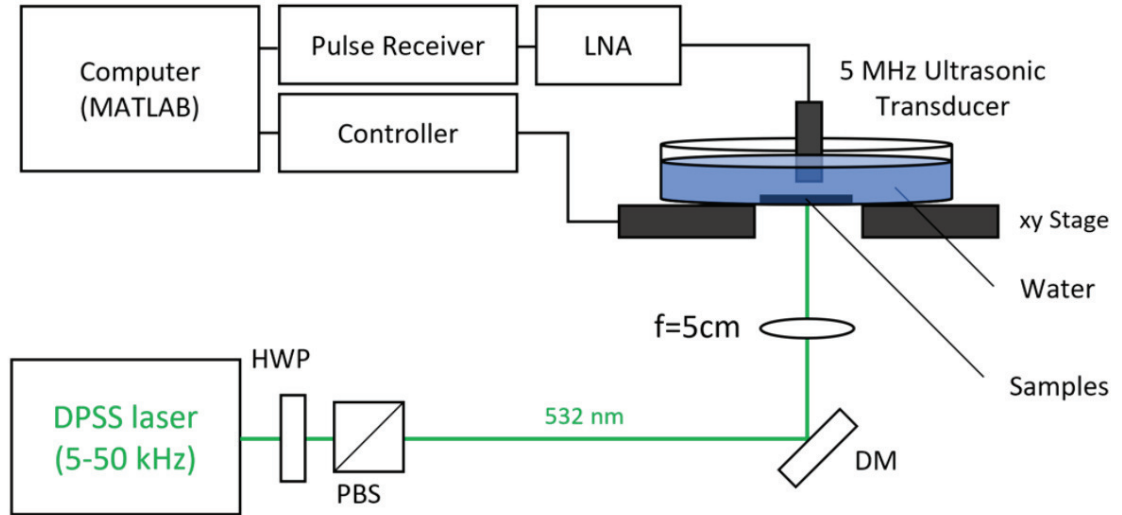


Figure 4.1 The setup used for photoacoustic imaging.

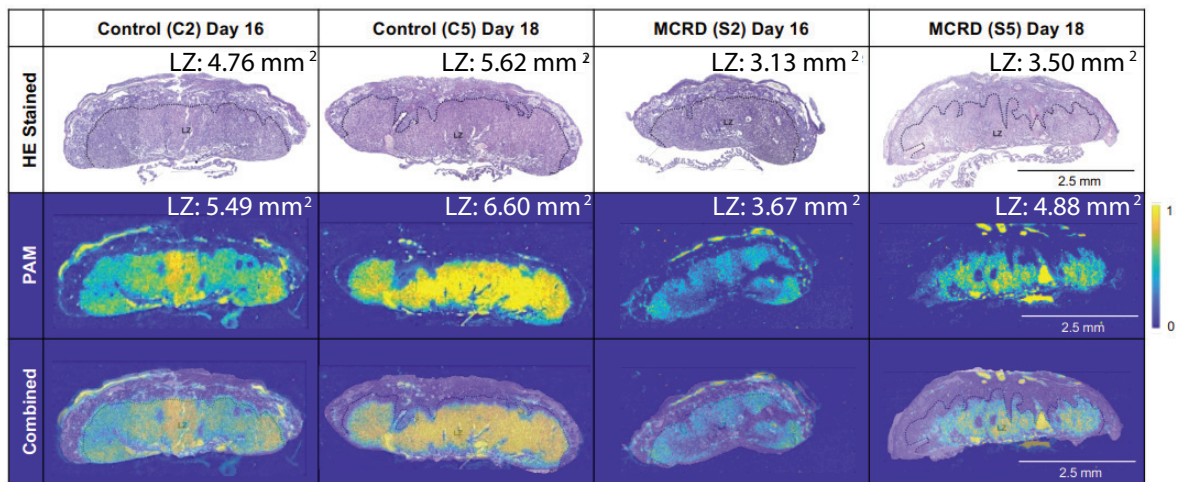


Figure 4.2 The HE stained and photoacoustic images for the Control and MCRD group at different days.

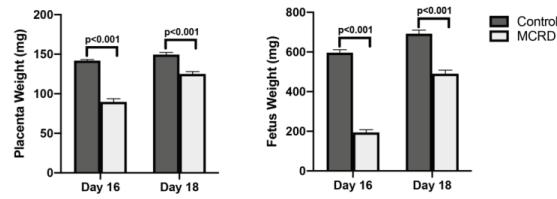


Figure 4.3 Weight data of placenta and fetus gathered from control and MCRD mice (N=6).

To support the link between placental condition and fetal health, we also measured fetal and placental weights in both groups. As illustrated in Figure 4.3, animals exposed to MCRD showed clear signs of intrauterine growth restriction (IUGR), with reduced fetal and placental weights on both gestational days. The insufficient expansion of the LZ appears to be a contributing factor to these underweight births. Notably, while the MCRD group displayed signs of placental compensation by day 18, their fetuses remained, on average, 29% lighter than those in the control group. This suggests that the compensatory mechanisms of the placenta were insufficient to support normal fetal growth. The results are presented in Tables 4.1 and 4.2 for the control and MCRD groups, respectively.

Table 4.1
Placental measurements in the Control group.

Days	Sample	PAM Labyrinth (mm ²)	HE Labyrinth (mm ²)
16	C1	3.74	4.45
16	C2	4.76	5.52
16	C3	4.30	5.06
Mean		4.26	5.01
18	C4	4.80	6.53
18	C5	5.62	7.74
18	C6	5.08	5.17
Mean		5.16	6.48

While the outcomes of this study offer valuable insights, it is important to ac-

Table 4.2
Placental measurements in the MCRD group.

Days	Sample	PAM Labyrinth (mm^2)	HE Labyrinth (mm^2)
16	S1	1.72	2.52
16	S2	3.13	3.94
16	S3	3.02	4.28
Mean		2.62	3.58
18	S4	2.88	5.70
18	S5	3.50	4.80
18	S6	2.69	3.32
Mean		3.03	4.61

knowledge certain methodological limitations. First, our imaging approach relies on paraffin-embedded tissue sectioning and two-dimensional imaging. While effective for comparative analysis, especially when validated against HE-stained images, this 2D approach inherently lacks volumetric representation of the placental structure. Additionally, tissue fixation introduces time-consuming steps and may alter some physiological features. Another limitation lies in the absence of calibration for absolute quantification of hemoglobin, potentially reducing the precision of blood content analysis in vascular-rich areas like the LZ.

Despite these constraints, the application of PAM has proven to be a promising and effective approach for evaluating tissue morphology in both healthy and pathological conditions. Its ability to non-invasively visualize and quantify blood-rich regions without the need for exogenous labeling is particularly advantageous for studies focused on vascular structures. Even under the current limitations, our findings affirm the potential of PAM as a valuable tool in biomedical imaging. With further refinement and optimization of the technique, we anticipate broader adoption of PAM in both research and clinical settings, particularly for applications in maternal-fetal medicine.

Ultimately, this study highlights the capacity of photoacoustic imaging to detect

morphological alterations in placental development resulting from circadian rhythm disruption. The clear distinctions between the control and MCRD groups reinforce the importance of maintaining proper circadian regulation during pregnancy and underscore the value of PAM in identifying and studying such developmental differences.



5. MANIPULATION OF JANUS PARTICLES USING NANOSECOND PULSED LASER

While the previous chapter demonstrated the biomedical potential of lasers through photoacoustic imaging, lasers also offer unparalleled opportunities in the manipulation and control of active matter, as introduced in Chapter 1. In this chapter, I return to the core theme of active matter by presenting my principal research contribution: the precise manipulation of Janus particles using nanosecond pulsed lasers. Leveraging our earlier discussion on laser-matter interactions (Chapter 2) and particle dynamics (Chapter 1), I demonstrate how controlled laser illumination can actively influence particle motion and organization.

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5.1 Introduction

Janus particles are known for their asymmetry, featuring two distinct surfaces with chemical and physical properties. Active motion on demand makes Janus particles a novel tool for imaging [141], drug delivery [142], and diagnostics [143, 144, 145] applications. To date, optical, chemical [22, 15, 23, 24, 25, 26, 27], and physical methods are reported, such as applying external magnetic [15] or electric [17, 146] fields. Optical methods, which involve illuminating particles with a laser, provide the highest flexibility and offer higher spatial resolution. It is understood that the underlying physical mechanism that initiates the active motion in Janus particles is thermophoresis

[147, 148]. In particular, for optical methods, thermophoresis is started by illuminating the Janus particle with light, where only the metallic cap absorbs the light, causing a rapid temperature elevation on the surface, leading to a localized, unsymmetrical, and uneven heating pattern. For nano- and micron-sized Janus particles, temperature differences are easily translated into directed movement [149, 29, 30, 31, 28]. In literature, many theoretical and experimental studies have been carried out on the optical manipulation of Janus particles using various approaches [45]. In 2010, Jiang et al [149], successfully demonstrated the active motion of Janus particles under laser-induced temperature gradients. Later, the core concept of propulsion was explained by calculating the flow patterns circulating around the Janus particles under the influence of focused laser light [150]. Further advances in the field have led to the development of techniques such as photon nudging to manipulate the position of microscopic swimmers [151], drive nanoparticle [152], and microparticle [153] motors with near-infrared light for drug delivery, and controlling the motion of micro and nanomotors for cargo transport and microfluidics [154]. However, despite the ability of Janus particles to navigate through random thermal noise and move in a directed manner, a significant challenge still lies in precisely controlling their dynamics. The widespread use of laser-based techniques underlines the need for refined control strategies to harness the potential of Janus particles.

Continuous-wave (CW) lasers are a common tool for manipulating Janus particles, and there are numerous studies in the literature investigating the behavior of Janus particles and controlling them under CW laser illumination [149, 155, 156, 157]. In this study, instead of common CW implementation methods, we examined the behavior of Janus particles under a nanosecond-pulsed laser regime. A standard Q-switched laser can generate kilowatts of peak power while maintaining an average power in the milliwatt range [158]. In pulsed laser interactions, the rapid deposition of energy within short time intervals leads to localized non-steady state heating. Above a certain threshold, rapid temperature elevation leads to the generation of pressure waves [159], shock waves [160], cavitation [161], and ablation [162], which might contribute to the propulsion mechanism.

5.2 Results and discussion

We investigated the interaction between nanosecond-pulsed lasers and Au-Janus particles, concentrating on the influence of the laser on the particles, their optical manipulation properties, and the ablation and damage threshold of the gold cap. In the first section, we showed that the pulsed laser influences the Brownian motion trajectories of the Au-Janus particles in three regimes. At the so-called high-influence regime, we observed superdiffusivity through mean square displacement (MSD) analysis. In the second section, we explored the novelty of the pulsed laser illumination during the optical manipulation of Au-Janus particles. Pulse energies above 4 nJ allowed us to translate the particles with 0.9 $\mu\text{m/s}$ up to 5.1 $\mu\text{m/s}$ with 50 nJ of pulse energy. In the final section, we validated our developed theoretical model that beyond 20 nJ the gold cap melts/damages and generates sub-micron particles.

