14 Physical Systems Biology and non-equilibrium Soft Matter

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in collaboration with:
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Work in the group of physical systems biology and non-equilibrium soft-matter is concerned with the study of developmental biology using physical techniques. In this, we are developing novel imaging techniques for in-vivo imaging in turbid environments, as well as studying the influence of mechanical stresses on developmental processes. This implies that we are developing tools with which to measure mechanical stresses in live biological tissues as well as methods to stimulate these tissues using suited levels of force. The biological model system we are studying is the wing imaginal disc of *Drosophila*, which is a proto-organ that develops into the adult wing of the fly during metamorphosis. In years of genetic characterisation, this tissue in the fly's larva has been extensively studied and a host of genetic manipulation tools have been developed. Thus it is possible in a system like the wing imaginal disc to investigate the interplay of genetic factors and mechanical properties, which are also implied by the environment. In these projects on the development of organs in *Drosophila*, we are closely collaborating with Biology groups. In addition, we take the study of elastic properties of biological tissues as a starting point in the investigation of the properties of growing soft matter, where our model system consists of two dimensional foams, which form structures akin to the epithelial tissues we study in Biology.

In addition, we are interested more generally in phase transitions and non-equilibrium behaviour. For this purpose, we also study Anderson localization of light in turbid media, the dynamics of granular gases under microgravity, as well as that of levitated three dimensional foams. These investigations in turn influence our development of imaging techniques, as well as the study of mechanical properties of soft condensed matter.

14.1 Granular materials

In collaboration with the University of Konstanz, we are studying the behaviour of granular gases using diamagnetic levitation (1). Due to the levitation of the particles, it is possible to study the behaviour of the grains as a function of time when the excitation is switched off. Under normal circumstances, this behaviour is completely masked by the gravitational effect of grains falling to the bottom of the container. Due to the inelasticity of collisions between grains, the particles continually loose energy, which is a fundamental ingredient in the theoretical description of granular gases using kinetic theory. This has led to a description of the freely cooling granular gas by Haff more than 25 years ago (2), which is used as a ground state in the description of excited granular gases (3).

Using a collection of monodisperse Bismuth shots, we have created a granular gas in the bore of a strong superconducting solenoid (4). At an applied field of 13.5 T, the field gradient at the edge of the solenoid is strong enough such that the diamagnetic susceptibility of Bismuth leads to a repulsive force that equals gravity. Exciting the granular gas using an alternating component of the levitating field, a stable granular gas is created. When switching off this excitation, the cooling of the gas can be observed directly by studying the mean speed of the particles. According to Haff, the mean speed in a homogeneous gas should decrease with time as

$$\langle |v| \rangle (t) = \frac{\langle |v|(0) \rangle}{1 + t/\tau_H}, \tag{14.2}$$

where τ_H is a time scale dependent on the mean free path of particles between collisions, their coefficient of restitution as well as the initial speed of the particles.

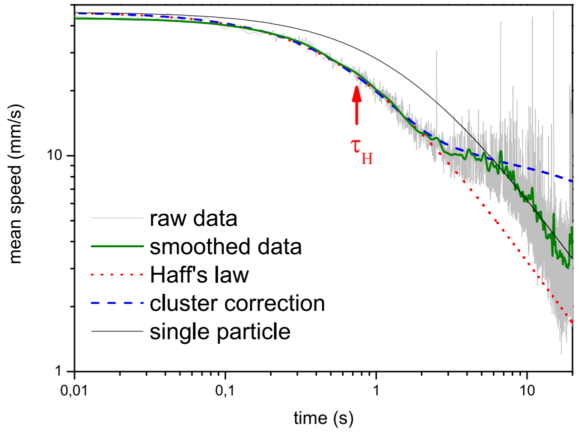

Figure 14.1:
The cooling of a granular gas as studied by video-imaging. As can be seen, the mean speed of the particles decreases as the excitation is switched off at time t = 0. The dotted line gives the prediction of Haff's law, which is adjusted for the presence of a cluster of particles in the gas in the dashed line. The thin solid line finally gives another Haff-like behaviour when the mean free path of particles becomes equal to the container size.

As can be seen in Fig. 14.1, the experimentally determined speeds are in good agreement with Haff's law at early times, where the gas is still homogeneous as indicated by the dotted line. At later times, the particles tend to form a cluster, which leads to an increase in the mean free path and thus a slowing down of the cooling process. This can also be seen in the data and the mean free path can be directly determined from the number of particles outside the cluster. Thus Haff's law can be adjusted to describe a clustering gas as well, indicated by the dashed line in Fig. 14.1, which is in good agreement with the data. Note that in the description of the data, no adjustable parameters were used since the parameters describing the Haff time τ_H can all be determined independently.

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14.2 Coherent backscattering of light

When shining light onto a turbid medium, there is an enhancement of the backscattered light in the exact back-direction (1). This is due to the interference between reciprocal paths inside the multiply scattering sample, a phenomenon giving rise to Anderson localization in the strong scattering limit (2). In spite of the fact, that this enhancement has been known experimentally for almost 25 years, the standard description of the effect (3) still leads to an excess of backscattered intensity for extremely turbid samples, which would break the conservation of energy. Using our carefully calibrated setup, which is able to cover almost the whole angular range of reflections (4), we have studied the absolute enhancement in coherent backscattering (5). There we could show that there is a suppression of enhanced intensity at higher angles that exactly compensates for the backscattered enhancement at small angles. This suppression is due to interference effects arising when the first and last scatterer are within a wavelength of the incoming light and can be described by diagrammatic theory (6), which can be applied to the problem of coherent backscattering and is in excellent agreement with our measurements (5), see Fig. 14.2.

