Optical manipulation and study of single gold nanoparticles in solution

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Introduction

In this thesis we aim to investigate the optical trapping of gold nanoparticles, both as an approach to study single gold nanoparticles in solution, as well as to explore the use of single gold nanoparticles as a tool for mechanical manipulations on the nanoscale. In this chapter we will motivate the subject and the chosen approach, and outline the contents of the thesis.

1.1 Nanoparticles: bridging the world between atoms and bulk matter

Consider a cube of solid gold with sides of 1 m, and imagine that we cut it into eight equal pieces. Apart from their reduced dimensions, the resulting smaller cubes will have the same intensive properties as the original in every sense: they will have the same elastic moduli, the same heat capacity per unit volume, the same thermal conductivity, the same melting temperature, the same density. If the original cubes looked shiny and yellowish-orange, the smaller cubes look shiny and yellowish-orange as well. You may say that this is obvious: the smaller cubes are still made out of gold, with the intrinsic material properties that belong to it.

However, knowing that matter is made out of atoms, we realize that we can not keep dividing the cubes of gold into smaller and smaller pieces and expect their material properties to remain constant; at some point we will

notice the discrete nature of matter. In this range, material properties will depend on the size and shape of the object, and may become very different from the bulk material properties. Clusters of matter in this size range –roughly 1 nm to 100 nm– are called nanoparticles.

It is one of the big challenges of science today to understand the properties of these nanoparticles as functions of their size and shape. Besides fundamental interest, the progress in this field has many real world applications. An example is the structure of computer chips that have steadily reduced in dimensions since their introduction in the early 1950s. The elements in computer chips are now reaching dimensions where the effects of deviations from bulk matter behavior are becoming important. Besides overcoming technical hurdles to allow the making of ever smaller devices, the study and engineering of nanoparticles and nanostructures allows for an entirely different approach: using the size and shape dependence of the properties to create novel materials with tailor-made functions, opening a wide range of exciting new applications. In recent years, technical developments have made it possible to have an ever increasing control over the size and shape of nanoparticles, and nanostructures of ever increasing complexity are fabricated. The science of nanoscale matter is characterized by a continuing exchange between fundamental insights and the development of new applications. This thesis serves as an example; we will investigate both the intrinsic properties of nanoparticles and their interaction with light, and we will explore the applications that are enabled by these properties.

Optical properties of noble metal nanoparticles

This thesis is about metal nanoparticles, and in particular about their optical properties. Among the various curious material properties of metal nanoparticles, their optical properties take a special place. Gold nanoparticles were already used by the Romans to give a ruby-red color to glass, the most famous example being the Lycurgus cup from the 4th century AD, on display in the British museum in London.[1] The production of gold-ruby glass was rediscovered in Europe only in 17th century by Andreas Cassius and Johann Kunckel.[2] The fact that the ruby-red color was due to colloidal gold particles was probably not known to either the Romans or the 17th century Europeans, and was only recognized clearly after the first scientific studies on the optical properties of metallic films and colloids by Michael Faraday[3] in 1857. The precise mechanism of the coloration was not understood until the beginning of the 20th century, when Gustav Mie developed the general theory to calcu-

late the absorption and scattering of light by spherical particles.[4–6] †

The special optical properties of gold nanoparticles are due to the collective oscillation modes of the conduction electrons in the particle, known as localized surface plasmons. Upon excitation by light, the conduction electrons in the metal will collectively shift with respect to the immobile ions. The shift of the electrons with respect to the immobile ions creates a restoring electric field at the particle's surface, that tends to restore electrical neutrality in the particle. Combined with the electron mass, this restoring force leads to harmonic oscillations. For spherical gold particles of sizes below about 100 nm, the resonance occurs at the frequency corresponding to green light for particles embedded in water or glass. Due to the strong absorption and scattering of light at this wavelength, colloidal solutions and glasses with gold particles appear greenish in scattering, and red when observed in transmission.