The Au-Janus particles utilized in our experiments are 4.1 μm polystyrene microbeads, half-coated with a 100 nm thick layer of gold. The schematic of the experimental setup is shown in Figure 5.13, where the laser beam was focused with a 10X (NA=0.25) objective lens, and the sample plane was imaged onto the camera with a 100X oil-immersed objective. The laser beam spot size was measured as $2\omega_0 = 2.7 \mu\text{m}$ using the knife edge method. The movement of the particle is recorded through digital video microscopy at a frame rate of 17 frames per second (FPS). Throughout this article, the experimental setup described above is used for all the experiments.

5.2.1 Influence of the Laser on the Au-Janus particle

We studied the Brownian motion of Au-Janus particles with and without laser illumination. We started by recording the Brownian motion of a particle when the laser was off. After 15 minutes, we turned on the laser, with a pulse repetition rate (PRR) of 10 kHz, and illuminated perpendicularly to the left side of the particle, which was

recorded for another 15 minutes. This procedure was repeated at pulse energies of 3.5 nJ, 10-50 nJ. Then, customized Python code was developed based on OpenCV [163] to extract the trajectories of the particles after each experiment and plotted in Figure 5.1(a,b,c). It is important to mention that a 100 nm thick layer of gold makes the particles relatively heavy (the gold cap accounts for 60 percent of the Janus particle total weight). Due to their weight, particles remain close to the surface of the glass slide, preventing diffusion in the z-direction.

Trajectories of the particle, shown in Figure 5.1(a)-(c), allow us to view the collected data comprehensively. 3-D histograms, in Figure 5.1(d)-(f), of the trajectories show the number of times that particle has been in a specific coordinate, revealing its predominant locations over time. The data suggest three distinct regimes based on the applied pulse energies.

In the first regime, what we call the low-influence regime, when the pulse energy is less than ~ 10 nJ (here 3.5 nJ), the particle continues to exhibit its Brownian motion, as indicated by the overlapping trajectories observed under both laser-off and laser-on conditions as shown in Figure 5.1(a) and (d). In the second regime, the medium-influence regime (less than ~ 40 nJ), at 10 nJ pulse energy, the particle experiences an increased range of motion, seemingly attempting to escape the laser influence, yet it remains in close proximity to laser zone while still undergoing Brownian motion, as shown in Figure 5.1(b) and (e). Lastly, in the third regime, high-influence regime (higher than ~ 40 nJ), at 50 nJ pulse energy, the particle experiences superdiffusion results in pushing the particle far away from the laser beam, establishing a new equilibrium location and continuing its Brownian motion at this new location, as illustrated in Figure 5.1(c) and (f).

Dashed circles in Figure 5.1(a)-(c) represent the laser zone, where the laser intensity decreases to approximately 0.03% of its maximum value. To illustrate the

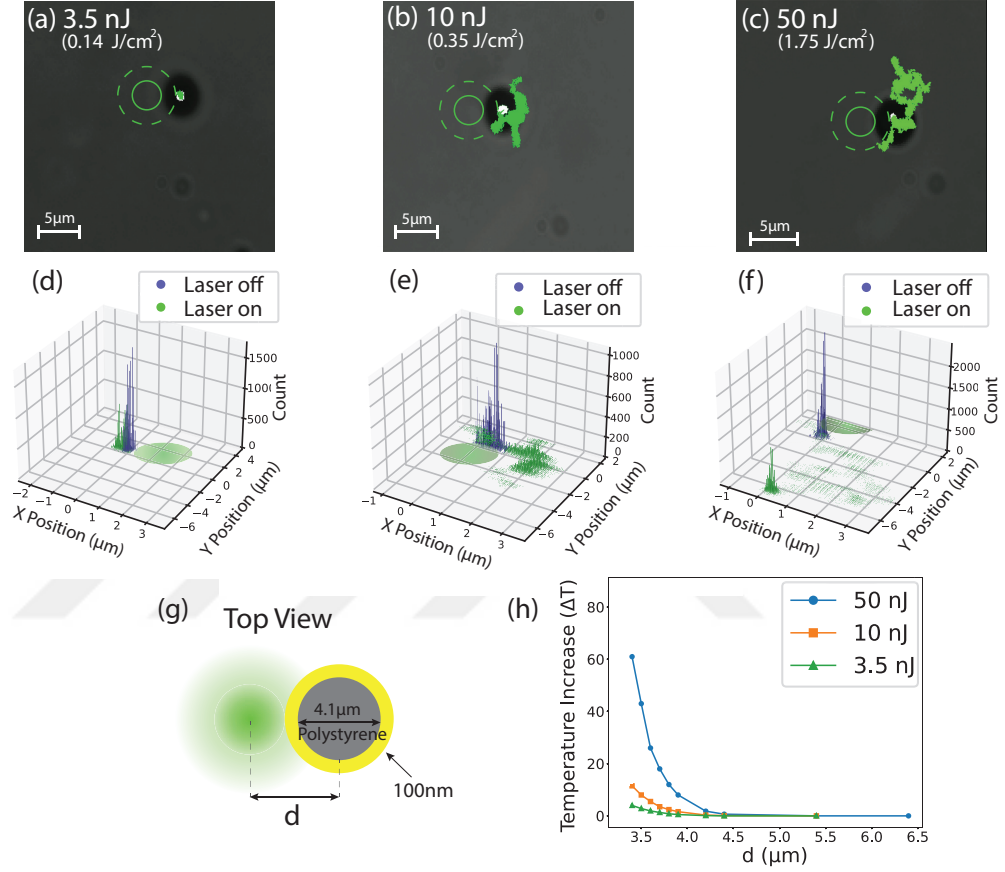


Figure 5.1 2D trajectory and 3D histograms of Janus particle under nanosecond pulsed laser illumination for $\omega_0=1.35 \mu\text{m}$ (a) The low-influence regime at 3.5 nJ, 0.14 J/cm^2 (b) the medium-influence regime at 10 nJ, 0.35 J/cm^2 , and (c) the high-influence regime at 50 nJ, 1.75 J/cm^2 . In (a)-(c), the white and green colors show the trajectory of the particle while the laser is off and on, respectively. The green solid and dashed circles show the laser spots at $r=\omega_0$ and $r=2\omega_0$. (d)-(f) The corresponding 3D histograms demonstrate how many times the particle was present in a certain coordinate, and the green-colored disk represents the position of the laser relative to the particle. (g) The schematic illustration of the laser spot at a distance d to the Janus particle. (h) The simulation result of the temperature increase of the gold Janus particle versus d for $E_P=3.5, 10, 50 \text{ nJ}$ and $\omega_0=1.35 \mu\text{m}$.

functioning of thermophoresis more clearly, we calculated the temperature increase of the gold cap as a function of the distance (d) from the center of the laser, as shown in Figure 5.1(g). The results, plotted in Figure 5.1(h), show that at $d_0=3.4\text{ }\mu\text{m}$, the temperature increases are calculated as 8°C , 15°C , and 60°C for the low-, mid-, and high-influence regimes, respectively. In the high-influence regime, this large temperature gradient causes the particle to settle at a final position approximately $d=7\text{ }\mu\text{m}$ away from the laser center. At this new location, sufficiently far from the laser, the effect of thermophoresis diminishes. As a result, the particle undergoes Brownian motion at this new location.

We compared the MSD behavior in three different regimes with the case when the laser is off. In this work, we calculated the MSD with respect to the initial position, r_0 , as

$$\text{MSD} = \frac{1}{N} \sum_{i=1}^N (r_i^2 - r_0^2) \quad (5.1)$$

where N is the total number of measurements, and r_i is the particle's position at the i -th measurement. We used this definition because we assessed how far the particle moves from its initial position under nanosecond pulsed laser illumination. Figure 5.2(a) shows the low-influence regime, where there is no notable difference in MSD between when the laser is on (green line) and off (blue line). As pulse energy increases and approaches the intermediate regime, the slope of the MSD increases (Figure 5.2(b)), and the particle exhibits Brownian motion over a broader range, as seen in the inset. In this regime, the particle remains affected by the laser and stays within the laser zone. In the high-influence regime, with the laser on, we initially observed superdiffusive behavior (green line). However, the particle is then pushed out of the laser zone, and once in the new position, it resumes Brownian motion, similar to when the laser is off (Figure 5.2(c)).

Figure 5.2(d) presents the MSD of the Janus particle at pulse energies of 3.5 nJ, 10 nJ, and 50 nJ. As shown, in the low- and medium-influence regimes, the MSD

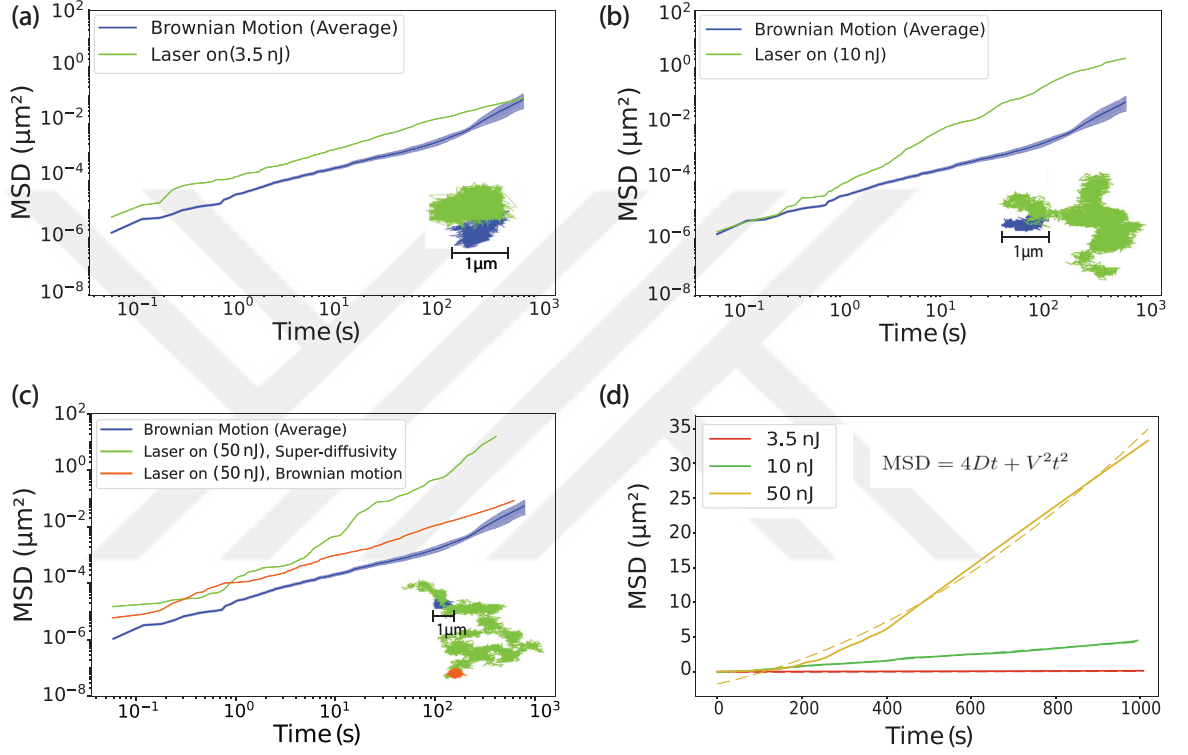


Figure 5.2 The MSD vs time plot for three regimes on a log-log scale for pulse energies at (a) 3.5 nJ (low-influence), (b) 10 nJ (medium-influence), and (c) 50 nJ (high-influence). Insets show corresponding particle trajectories. The MSD vs time plot for three regimes on a (d) linear-linear scale. Dashed lines represent the fitting curves. In the low-influence regime (a), the particle exhibits similar trends in laser on (green line) and off (blue line) states. In the medium-influence regime (b), the MSD slope is steeper when the laser is on (green line) compared to when it is off (blue line), and in the high-influence regime (c) particle experiences super diffusion with a parabolic shape MSD (green line) and then relocated in a new location and exhibited Brownian motion (orange line) as if the laser is off (blue line).

increases linearly with time, which can be expressed as [13]:

$$\text{MSD} = 4Dt \quad (5.2)$$

where D represents the particle's diffusion constant. On the other hand, in the high-influence regime, the MSD follows a quadratic dependence on time and can be described by [149]:

$$\text{MSD} = 4Dt + V^2t^2 \quad (5.3)$$

where V is the particle's self-propelling velocity.