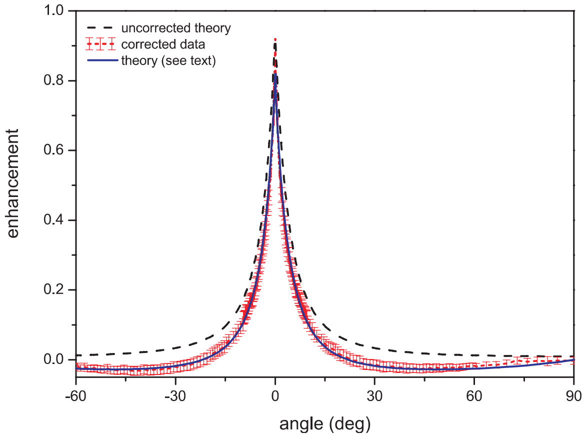

Figure 14.2:
The enhancement of backscattering due to path reciprocity in turbid media over a wide range of angles. Due to the wide angular resolution, it is possible to see a reduction of enhancement at angles around 45°, which makes sure that the enhancement in intensity fulfills conservation of energy. This can be described theoretically using a Hikami box [6], which describes the diffraction limit effect of two sources moving closer than a wave length. The corresponding theory is plotted as the dashed line. Without this effect, the dotted line is obtained which would be in conflict with conservation of energy.

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14.3 Measurements of mechanical stress in the wing imaginal disc of Drosophila

On the side of organ development, we have recently studied the regulation of growth in the wing imaginal disc theoretically and proposed a model for size regulation with an important role for mechanical forces creating a feedback acting on the growth rates of the system (1). Here, the main point was to show through simulations of a simplified model that inhomogeneous growth as is probably present in the initial stages of the wing imaginal disc due to a graded presence of growths factors, such as decapentaplegic or wingless can lead to a homogenization of the growth rates via mechanical feedback. In addition, the distribution of stresses in the tissue, which was assumed to be completely elastic, leads to a regulatory feedback controlling the cessation of growth via compressional forces in the locations of high growth factor concentration. A similar model has been put forward independently by another group as well (2; 3), which together with our study has lead to an increased interest in the study of mechanical forces in the development of organs in Drosophila.

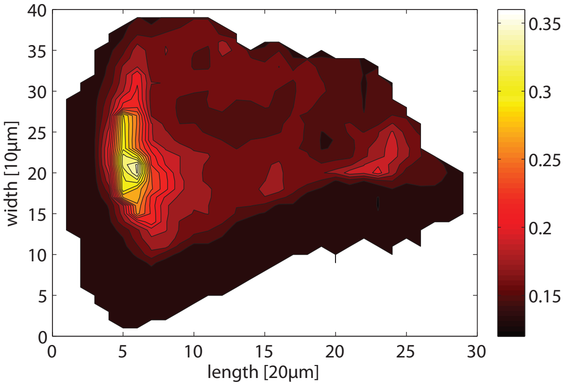

Figure 14.3:
Distribution of retardance in the wing imaginal disc of a late third instar larva. As can be seen, the retardance is highest in the centre of the wing pouch, where the orientation of the retardance and hence the stress can be checked by a rotation of the incoming polarization of the light. This shows that the stresses in the wing pouch are roughly radially distributed as is predicted by the models [1; 3].

In order to study the implications of this model, we have in the following begun the experimental study of the mechanical properties of the wing imaginal disc. As a starting point, we have studied the stresses present in wing discs of different ages using a setup to accurately measure birefringence and thus determine the stresses via photoelasticity. In a photoelastic experiment, the change in retardance of a material is measured under an applied stress. This retardance is given by the birefringence of the material as well as its thickness. Under an applied stress, the birefringence changes in proportion to the stress, because of the change in the electronic properties induced by the stress. In these experiments, we have used a sophisticated method of measuring the retardance directly (4), which yields the phase difference due to birefringence and thus the stress. The nature of this setup leads to a poor spatial resolution since the illumination needs to be scanned across the sample and thus is limited to 20 μm. This can however be increased in principle to the sub-cellular level by the inclusion of such a setup to a wide field microscope (5), which we are currently building up. We should therefore be able to measure the stress distribution to the cellular and sub cellular level in in-vitro wing imaginal discs in the future.

The present, preliminary investigations have already indicated the presence of a mechanical stress distribution with a radial maximum at the centre of the wing pouch, where compressional stresses are predicted by the models discussed above (1; 3), see Fig. 14.3. The extent of these stresses inside the wing imaginal disc is also seen to increase with age of the wing disc(6), still as predicted by the theoretical models. In addition, other predictions concerning the stress distribution could be tested, such as the temporal development of the peripheral tensile stress, where the predictions of the two models differ strongly. One of the models predicts an increasing stress (3), whereas the other predicts a constant or slightly decreasing stress (1). Our results indicate a temporally constant stress in the periphery of the wing disc in agreement with (1). These results are currently being submitted for publication (6).

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