Because of the resonant character of the oscillation, gold nanoparticles are very efficient scatterers and absorbers of light. This property can be exploited in numerous applications. One example is the use of gold nanoparticles as labels in biological studies, where the nanoparticle is attached to a protein of interest that would be invisible otherwise.[8–16] An important advantage of metal nanoparticles in these kinds of applications is that they are photostable. Alternative labels as organic fluorophores or semiconductor quantum dots display an erratic on-off switching of their fluorescence known as blinking and eventually photobleach. In contrast, the many electrons in metal nanoparticles never stop interacting with light. The Lycurgus cup may serve as a vivid illustration; after more than two millennia it is still as brightly colored as when it was made. In other applications, the strong absorption of nanoparticles is used to heat the particles, that can then act as a very local heat source. In combination with specific labeling to certain cells, this heating can be used to selectively destroy certain cells, for example in cancer therapy.[17]

The restoring force on the electrons – and thereby the plasmon resonance frequency – depends on the material of the particle, on its shape, and the dielectric constant of its environment. The sensitivity of the plasmon resonance to the environment can be exploited to sense the specific binding of molecules that have a different refractive index than the buffer solution, and provides new avenues to detect analytes in very low concentrations or in very small

† The solution for scattering of light by a sphere is generally referred to as Mie theory, after Gustav's Mie's seminal work[4] from 1908. Several important contributions had been made by Thomson, Rayleigh, Lorenz, Love and others, going back to the work of Clebsch in 1863, and an independent derivation has been given by Debye (1909). For a historical overview, see Kerker (1969).[7]

devices.[18,19] The shape dependence is most clearly presented in nanorods, where the plasmon resonance frequency decreases with increasing particle aspect ratio, and can be shifted from the green all the way to the near infrared. This tunability of the optical properties provides exciting options to tailor the optical properties to the demands of the experiment at hand.

Another property of the localized surface plasmon in particles is that the local electric field at the surface of the particle can be much larger than the electric field of the light exciting the plasmon. This property has various uses. In much the same way as antennas for radio-frequency waves, metal nanostructures can be used as antennas for optical frequency waves, for light. This can be used to enhance the coupling between molecular scale objects and light,[20] as has been exploited in surface enhanced Raman scattering.[21–23] Also the fluorescence of molecules can be modified, and can be either enhanced or quenched[24–26] or directed,[27] depending on the details of the used geometry.

1.2 Why study single metal nanoparticles

In this thesis we study gold nanoparticles with far-field optical microscopy, and focus on experiments on *single* gold nanoparticles. It is important to motivate why we make these restrictions.

Far-field optical studies of metal nanoparticles

A major advantage of optical microscopy is that it can access objects in solid or liquid matrices far away (up to hundreds of microns) from surfaces, with the only restriction that the matrix is (at least partly) transparent at the used wavelength. This opens the possibility of studying nanoparticles live in action in matrices of interest. Relevant examples are biological tissue or cells, or colloidal solutions. With optical microscopy, we can make use of a rich toolbox of time-resolved and frequency-resolved techniques. This thesis itself is an example of the possibilities available; we use powerful infrared continuous wave lasers for optical trapping, broad-band thermal light sources for nanoparticle characterization and ultra-fast wavelength-tunable pulsed lasers for investigation of nanoparticle dynamics on the picosecond timescale.

The biggest disadvantage of far-field optical microscopy is its limited spatial resolution. As with any wave phenomenon we are limited by diffraction, and light can not be focused to a spot smaller than about half its wavelength. For optical studies in the visible region of the electromagnetic spectrum, this limits the spatial resolution to several hundred nanometers. Tech-

niques based on electrons -scanning electron or scanning tunneling microscopy- or atomic forces can achieve much higher spatial resolution, and even resolve single atoms. However, these techniques are much more restrictive in the types of environments that can be studied, and either require vacuum conditions or are restricted to work very close (within nanometers) to the surfaces of materials.

Single particles

During many decades, metal nanoparticles have been studied on large ensembles of particles,[2,9,28–38] and until today, the bulk of studies on nanoparticles is performed on ensembles.[39] The reason that ensemble studies remain a popular choice is that optical studies can reveal a wealth of information, and studies of ensembles can be performed with relatively simple equipment, such as a spectro-photometer present in every (physical)- chemistry laboratory, and with straightforward sample preparation.