Using the Eq. 5.2 and Eq. 5.3 to fit lines on the MSDs shown in Figure 5.2(d) highlights the effect of the laser illumination on the particles' diffusion behavior. In the low-influence regime, at a pulse energy of 3.5 nJ, the MSD versus time shows a diffusion coefficient, D , of $0.3 \times 10^{-4} \mu\text{m}^2/\text{s}$, with no notable difference compared to when the laser is off. As the energy increases, entering the medium-influence regime, the MSD remains linear while the D values rises. At 10 nJ, the calculated D is $1.1 \times 10^{-3} \mu\text{m}^2/\text{s}$. At 50 nJ, the quadratic behavior of the MSD indicates superdiffusion, the particle's velocity, V , is $4.7 \times 10^{-3} \mu\text{m}/\text{s}$, and the D is $3.3 \times 10^{-3} \mu\text{m}^2/\text{s}$.

In the high influence regime, the calculated temperature transient of the gold cap reaches 60°C for tens of nanoseconds. During this transient period (30-100 ns, Figure 5.9(c)), the viscosity of the surrounding medium may vary. However, shortly thereafter, the particle stabilizes in a cooler region where the temperature remains constant, owing to the thermal dissipation characteristics of the water medium. Given the experimental time frame-58 ms per frame (with the camera operating at 17 FPS), a total duration of 15 minutes, and considering that viscosity fluctuations occur on timescales much shorter than those experimentally accessible-we conclude that the average viscosity of the water medium remains effectively constant throughout the measurement period.

5.2.2 Influence of the Laser spotsize on the Au-Janus particle

This section is dedicated to investigating how the laser beam influences the Brownian motion of the particle at a distance defined by d . For this experiment, the particles were recorded for 15 minutes, and then the laser having a spot size of $\omega_0=1.35 \mu\text{m}$ turned on the left side of the particle with the initial distance of $d_0=3.4 \mu\text{m}$ and then recorded for 15 minutes again. After we completed this, we repeated the same procedure for approximately two times larger laser beam spot size $\omega_0=2.80 \mu\text{m}$ with the initial distance of $d_0 = 4.8 \mu\text{m}$. Since the laser beam has a Gaussian beam profile, depending on d , the gold part of the Janus particle experiences an effective energy transfer. The effective energy transfer (E_t) to the Janus particle is defined as

$$E_t = \int_d^\infty \frac{2E_0}{\pi\omega_0^2} \exp\left[-\frac{2r^2}{\omega_0^2}\right] 2\pi r dr, \quad (5.4)$$

where d is the distance from the center of the particle to the center of the beam, and E_0 is the incident pulse energy. The transferred energy as a function of d and ω_0 becomes:

$$E_t = E_0 \exp\left[-\frac{2d^2}{\omega_0^2}\right]. \quad (5.5)$$

To demonstrate how strong this dependence is, we calculated the energy transfer (E_t) and resulting temperature increase (ΔT) with respect to the beam waist spot size (ω_0) and plotted in Figure 5.3a for $E_0=50 \text{ nJ}$. As ω_0 increases, due to the fixed $d_0=3.4 \mu\text{m}$, the effective energy transfer increases because of a larger overlap with the laser spot, which in turn raises the temperature of the gold cap.

Building on this, we further investigated the effect of the laser beam waist spot size on particle trajectories and range of motion. The calculated temperature increase

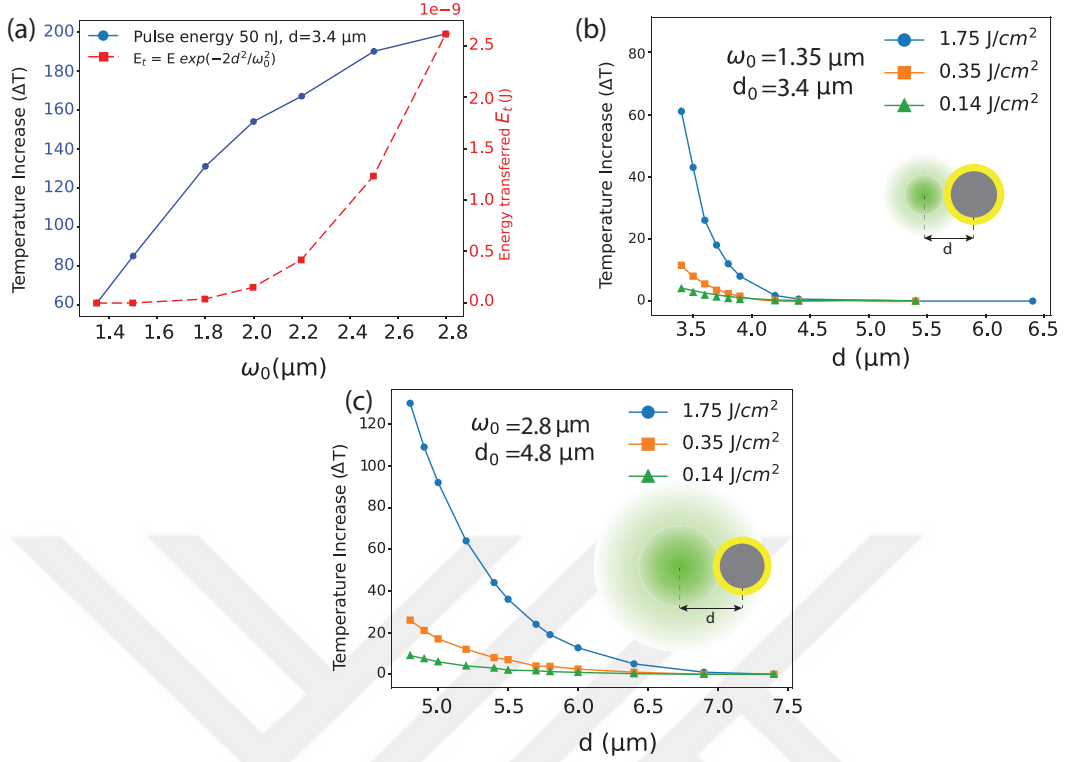


Figure 5.3 (a) The calculated temperature increase (ΔT) and transferred energy (E_t) versus laser beam spot size (ω_0) at $E_0=50 \text{ nJ}$ and $d_0=3.4 \mu\text{m}$. The temperature increase (ΔT) versus (b) d at given laser fluences (J/cm^2) for $\omega_0=1.35 \mu\text{m}$ and (c) $\omega_0=2.8 \mu\text{m}$.

(ΔT) with respect to d for two laser beam waist spot sizes: $\omega_0=1.35 \mu\text{m}$ (Figure 5.3b) and $\omega_0=2.8 \mu\text{m}$ (Figure 5.3c), indicates the region where thermophoresis has an influence on the Janus particle. As observed in these figures, a larger spot size with the same laser fluence (J/cm^2) effectively increases the temperature of the gold cap over a broader area.

To further analyze the impact of spot size on particle motion, the following sections will present recorded particle tracking data separately: results for $\omega_0=1.35 \mu\text{m}$ in Section 2.1 and for $\omega_0=2.8 \mu\text{m}$ in Section 2.2.

Influence of Laser Beam Spotsize of $\omega_0 = 1.35 \mu\text{m}$: The plot of the trajectories in Figure 5.4 reveal three different behaviors for the Janus particles. At 3.5 nJ , the particle does not show any significant change in its motion. At $10\text{-}30 \text{ nJ}$, the Janus particle motion shows that the range of the Brownian motion increases, and at $40\text{-}50 \text{ nJ}$, the Janus particle escapes from the laser zone and settles in a new location, and

continues Brownian motion.

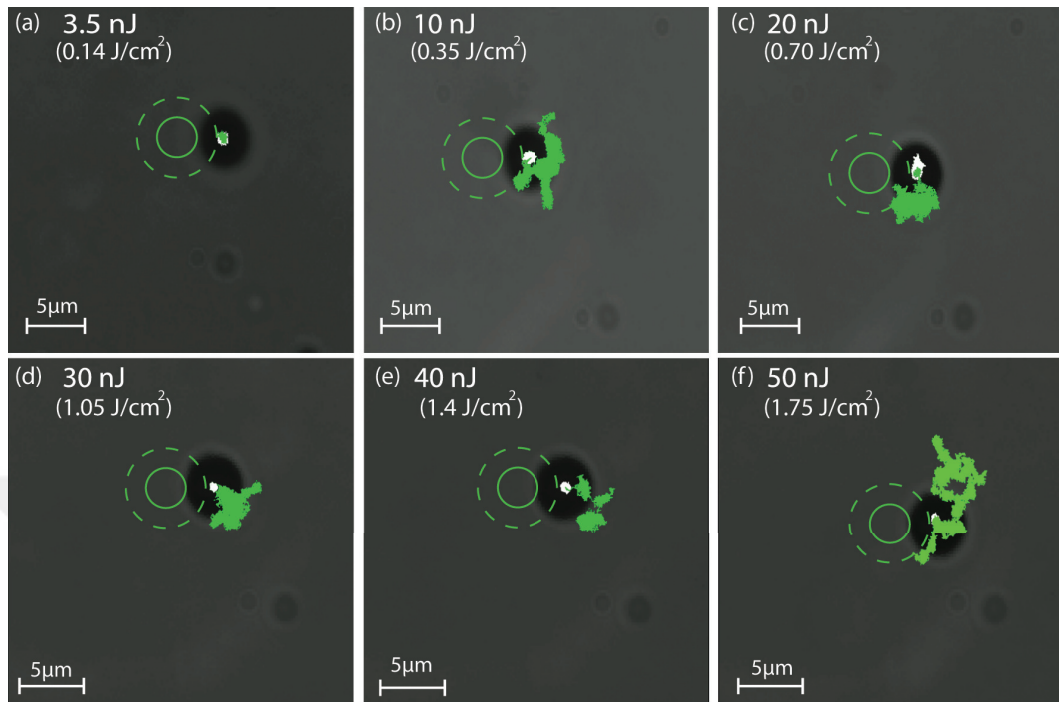


Figure 5.4 Janus particle Brownian motion analysis in pulse energies ranging from 3.5 nJ to 50 nJ. White lines show the trajectory of the particle while doing Brownian motion. The Green lines show the trajectory of the particle when the laser is present on the left side of the particle (The green circle shows the location of the laser spot).