Recently, it has become possible to perform studies on single metal nanoparticles. Since the first reports on the detection of single particles about a decade ago,[8,10,40–42] the field has rapidly developed, expanding the range of particle sizes that can be detected,[43–46] either by scattering, absorption, the generation of new wavelengths by higher harmonics[47] or fluorescence, and a range of new applications has opened up.[48–51] While the experimental methods become more challenging, single-particle experiments present several important advantages:

Sample inhomogeneity is suppressed – Even the best synthesis methods yield ensembles with a distribution of particle sizes and shapes. In single-particle studies this inhomogeneity due to the distribution of particle properties in an ensemble is removed, and intrinsic particle properties can be directly observed. Especially valuable is the correlation of several properties on the same particle, and the correlation of the optical properties of the particle to the exact particle morphology by electron microscopy. This is only possibly in single-particle studies.

Time dependent fluctuations are accessible – Using single particles, time dependent processes can be studied without the need for synchronization. For ensembles, synchronization is often difficult, or only possible within limits, as particles of different sizes and shapes react differently to a synchronized external perturbation. Another example is

the study of processes that are intrinsically random, such as fluctuating two (or more) level systems. For single particles these fluctuations can be directly observed, whereas in ensembles these fluctuations are averaged out.

Rare configurations can be observed – Particles with rare properties within a sample -or rare configurations of particles- can be studied without the requirement to reliably produce these configurations in large numbers, an often impossible task in the preparation of samples.

Single particle as local reporter or actuator – With single particles, qualitatively new types of experiments are possible. As labels of single entities in cells, they can report not only on their position, but on their three-dimensional trajectories in time. Single particles can become local actuators with optical control, acting either as highly localized sources of heat, or as transducers of force and torque.

1.3 Study of a single nanoparticle in solution

The majority of single particle measurements thus far have met a fundamental limitation: to enable detection of the particle with sufficient signal-to-noise ratio, it had to be immobilized on a solid substrate, such as a microscope coverslip. The underlying reason is that to visualize single particles, typically light has to be focused to a small spot using a high-numerical-aperture objective, and the nanoparticle needs to be immobilized with respect to this tiny focal volume for the duration of the desired experiment. In solution, the nanoparticle will drift away from the focus due to Brownian motion. The time for a nanoparticle to pass the focal volume is on the order of milliseconds (in water), too short for many experiments of interest.

The proximity of the substrate provides a perturbation to the optical, mechanical and thermodynamical properties of the particle. This perturbation complicates modeling of experiments, making it more difficult –or simply impossible– to acquire the desired information. In addition, some experiments inherently take place in solution. For these reasons, it would be highly desirable to perform experiments on single nanoparticles in a homogeneous liquid environment. Some examples of experiments that would benefit from this geometry:

-The particle's plasmon resonance is influenced by the proximity of the substrate, whenever the index of refraction of the substrate differs from that

of the environment. Mie theory[4,6] qualitatively describes the optical properties of spherical particles embedded in an isotropic medium with an analytical expression, but no such solution exists for a particle on the boundary between two media. Usually the influence of the substrate on the plasmon is simply included as an effective refractive index –the average index of the substrate and the environment. It has not been possible so far to directly measured the influence of the substrate.

-The acoustic vibrations of nanoparticles are influenced by the boundary conditions between the particle and the environment. For a single spherical particle embedded in a homogeneous medium both the frequencies[52] and damping[53] of the vibration modes can be calculated exactly, but a direct experimental test has been lacking. Experiments on ensembles are plagued by the distribution of particle sizes that is inherent to nanoparticles; synchronously launched vibrations quickly get out of phase as particles of different sizes vibrate with different frequencies. The resulting inhomogeneous damping limits the resolution with which the vibration frequencies can be measured and makes it impossible to investigate the loss of vibrational energy to the environment by a measurement of the vibrational damping time. In single-particle measurements the vibrational damping time can be directly accessed. However, here the presence of the substrate provides a perturbation that is very difficult to quantify in experiments. In Chapter 6 we describe our approach to this problem, with a single gold nanoparticle in solution.