Histogram plots in Figure 5.5 depicts the distribution of trajectories in Figure 5.4 in 3D.

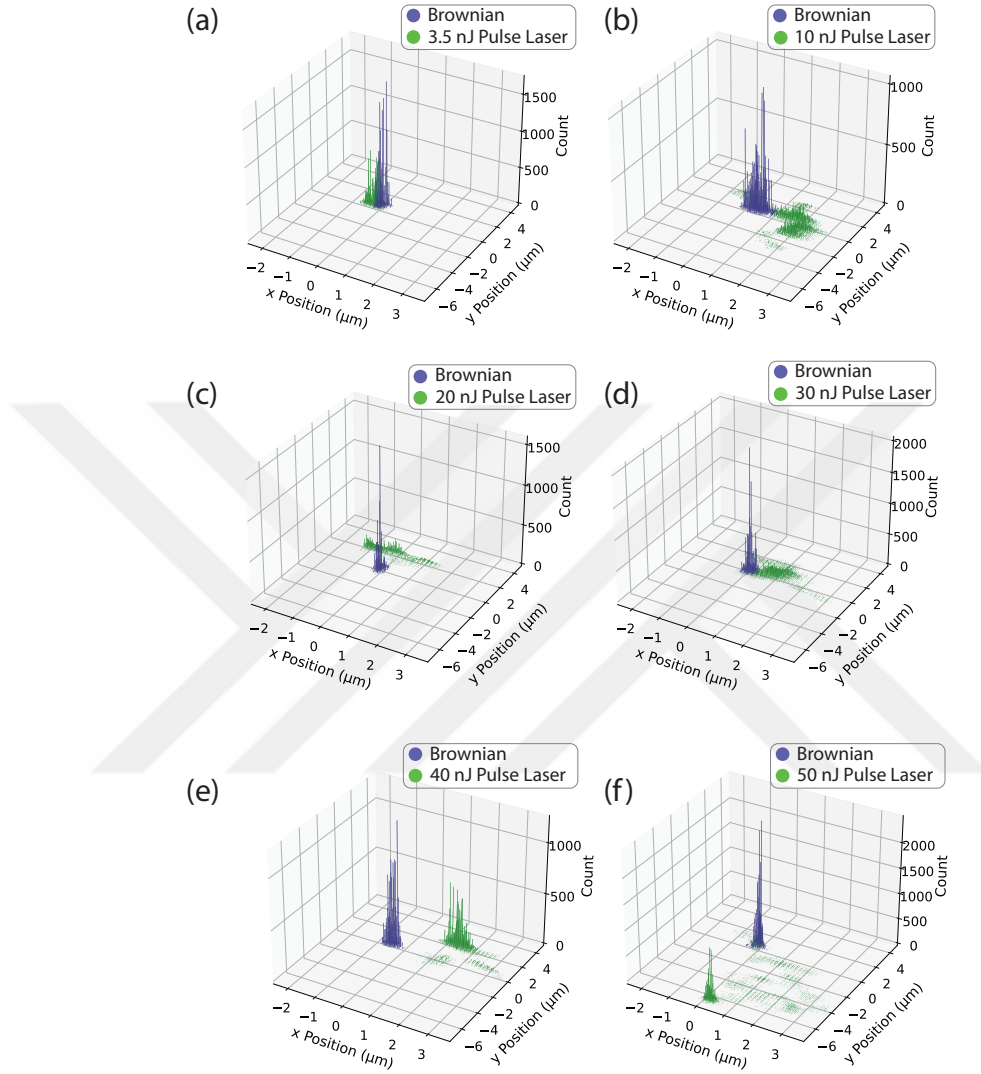


Figure 5.5 3D histograms of the trajectories in Figure 5.4.

The mean square displacement (MSD) of the particles above is plotted in Figure 5.6. The average of all the Brownian motions when the laser is off is shown in black. Figure 5.6a shows a log-log scale to highlight the differences in the behaviors in Brownian motion.

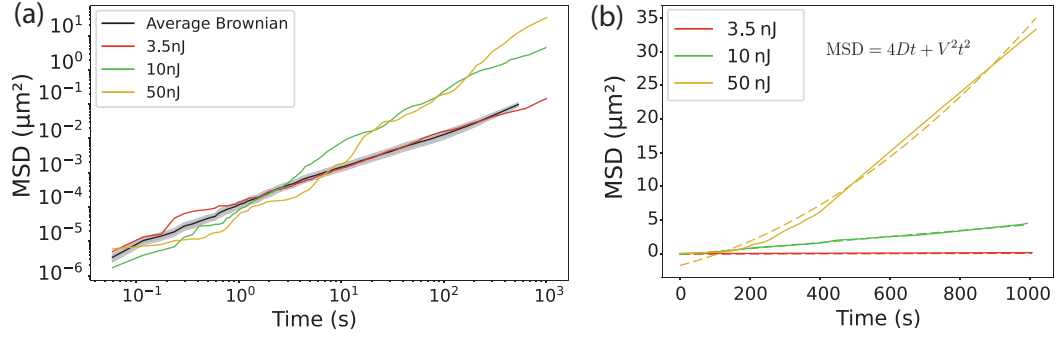


Figure 5.6 MSD of the Janus particles. 3.5 nJ and the average of Brownian motion have almost the same slope, showing that the laser did not affect the particle Brownian motion. For 10 nJ, the slope is steeper than 3.5 nJ, and for 50 nJ, the line goes parabolic, indicating the super-diffusivity state in (a) log-log scale and (b) linear-linear representation.

Influence of Laser Beam Spotsize of $\omega_0 = 2.8\mu\text{m}$: We repeated the experiments from Section 2.1 using a laser spot size approximately twice as large ($\omega_0 = 2.8\mu\text{m}$) while keeping the laser fluence constant. The 3D histogram data for both spot sizes are plotted in Figure 5.7. In both cases, the particles exhibit similar histogram counts corresponding to low-, medium-, and high-influence regimes. Additionally, the larger spot size allowed the particles to travel farther from their initial positions.

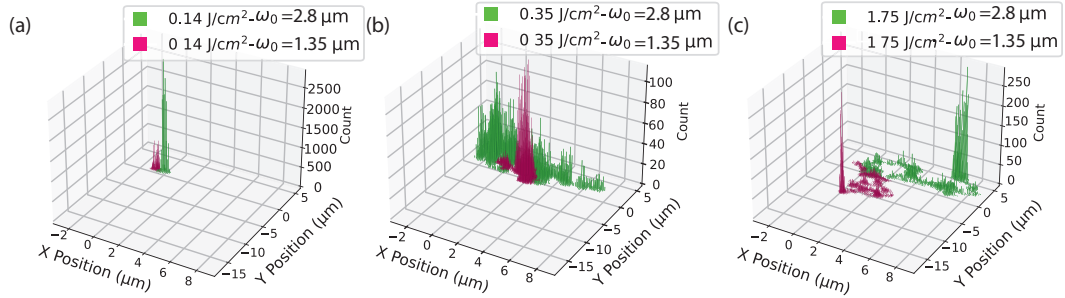


Figure 5.7 3D histogram in three regimes (a) low- (b) medium- and (c) high-influence regime for (green) $\omega_0 = 2.8\mu\text{m}$ and (red) $\omega_0 = 1.35\mu\text{m}$.

The MSD curves obtained from particle tracking data presented in Figure 5.8 further confirm that a larger spot size extends the range of motion, highlighting the role of thermophoresis in the movement of the Janus particle.

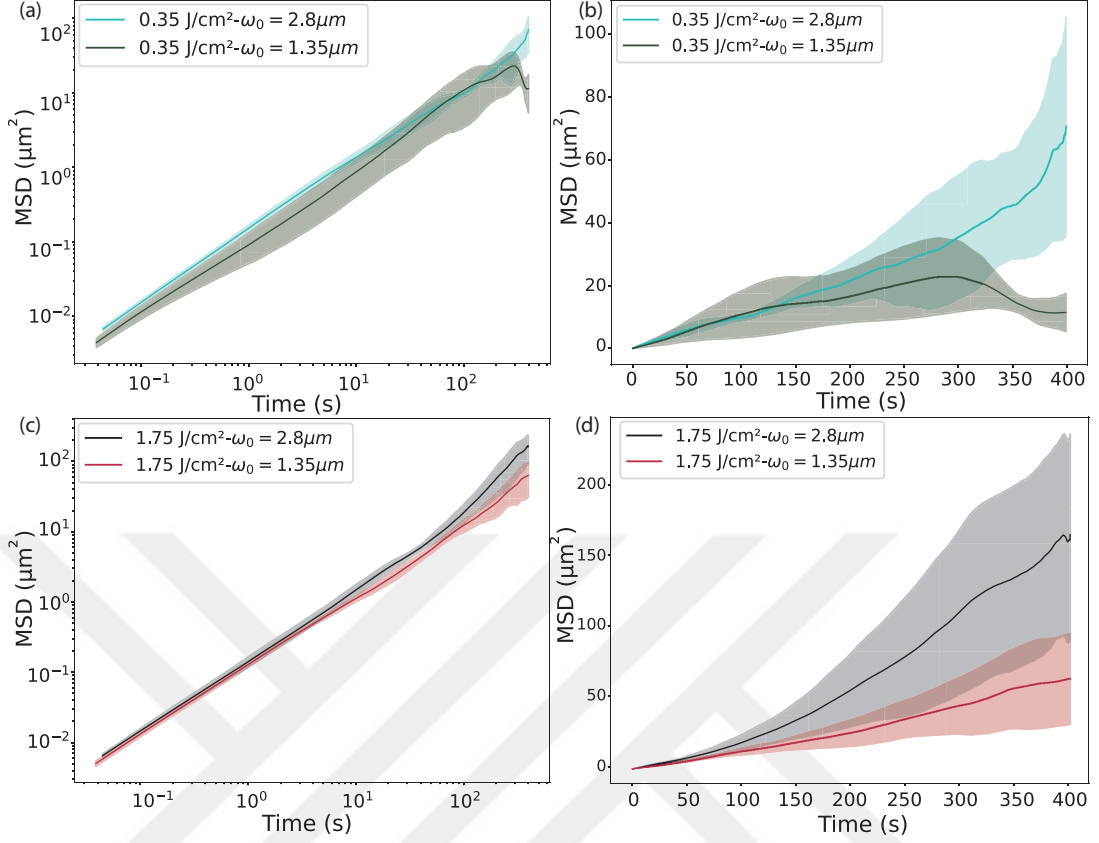


Figure 5.8 MSD vs time plots of the Janus particles for spot size comparison in log-log scale for (a) laser fluence of 0.35 J/cm^2 and (c) 1.75 J/cm^2 and in linear scale for (b) laser fluence of 0.35 J/cm^2 and (d) 1.75 J/cm^2 .

5.2.3 Manipulation of the Au-Janus Particles

In this section, we present our investigation into the optical manipulation of Au-Janus particles using nanosecond-pulsed laser illumination. The experiments were conducted using the same setup detailed in the previous section.

As illustrated in Figure 5.1(a), the laser beam was focused on the particle plane at a distance defined as d from the center of the particle. The translational displacement of the Au-Janus particles suspended in the water together with the laser spot (illustrated in Figure 5.9(a)) was measured at pulse energies between 3.5-50 nJ, with an average power of 35-500 μW , respectively. The threshold pulse energy required to attain translational movement was measured to be approximately 3.5 nJ. We manip-

ulated the position of Janus particles by moving the sample holder stage against the laser spot and arranged them into the desired pattern depicted in Figure 5.9(b). When the laser approached approximately $d = 3.4 \mu\text{m}$ to the Janus particle, the laser began to exert influence on it due to the laser absorption ($\alpha_{\text{gold}} = 5.41 \times 10^5 \text{ cm}^{-1}$ at 532 nm). As we push the Janus particle against the laser spot, we observed that depending on the pulse energy of the laser, the separation defined as d in Figure 5.1(g) has increased. For example, at pulse energies near the threshold, the average separation was $d = 1.6 \pm 0.4 \mu\text{m}$. However, at 50 nJ, this distance was raised to $d = 2.6 \pm 0.2 \mu\text{m}$. This observation suggests that the particle adjusts its distance from the laser spot based on the applied pulse energy. To see how it affects the maximum temperature elevation, we calculated the temperature increase of the gold cap, taking into account the corresponding separations of d measured from recorded movies at pulse energies of 4 nJ, 20 nJ, and 50 nJ. We used the model we developed based on heat transfer equations for pulsed laser illumination. The calculated temperature profile over 100 ns is plotted in Figure 5.9(c). Shaded areas correspond to the temperature profiles calculated with minimum/maximum separation values of d where the particle is translated together with the laser, and the solid line represents the average temperature elevation profile. From Figure 5.9(c), it is understood that a wide range of temperature elevations are eligible to induce translational movement, starting at a minimum of 50°C up to 290°C scaling with incident pulse energy. The pronounced temperature gradient around the particle [153] drives slip flows due to the tendency of fluids to move from colder to hotter regions [164], generating a force that moves the particle in the opposite direction of the temperature gradient [151]. Later we estimated the translation velocity of the particles while they stayed coupled with the laser spot from the recorded movies in Figure 5.9(d). The average elevated temperature of $\Delta T = 170^\circ\text{C}$ lasted for tens of nanoseconds at 50 nJ of pulse energy allowed us to translate the particles 5.7 times faster ($5.1 \mu\text{m/s}$) as opposed to the threshold value of 4 nJ where it was only estimated as $0.9 \mu\text{m/s}$ (Figure 5.9(d)). Consequently, the interplay between the pulse energy, the induced temperature gradient, and the resulting thermophoretic forces governs both the translation velocity and the particle's ability to stay coupled with the laser spot.

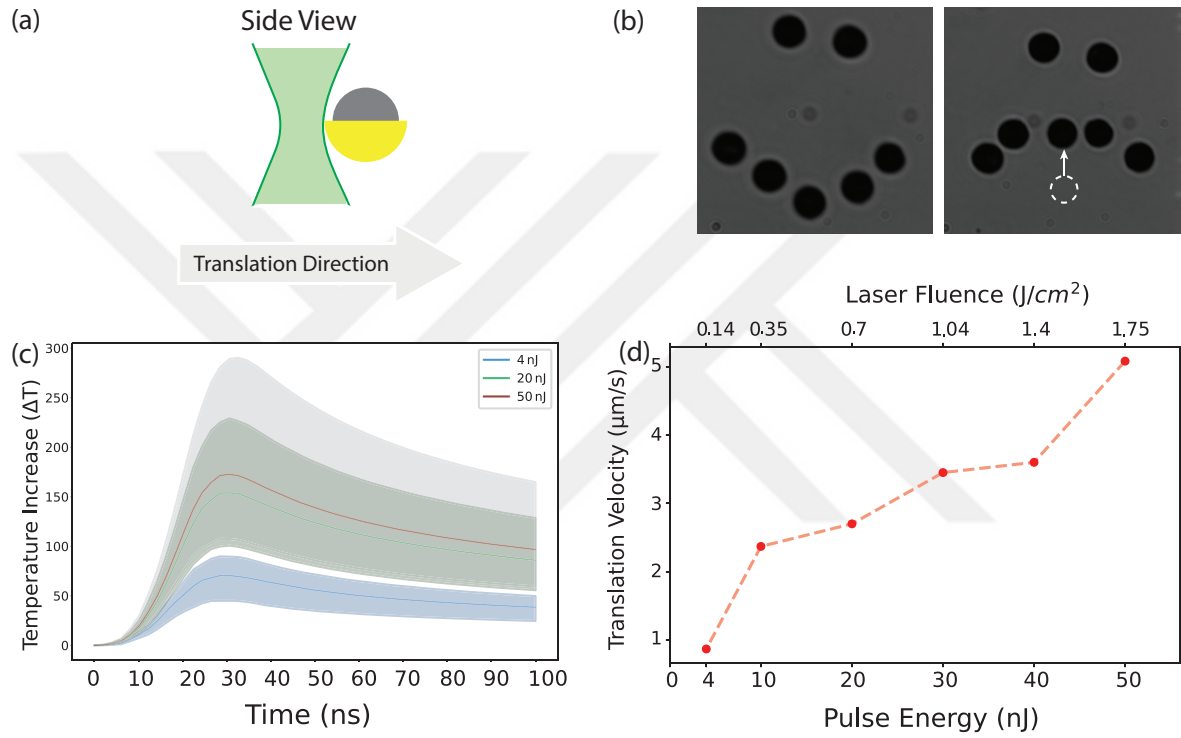


Figure 5.9 Au-Janus particle manipulation. (a) The schematic of the Janus particle and the laser beam arrangement together with the translation direction. On the side view, solid lines represent $1/e^2$ profile. (b) Janus particles in the desired pattern, the white arrow shows the direction of movement, and the dashed circle represents the initial position. (c) Calculated temperature profiles by considering the minimum and maximum values measured for the separation, d , at pulse energies of 4 nJ, 20 nJ, and 50 nJ. (d) The translation velocity of the particles moving together with the laser at given pulse energies and corresponding laser fluences.

To show the effective energy deposition ability of pulsed laser illumination, we estimated the required CW laser power to achieve similar temperature elevations acquired in the tens of nanoseconds time range with the pulsed laser. To do that, we have incorporated the expressions derived to estimate the temperature elevation of the gold cap [165] with a CW laser source. For example, with 20 nJ of pulse energy, we achieved an average temperature elevation of $\Delta T = 170^\circ C$ for 10 ns. According to the expression derived in [165, 150] CW power of 8.5 mW is necessary to achieve such ΔT . Furthermore, we experimentally tried to initiate the movement of Au-Janus particles with a CW laser source using the experimental setup similar to the pulsed laser one. However, even though we exposed the particles to as high as 6 mW of power at 532 nm, we did not observe any discernable movement. Notably, the movement threshold in the pulsed laser was 4 nJ in 10kHz, corresponding to the average power of 40 μW . The results of the CW experiments demonstrate that a nanosecond pulsed laser can move the Janus particles with significantly lower average power compared to a CW laser.

We additionally investigated the role of the gold cap in the movement. An uncoated, polystyrene (the same polystyrene particles were used to make the Janus particles) was exposed to the same pulse energies. We did not observe any movement in the lateral direction, but a perpendicular movement to the sample plane was observed with pulse energies as high as 700 nJ (7 mW at 10 kHz), indicating the effect of the laser radiation pressure wave pushing the particles in the direction of laser beam propagation.

Figure 5.10(a) shows the effect of distance on the temperature elevation with 4 nJ of pulse energy. Figure 5.10(b) illustrates the temperature variations with different pulse energies, maintaining a constant distance of 3.4 μm between the particle and the laser spot in the simulation. Figure 5.10(c) shows the distance of the particle and the center of the laser spot in a trial. The distance varies according to the pulse energy, as shown in Table 5.1.

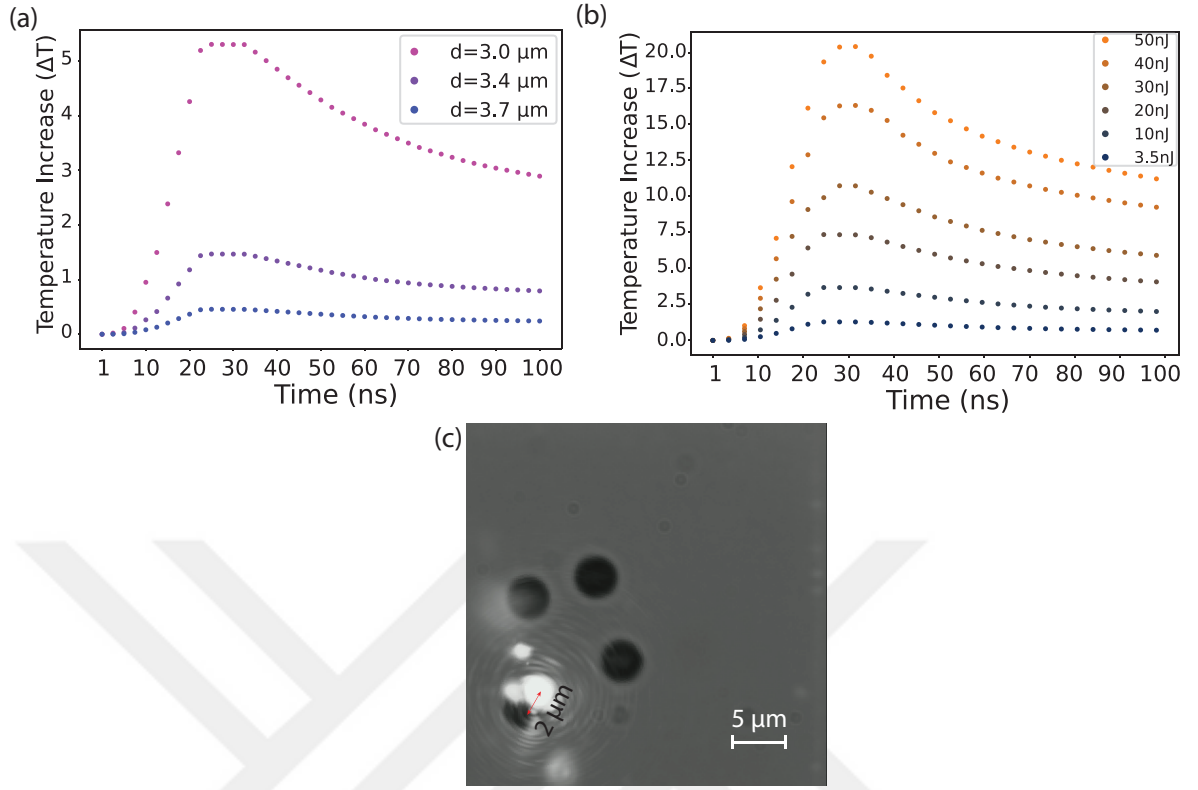


Figure 5.10 (a) The temperature of the Janus particles varies based on their distance to the laser beam. (b) The temperature increase of the Janus particle when the distance between the laser and particle is $3.4 \mu\text{m}$. (c) The distance from the particle to the center of the laser spot was recorded during a trial.