Besides these examples, we could think of a whole class of experiments in thermodynamics on the nanoscale, probing heat conduction, nano-bubble formation, particle-reshaping, surface melting, solution based catalysis, etc.

Approach in this thesis: immobilization in solution by optical trapping

In this thesis we achieve the effective immobilization of a single particle in solution, by confining it to the focal volume of a high-numerical-aperture objective with an optical trap. We will discuss the physical principles underlying the trapping in more detail in Section 1.4 and Chapter 3, for now it suffices to say that the optical forces in an intense focused light beam can localize a particle to the focus, enabling the study of single particles in an homogeneous liquid environment. Even though optical trapping of metal nanoparticles was introduced more than 15 years ago and the field has expanded considerably since then (see section 1.4), optical trapping has thus far not been much exploited as a means to study single gold nanoparticles.

The use of an optical trap has several advantages. In optical trapping no feedback is needed to keep the particle in focus. Once the particle is trapped, it can be followed and studied at leisure for extended periods of time, provided that the trap potential is deep enough. This is an important practical advantage, especially when the complexity of the experiments performed on the particle increases. Furthermore, optical trapping requires no special micro-fluidic devices; any chamber with a liquid between microscope coverslips can be used. Lastly, with the optical trap the particle can be brought from the solution to a substrate to systematically investigate the influence of the substrate.

A further advantage of the optical trap is that it enables a range of other exciting applications for active local manipulation. The ability to locally exert a true force and/or torque on a particle enables applications not accessible with either the passive tracking or trapping by manipulation of solvent flows. We will discuss these possibilities in section 1.4.

Alternative methods for immobilization in solution

In recent years, several methods have been developed that could serve as alternatives to optical trapping as a means to immobilize nanoparticles in solution.

The first possibility is a form of particle tracking.[54–59] Here, the movement of the particle away from the focus is deduced from an optical signal, for example the light scattered by the particle. This information is inserted in a feedback loop, that moves the complete sample chamber to bring the particle back in the focus (or moves the laser focus back to the particle).

The second possibility is a combination of particle tracking and the use of the feedback signal to induce a flow in a micro-fluidic device to counteract the Brownian motion, a configuration known as the Anti Brownian Motion Electrokinetic trap or ABEL trap.[60,61] With the ABEL trap, single molecules[62] and particles down to 1 nm in size[63] can be trapped in two dimensions.

A third possibility is geometry-induced electrostatic trapping, where charged objects can be trapped in solution in the vicinity of tailored micro-fluidic slits and pits.[64] In this method, a spatially modulated electrostatic potential is formed in an ionic solution, by the distribution of charges around the slit. The properties of the trap can be tuned by tuning the ionic strength of the solution, and the precise topography of the slit.

The possibilities above may be complementary methods for the study of single gold nanoparticles in solution. In particular, they may be used to study

particles of sizes too small to be optically trapped. As we shall see, inherent to optical trapping of metal nanoparticles is heating due to absorption of the trapping laser. Single-particle-tracking or the ABEL trap provide avenues to study single particles in solution for experiments when such heating would pose a problem. However, three-dimensional trapping is difficult with the ABEL trap, and the need for a specialized micro-fluidic device restricts its applicability. Both particle tracking and the ABEL trap require a dedicated fast feedback system, with highly optimized optical and electronic components of the setup, adding significantly to the overall complexity of the experiment. The electrostatic trap requires charged particles, trapped in close vicinity (up to several hundred nanometers) of a solid substrate. This restricts its use for thermodynamic and mechanical study of single particles in an homogeneous liquid environment.

1.4 Optical manipulation of single gold nanoparticles in a liquid: the use of nanoparticles as a tool

With control over particle position and the possibility to exert forces on particles, the metal nanoparticle is not only a study object, but it can be used as a tool to manipulate an investigate matter on a nanometer scale.