Table 5.1

Distance between the particle and the center of laser spot.

Pulse Energy	Average Distance	Minimum / Maximum
4 nJ	$1.6 \mu\text{m}$	0.4
20 nJ	$2.2 \mu\text{m}$	0.2
50 nJ	$2.6 \mu\text{m}$	0.2

To calculate the temperature of the Au-Janus particle under CW illumination, we used the equation below [150].

$$P = 2(2 + \pi)\kappa_{\text{water}}R\Delta T \quad (5.6)$$

where κ_{water} (0.6 W/m.K) is the heat conductivity of water, R ($2.05 \mu\text{m}$) is the ra-

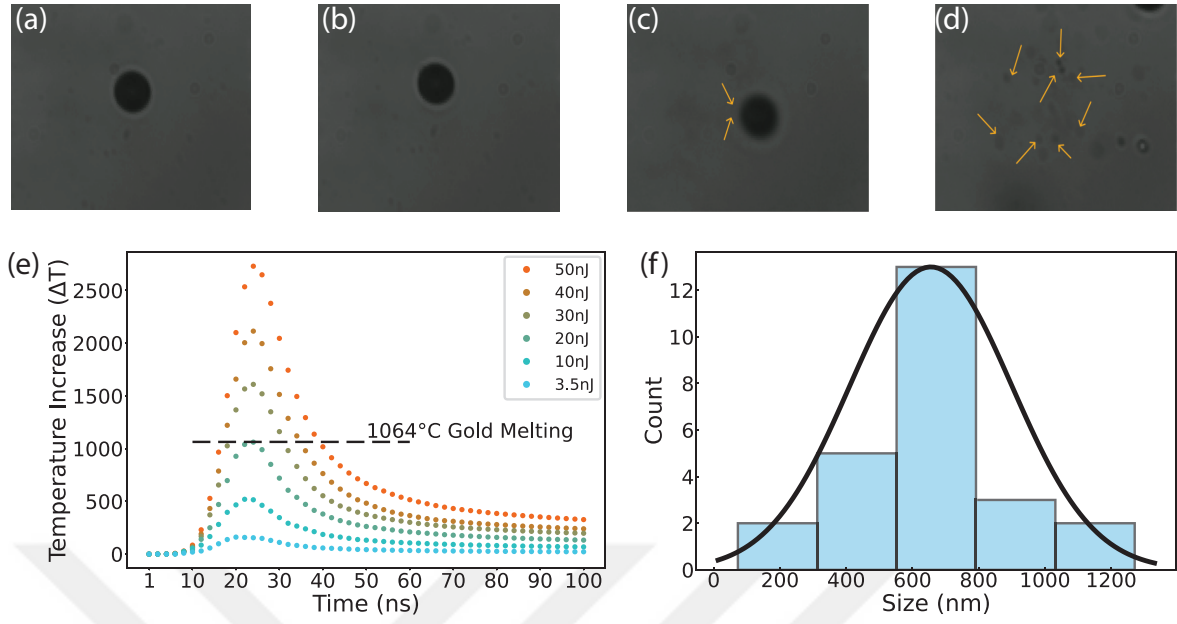


Figure 5.11 The single laser pulse experiment result. Janus particle (a) before laser illumination and after exposure to pulse energies of (b) 3.5 nJ, (c) 20 nJ, and (d) 50 nJ. (e) Calculated temperature increase of Janus particle at the center of the laser pulse illumination. (f) Size distribution of gold particles generated by a single 50 nJ, 10 ns pulse with fluence of 1.75 J/cm^2 .

dius of the particle, P is the power absorbed by the metal cap. When we place all the known values to equation 5.6, the required power (P) to elevate the temperature between $100\text{-}200^\circ\text{C}$ is estimated to be $5\text{-}10 \text{ mW}$.

5.2.4 Damage Threshold and Ablation of Au-Janus particles

In this section, We explored the interaction between a single laser pulse and Au-Janus particles with the experimental setup depicted in Figure 5.13. The laser pulse duration (FWHM) is 10 ns and focused on the particle. The pulse energies in this experiment ranged from 3.5 nJ to 50 nJ, similar to what we used in the aforementioned experiments.

Figure 5.11(a) shows the Au-Janus particle shows the particle before the laser incidence. Figures 5.11(b-d) demonstrates particles exposed to 3.5 nJ, 20 nJ and 50

nJ. Figure 5.11(d) left the field of view by ejecting the finer particles. We employed a model based on heat transfer equations to calculate the gold cap's surface temperature after the laser pulse's arrival. The calculated results in Figure 5.11(e) imply that a pulse energy of 20 nJ provides sufficient heating to melt the gold cap, considering the melting point of gold is 1064°C. Although gold's absorption is temperature-dependent, its absorption barely changes even when the gold reaches high temperatures under laser illumination at 532 nm [166]. We carried out experimental tests to validate our theoretical calculation. Focused single laser pulses with 20 nJ of pulse energy (0.7 J/cm²) were sent at the Au-Janus particle, and it was observed that debris detached from the particle. We found that the calculated temperatures are consistent with experimental results Figure 5.11(c).

In 50 nJ of pulse energy (1.75 J/cm²), the gold cap's ablation generates micron and sub-micron size gold particles [167, 168], and the particle escapes the field of view. Figure 5.11(f) illustrates the size distribution of these ablated particles in a histogram, with a Gaussian function fitted to the data.

This experiment also uses 3.5 nJ, 10 nJ, 20 nJ, 30 nJ, 40 nJ, and 50 nJ of pulse energies. In figure 5.12, the laser effect on the particles. The "Laser Off" column shows the Janus particle right before the laser incident. The middle column, "Right After Laser Pulse," shows the Janus particle exactly after the laser incident, and in the third column, "Long After Laser Pulse," the particle's image is taken one second after the laser incident.

5.3 Conclusion

Our study demonstrates the potential of nanosecond-pulsed lasers as an effective tool for manipulating Au-Janus particles with significantly reduced power requirements compared to continuous-wave lasers. The study highlights the effectiveness of nanosecond pulsed lasers for particle manipulation, presenting a novel and efficient alternative

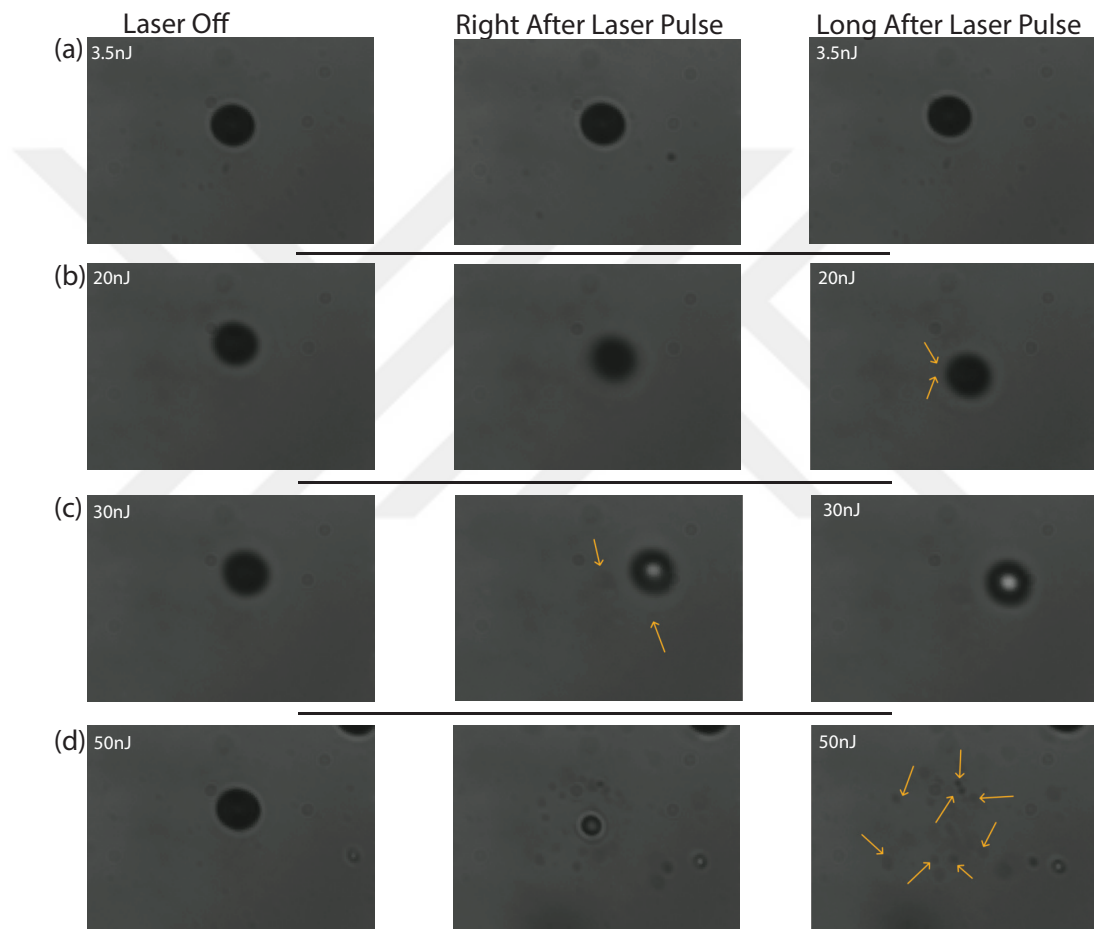


Figure 5.12 The single laser pulse experiment. Particles are shown when the laser is off, right after, and long after turning on the laser.

to continuous-wave lasers. Our study concluded with three sections. We studied the influence of nanosecond-pulse lasers on the Brownian motion of the particles. We observed three regimes: in the first regime, the particle's Brownian motion remains undisturbed; in the second regime, the particle does a broader Brownian motion; and in the third regime particle shows a superdiffusive behavior and continues its Brownian motion at a new location. In the second section, we examined the threshold pulse energy needed to initiate the movement of the Au-Janus particle. We found that this threshold pulse energy is 4 nJ. Additionally, we discussed how the minimum distance between the particle and the laser spot changes as the pulse energy varies. Finally, through theoretical calculations and experimental validation, we determined the critical pulse energy required for gold cap ablation and observed the formation of micron- and sub-micron-sized gold particles. These findings not only validate the precision and versatility of pulsed lasers in particle manipulation but also open new avenues for power-efficient techniques in the design and application of asymmetrical materials.

5.4 Methods

Experimental Setup:

Figure 5.13 presents a schematic of the experimental setup. A 10X objective and a convex lens ($f=5$ mm) were incorporated into the optical path to achieve two laser beam spot sizes, as illustrated in Figure 5.13. The laser beam spot sizes were measured using the knife-edge technique, yielding $\omega_0=1.35$ μm for the 10X objective and $\omega_0=2.8$ μm for the $f=5$ mm convex lens.

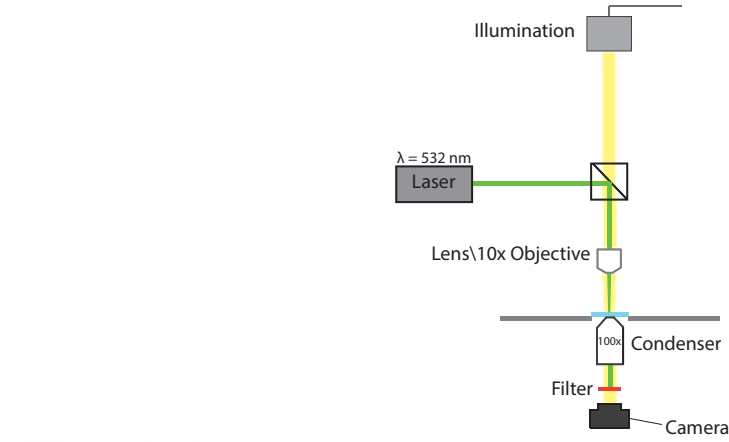


Figure 5.13 Schematic of the experimental setup. The laser beam was focused with a 10X objective/convex lens ($f=5$ mm) on the sample plane, and a 100X objective collect the images from the sample plane. A red filter is also used in some experiments to block the laser from entering the camera.

Janus Particles:

The Janus Particles were prepared by metal coating one hemisphere of dielectric spherical particles. First, 60 μL of a 5 mg/mL particle suspension was spread on a microscopy slide and allowed to dry. The obtained monolayer was subsequently coated with a 100 nm Au layer using a sputter coating device (Safematic, CCU-010), dispersed in 50 μL milliQ water by sonication, and concentrated to a final volume of 0.5 μL . The dielectric particles used included polystyrene spheres with $d=4.1$ μm (Microparticles GmbH, batch code: PS/Q-R-KM427).

Pulsed Laser System Setup:

The experimental setup and the schematic is shown in Figure 5.13. The laser (Spectra-Physics, Explorer One) was operating at 532 nm and equipped with an electro-optic Q-switch that allowed us to modify the temporal output of the laser on demand. This allowed us to send a single pulse or burst of pulses to the sample to study the interaction between the optical pulses and Janus particles. The laser was focused with a 10X objective lens (Olympus PLN 10X Objective NA=0.25) to a beam waist spot size of 2.7 μm , measured by knife-edge technique, with the objective being underfilled. We

sent 4 nJ, 10 nJ, 20 nJ, 30 nJ, 40 nJ, and 50 nJ of pulse energies to the Janus particle. The sample was illuminated by an LED source and imaged with an oil-immersed 100X objective onto the camera (AM-Scope), where the transmitted laser was blocked by a filter (DMLP-550 nm). Finally, we navigated the sample manually with translational stages in X and Y directions (Thorlabs, XRN-25P/M). The samples were prepared by cleaning a glass slide and sticking a double-sided tape mask to the slide. Afterward, 15 μL of the particles were poured onto the glass slide, and finally, a cover slip was put on the glass slide.

Temperature Calculation:

Theory: To study the interaction between the Au-Janus particles and the laser, we conducted Finite Element Method (FEM) to simulate the heat transfer from the laser to the gold cap of the particles. Therefore, the key equation within our simulations is the heat conduction equation, written in cylindrical coordinates due to the axial symmetry of the system. The formulation of this equation is as follows:

$$\rho_{\text{gold}} C_p \left(\frac{\partial T_{\text{gold}}}{\partial t} \right) = \frac{k_{\text{gold}}}{r} \frac{\partial}{\partial r} \left(r \frac{\partial T_{\text{gold}}}{\partial r} \right) + k_{\text{gold}} \frac{\partial}{\partial z} \left(\frac{\partial T_{\text{gold}}}{\partial z} \right) + Q(r, z, t) \quad (5.7)$$

Where T_{gold} , ρ_{gold} , C_p , k_{gold} , and $Q(r, z, t)$ are defined as gold density, the specific heat of the gold cap, heat conductivity of gold, and the laser heat generation density, respectively.

$Q(r, z, t)$ can be written as

$$Q(r, z, t) = Q_0 \exp\left(\frac{-2r^2}{\omega_0^2}\right) \exp\left(\frac{-t^2}{2\tau^2}\right) \exp(-\alpha z) \quad (5.8)$$

r and t represent the spatial and temporal variables, respectively. $2\omega_0$ is the beam waist spot-size, and τ denotes the standard deviation of the pulse duration, P_d , to make a Gaussian temporal profile ($\tau = \frac{FWHM}{2\sqrt{2\ln 2}}$). α expresses the absorption coefficient of gold, which states how much the beam penetrates into the material. The heat that is generated by the laser can be written as:

$$Q(r, z, t) = Q_0 \exp\left(\frac{-2r^2}{\omega_0^2}\right) \exp\left(\frac{-t^2}{2\tau^2}\right) \exp(-\alpha z) \quad (5.9)$$

By integrating equation 5.9, we have

$$\int \int Q dV dt = E_{\text{Pulse}} \quad (5.10)$$

E_{Pulse} designates the pulse energy of the laser. By substituting Eq. 5.9 into Eq. 5.10, the integration yields

$$Q_0 \int_0^{2\pi} d\phi \int_0^\infty r \exp\left(-\frac{2r^2}{\omega_0^2}\right) dr \int_0^\infty \exp\left(-\frac{t^2}{2\tau^2}\right) dt \int_0^l \exp(-\alpha z) dz = E_{\text{Pulse}} \quad (5.11)$$

Since $\alpha l \ll 0$

$$Q_0 = \frac{2E_{\text{Pulse}} \alpha}{\pi \omega_0^2 \tau \sqrt{\frac{\pi}{2}}} \quad (5.12)$$

The final form of the $Q(r, z, t)$ is

$$Q(r, z, t) = \frac{2E_{\text{Pulse}} \alpha}{\pi \omega_0^2 \tau \sqrt{\frac{\pi}{2}}} \exp\left(\frac{-2r^2}{\omega_0^2}\right) \exp\left(\frac{-t^2}{2\tau^2}\right) \exp(-\alpha z)(1 - R_{\text{ref}}) \quad (5.13)$$

R_{ref} is the reflection coefficient.

Upon formulating the heat conduction equation and the laser heat generation density, it's essential to define the boundary conditions for the simulation. These conditions help govern the temperature changes at the interfaces of different materials within our system.

The boundary conditions used in this simulation are as follows:

On the gold cap and water boundary at $r = R + l$ and $-\pi < \theta < 0$:

$$k_{\text{gold}} \vec{\nabla} T_{\text{gold}} = k_{\text{water}} \vec{\nabla} T_{\text{water}} + h(T_{\text{water}} - T_{\text{initial}}) + \epsilon_{\text{gold}} \sigma (T_{\text{water}}^4 - T_{\text{initial}}^4) \quad (5.14)$$

Where ϵ_{gold} is the emissivity of the gold cap, σ is the Stefan-Boltzmann constant, and h is the heat transfer coefficient, and R is the radius of the particle and l is the thickness of the gold cap.

On the gold cap and core at $r = R$ and $-\pi < \theta < 0$:

$$k_{\text{gold}} \vec{\nabla} T_{\text{gold}} = k_{\text{core}} \vec{\nabla} T_{\text{core}} \quad (5.15)$$

On the core and water at $r = R$ and $0 < \theta < \pi$:

$$k_{\text{core}} \vec{\nabla} T_{\text{core}} = k_{\text{water}} \vec{\nabla} T_{\text{water}} + h(T_{\text{water}} - T_{\text{initial}}) \quad (5.16)$$

Finally, the temperature of water at the borders of the water container is set to room temperature (298K).

Table 5.2 below shows the values used in the calculation.

Table 5.2
Properties and values required for numerical analysis.

Property	Symbol	Value	Reference
Reflection coefficient	R_{ref}	0.76	[169]
Absorption coefficient	α	$5.41 \times 10^5 \left(\frac{1}{\text{cm}}\right)$	[170]
Pulse duration	τ	10 ns	
Beam waist	ω_0	$1.3 \mu\text{m}$	
Pulse energy	E_{pulse}	3.5–50 nJ	
Heat conductivity of gold	κ_{gold}	$314 \frac{W}{m K}$	[171]
Heat conductivity of water	κ_{water}	$0.6 \frac{W}{m K}$	[171]
Emissivity of gold	ϵ_{gold}	0.3	
Stefan-Boltzmann constant	σ	$5.67 \times 10^{-8} \left(\frac{W}{m^2 K^4}\right)$	[150]

Figure 5.14 depicts two laser incident orientations on the gold cap. In the Brownian motion analysis and manipulation of the Janus particles, the laser illuminated the side of the Janus particles, and in the damage threshold studies, the laser illuminated the center of the gold cap.

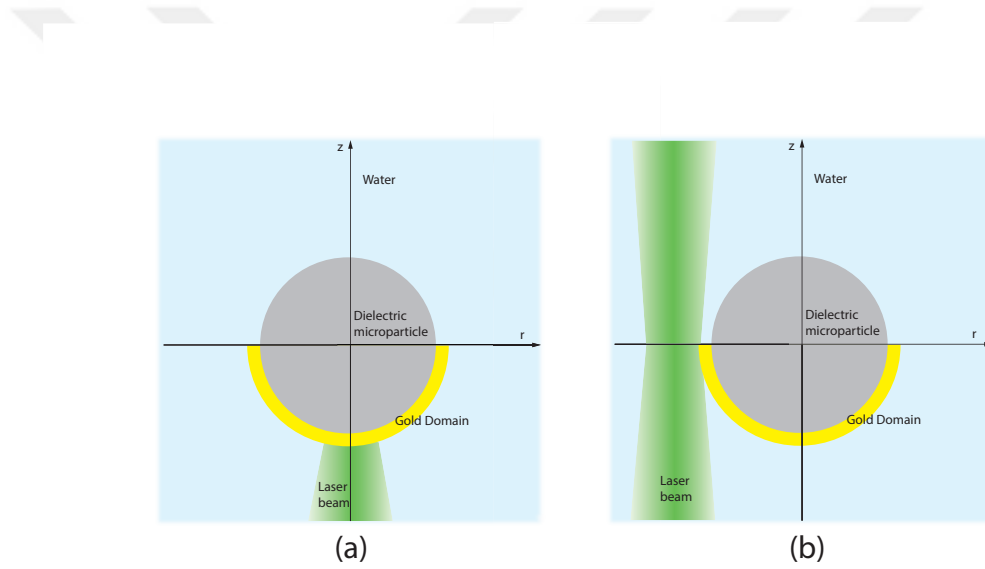


Figure 5.14 The orientation of the laser beam and gold cap of the Janus particle in the simulation. (a) the laser illuminates the center of the gold cap, (b) the laser illuminates the side of the gold cap.