Optical trapping

Light carries both momentum and angular momentum and can be used to exert forces and torques on matter. For macroscopic objects and the light intensity of most thermal light sources, these forces and torques are so minute that their effects are hardly measurable. For a microscopic particle in an intense laser beam, however, these effects can be substantial, as first realized by Arthur Ashkin.[65,66] When such a laser beam is strongly focused, these forces can act to localize a particle to the focus, a configuration known as optical tweezers. The ability to exert forces on microscopic particles and manipulate matter on the microscopic scale has been tremendously valuable in physics, biology and chemistry, in a wide variety of applications, ranging from the measurement of the mechanical properties of single (bio-)molecules,[67–70] to micro assembly,[71,72] to nano-surgery.

Most applications to date have used dielectric objects as trapping handles, typically glass or polymer beads, with a size typically one to several micrometers in diameter. Gold nanoparticles can also be trapped, and enable

exciting new possibilities. Due to the higher polarizability of metals, gold nanoparticles can be trapped down to smaller sizes than dielectric objects. The small volume of the particle opens up potential applications of optical manipulation in environments that exclude micron-sized trapping handles. An exciting application would be the optical trapping in living cells, to study the mechanical properties of single bio-molecules in living cells.[73]

Due to the smaller size, the hydrodynamic friction of nanoparticles is smaller than for micron-sized dielectric particles. This gives rise to shorter relaxation times, and provides access to dynamics of objects attached to the particle on shorter timescales. This holds in particular for rotational motions, for which the friction scales as the particle volume.

Optical trapping of metal nanoparticles

The optical trapping of metal nanoparticle was pioneered by Svoboda and Block in 1994.[74] Since then, several groups have demonstrated optical trapping of metal nanoparticles. The range of particle sizes that can be trapped has been expanded to particles up to 250 nm in diameter[75] and down to 10 nm in diameter.[76] Stable three dimensional optical trapping has been reported for gold[75,77] and silver[78] nanospheres, and gold nanorods[79] with off-resonant trapping with a near-infrared continuous trap laser. Trapping has also been demonstrated using near-resonance geometries,[80–82] and with pulsed lasers.[83] Also, anisotropic nanoparticles and nanowires have been shown to align -and rotate- with the polarization of the trap laser,[84] and the optical forces between two trapped particles have been studied,[85] characterized by their scattering spectra.[86]

However, compared to the rich toolbox of techniques that has been developed for dielectric trapping objects, and the wide variety of applications trapping has been used for, optical trapping of metal nanoparticles is still very much in an early stage,[87] and many of the unique possible applications of trapping metal nanoparticles are thus far unexplored.

Challenges and open questions in optical trapping of metal nanoparticles

The trapping of metal nanoparticles raises several interesting technical issues and poses new physical questions.

Firstly, a technical issue arises due to the particle volume. Whereas micron-sized dielectric trapping objects have a size comparable to the focal size, or

larger, metal nanoparticles that can be used for trapping are much smaller in size than the trap focus. The metal nanoparticle may explore inhomogeneities and fine structure in polarization and intensity in the trap focus, that are averaged out for the larger dielectric particle. Methods to detect the motion of the particle in the trap are optimized for particles of a size comparable to the focal volume. Are the same methods still optimal for particles much smaller than the focus?

Secondly, an issue inherent to metal nanoparticles is the absorption of photons of the trapping laser, and the resulting heating.[77,88,89] For nanoparticles the absorption at a wavelength far off-resonance with the trapping laser can be very small, but it is not zero. Due to the high intensities required for trapping, absorption may be significant. How much light is absorbed? How hot will the particle become? How can we measure the temperature of the nanoparticle in the trap?

Furthermore, the motion of the trapped particle is strictly speaking not Brownian motion. Rather, the hot particle diffuses in an inhomogeneous temperature and viscosity profile.[90,91] Here the question becomes: can an effective temperature and an effective viscosity be found that describe the motion of the particle subject to the fluctuations of the bath? If so, what are they? More interestingly still, are rotational and translation movements described by the same effective temperature?[92]

The heating that is inherent to the optical trapping of nanoparticles can be considered a nuisance, or an opportunity. For biophysical experiments, the heating of the nanoparticles is certainly of concern. The health of living cells as a whole is most likely not influenced by a single hot nanoparticle, as the heat is very much localized. Molecules directly attached directly to the surface of the particle may be more significantly affected. This provides a challenge to the common use of trapped particles as a way to measure the mechanical properties of single (bio-)molecules. This challenge is probably the reason why thus far no single-molecule force measurement using a metal nanoparticle has been reported. However, it is not a priori clear that the challenge of heating is an insurmountable obstacle. For example, one property that may be used to work around this obstacle is that the temperature around the metal nanoparticle falls off rapidly with distance, with a characteristic length scale given by the particle radius. A few radii way from the particle, the temperature is close to the temperature of the bath. If a bio-molecule can be kept at this distance from the particle surface by a heat-resistant spacer that still allows for transduction of forces and torques, it may not be significantly affected. We may also turn around the problem entirely and decide to

use the heating of the particle. Having the ability to control the motions of a hot nanoparticle in space and time, we may envision performing a new type of laser surgery on the nanoscale.

1.5 This thesis

In this thesis, we will address the physics and applications of optical trapping of single gold nanoparticles in solution. We explore this general theme by addressing several inter-related topics in individual chapters: single particle detection, optical manipulation of single particles and study of single-particle properties in solution.

In the topics that will be discussed, one common theme is heat. We will use heat explicitly as a way to detect gold nanoparticles and as a way to excite ultra-fast mechanical vibrations. Wherever heat arises we will try to quantify it, by its effects on the optical properties of the particle or its environment, or on the motions of the particle in solution. A second common theme is (an)isotropy. We will use both spherical and rod-like gold particles when appropriate, and characterize and use their isotropic or anisotropic properties; either optical, thermal or mechanical.

The chapters in this thesis can be read largely independently. To facilitate the reader's choice, we provide here a short description of each chapter, highlighting the main results.

> **Chapter 2** – A prerequisite to working with single nanoparticles is that you are able to detect them. In this chapter we investigate the detection limits of photothermal microscopy. In this far-field optical detection method absorbing particles are detected by the refractive effects of the heat dissipated into their environment upon illumination. This technique had been shown previously to be able to detect gold nanoparticles of only 67 gold atoms,[44] a record sensitivity. We show in this chapter how the sensitivity can be pushed even further, enabling the detection of even smaller particles, or smaller amounts of dissipated heat. An important improvement was the realization of how to make optimal use of the optical and thermal properties of the liquid medium surrounding the particle. The achieved improvement in sensitivity of the photothermal method enabled us to detect single non-fluorescent organic dye molecules at room temperature, by the refractive effects of the heat released in their environment upon light absorption. This achievement had been an outstanding challenge since the first far-field

optical detection of single molecules at liquid helium temperatures in 1989.

Chapter 3 – We introduce the optical trapping setup that was built during this thesis. We demonstrate the capabilities of the setup by showing stable three-dimensional trapping of single gold nanorods and perform an experimental characterization of the particles in the trap, with a close look at the thermal stability of the nanorods in the trap, their alignment with respect to the polarization of the trap laser, and the dynamics of their rotational and translational fluctuations in the trap.

Chapter 4 – We quantify the optical torque acting on a single gold nanorod in an optical trap, and show that this torque would be large enough to twist single (bio-)molecules. With the optical force acting on the rod at time same time, the single gold nanorod in the trap could be used as an ultra-small simultaneous transducer of forces and torques. In addition, we quantify the laser-induced heating of the gold nanorod, and we report on the first observation of the combined translational and rotational Brownian motion of a hot object.

Chapter 5 – We study the spectral width of the plasmon resonance of gold nanorods, as a method to measure the temperature of the nanoparticle. We apply the method to the particle in the trap, where the temperature is varied by variation of the trapping power, and for particles immobilized on a substrate, where the temperature of the sample chamber is varied by a known amount.

Chapter 6 – As a demonstration of the advantage of studying single particles in a homogeneous liquid environment, we study the acoustic vibrations of a single gold nanoparticle in the optical trap. With the particles embedded in a homogeneous liquid environment, the damping of acoustic vibration can be directly compared to established theory. Surprisingly, we find that the acoustic vibrations are not only damped by dissipation into the liquid, but damping mechanisms intrinsic to the particle are a significant fraction of the overall damping.