6. ADDITIONAL WORKS

6.1 The Simulation of Acoustic and Optical Tweezer

One of the objectives of my scholarship was to simulate a setup where a particle is simultaneously trapped using both acoustic and optical tweezers. This simulation aimed to establish a theoretical foundation for a future experimental setup intended to measure interaction forces in systems exhibiting collective behavior. Collective motion refers to coordinated movement patterns observed in groups of active particles, where interactions among individual entities lead to organized behaviors such as clustering, alignment, and directional migration. Understanding and controlling collective behavior can significantly advance applications in biomedical engineering, microfluidics, and targeted drug delivery.

To simulate this dual trapping setup, the main governing equation (as introduced in Chapter 1, Eq. 1.8) was extended to include the forces contributed by acoustic and optical tweezers. For acoustic trapping, it was assumed that an acoustic transducer generates a standing acoustic wave. The acoustic radiation force exerted by this wave on spherical particles along the x-axis is given by:

$$F_y = 4\pi\Phi(\tilde{\kappa}, \tilde{\rho})kr^3 \sin(2ky). \quad (6.1)$$

To incorporate the acoustic force into the simulation, it was normalized by the friction coefficient ($\zeta = 6\pi\eta r$) of the particle, resulting in:

$$x_i = x_{i-1} + \sqrt{2\Delta t}\xi_x + \frac{F_{Acoustic}}{\zeta}dt \quad (6.2)$$

The optical trapping force, typically represented by restoring force ($F = -kx$). Where k is the stiffness of the optical trapping potential, and was similarly normalized by the friction coefficient, giving the updated equation:

$$x_i = x_{i-1} + \sqrt{2\Delta t}\xi_x + \frac{F_{Acoustic}}{\zeta}dt + \frac{F_{Optical}}{\zeta}dt, \quad (6.3)$$

which can be written as

$$x_i = x_{i-1} + \sqrt{2\Delta t}\xi_x + \frac{4\pi\Phi(\tilde{\kappa}, \tilde{\rho})kr^3 \sin(2kx_{i-1}) - kx_{i-1}}{\zeta}dt. \quad (6.4)$$

Although the optical force presented above utilizes a basic harmonic potential model, it is a widely accepted simplification. A neural network model trained within the "ACTIVEMATTER" [172] research initiative could offer more accurate predictions, indicating a promising direction for future simulations. The finite element method (FEM) was employed to perform numerical simulations, as detailed earlier in Chapter 1. Acoustic waves in the MHz range were propagated through water, and three simulation scenarios, each initialized with different random seeds, were conducted to emphasize the direct impact of acoustic forces on particle dynamics. Results consistently showed that increasing acoustic force progressively displaced particles from their optical trap equilibrium positions, providing clear computational evidence of the interplay between acoustic and optical forces. These findings establish a strong theoretical basis for further experimental setups aiming to measure forces and dynamics in systems exhibiting collective behavior. The result is shown in the Figure 6.1.

6.2 Polystyrene Particles Getting Pushed via Dyed Medium

In this additional study, we investigated the propulsion of polystyrene particles suspended in a dyed medium, driven indirectly by acoustic waves generated through laser-induced heating. This innovative approach diverges from traditional direct optical manipulation by exploiting photothermal effects: laser interaction with the dye in the medium produces localized heating, leading to rapid thermal expansion and the generation of acoustic waves that propel particles indirectly.

Figure 6.2 visually illustrates the fundamental mechanisms underlying this indirect propulsion approach. Panel (a) shows a pulsed laser spot inducing photoacoustic waves, which indirectly push the polystyrene particle away from the laser spot. Panel (b) depicts a pulsed laser configured as a ring, generating concentric photoacoustic

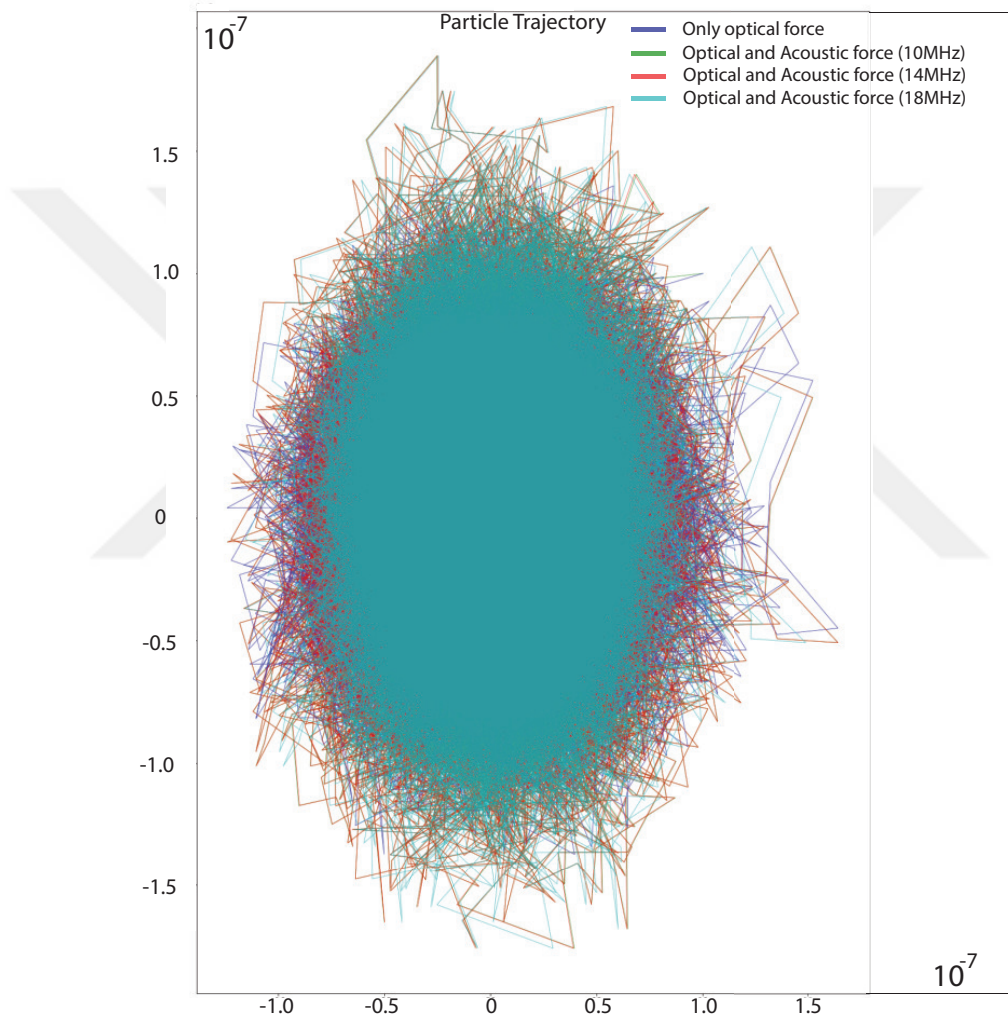


Figure 6.1 The simulated trajectories for a particle that is acoustically and optically trapped.

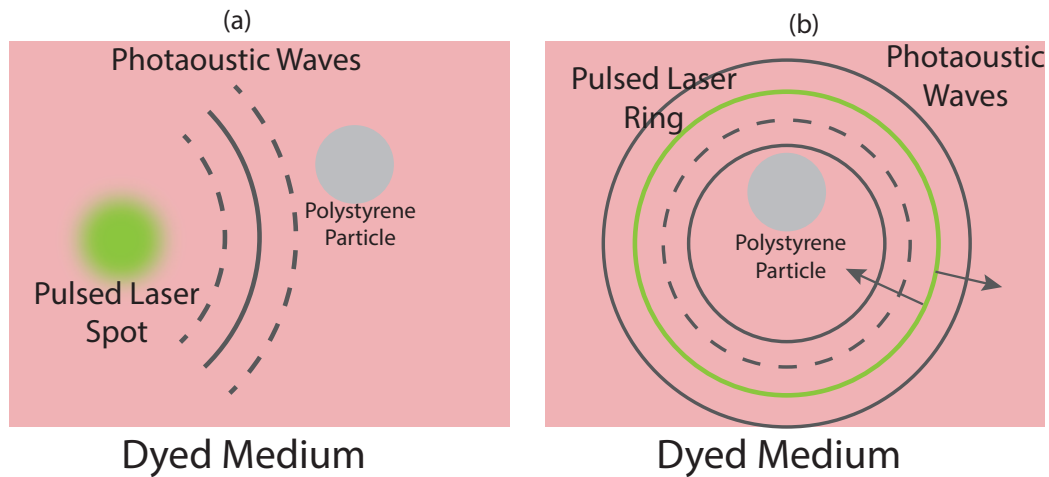


Figure 6.2 Photoacoustic waves generated in dyed medium. (a) When the spot of the laser illuminates the dyed medium (due to absorption of the laser by the medium), acoustic waves are generated, and these waves can push the polystyrene particles. (b) Transitioning from a spot to a ring-shaped laser changes how acoustic waves propagate, generating waves that propagate both toward the center of the ring and outward from it.

waves that effectively trap and control the particle's movement. At this configuration, the ring laser generates acoustic waves in two directions one is inward and outward of the ring.

This study was inspired by pioneering work from Zharov et al., who first demonstrated the effectiveness of photoacoustic manipulation using continuous and pulsed laser sources. Zharov's research illustrated the creation of stable acoustic pressure nodes and anti-nodes capable of trapping or propelling particles through gradient acoustic forces [173, 174]. Additionally, Galanzha et al. successfully applied similar principles in vivo, demonstrating non-invasive cellular manipulation, thereby highlighting the considerable potential of this technology for biomedical applications [175].

Our research specifically aimed to validate and extend these foundational studies, assessing the impact of variables such as dye concentration, laser intensity, and medium properties on particle propulsion efficiency and controllability. Initial results indicate that this indirect acoustic propulsion technique provides significant advan-

tages, including minimized risk of photodamage and enhanced precision, making it highly suitable for sensitive biological applications. Future work will focus on quantitative evaluations, optimization of system parameters, and comprehensive experimental validation, potentially broadening the scope of active matter manipulation in biomedical fields.



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