MSc thesis/examensarbete Biophotonics

Developing techniques for optical imaging deep inside the body

We develop techniques to look deep into the body by creating structures where light propagate at a speed of just a few km/s. Light in general offers imaging opportunities not available with *e.g.* MRI, ultrasound or X-rays. In particular light has molecular sensitivity, e.g. through interaction with fluorescent markers, in our case we in particular intend to look at blood oxygenation. It appears that light soon will start to be used as a medical probe down to a depth of a few cm using Photo-Acoustic Tomography (PAT) and the question here is whether optical imaging techniques can reach still further into the body.

Light propagation in tissue is characterized by a scattering coefficient, μ_s, and an absorption coefficient, μ_a. Even within the so called tissue optical window between 700 and 1100 nm human tissue absorbs light. Due to scattering, the actual optical path length for light to reach a particular depth, d, in tissue is about 1-2 orders of magnitude larger than d. This means that for sufficiently large depths basically no photons will penetrate unless they can take a shorter path. However indeed some photons do take a shorter path (since scattering is a random process) and there is extensive work on developing techniques for making as large fraction as possible of the photons to take a more direct path between two points when they propagate in scattering media. In general this is done by controlling/manipulating the spatial waveform of the incoming light.

Taking a short route through scattering media is to some extent connected to the problem of focusing light deep into tissue, either for treatment or for improved diagnostics. In a scattering but non absorbing medium light emanating from a single point, P, exiting the medium can be refocused to the point P by utilizing phase conjugation. However, if some light is lost, *e.g.*, not reflected or absorbed, complete refocusing will not be possible.

We would like to know how large fraction of light entering a medium could be forced to take a short path to some point in tissue and the objective here is to start to learn about this by working experimentally and theoretically with digital phase conjugation in tissue phantoms

We cooperate with Mats Gustafsson & Johan Lundgren at the Division of Electro-magnetic Field Theory at the Electrical Engineering (EE) Department on this task. Light propagation in scattering media is a well researched problem. We can achieve spatial resolution in the scattering object by tagging the light at a specific point through interaction with a localized ultrasound pulse. What is unique in our case is that we have developed slow light filters where we can lower the speed of light to a few km/s which enable us to better discriminate the tagged light from the non-tagged light. We believe this can make a feedback process based on phase conjugation more efficient. An initial experimental set up would look as in Fig. 1 or Fig. 2 on the next pages.

Mats & Johan's simulations indicate that the phase front of the input wave can be modified such that the scattered light interferes constructively along certain paths. Quite surprising it seems "express routes" are formed through the scattering medium where light takes shorter paths. If we could mimic and study these effects experimentally it would be very interesting.

Scattering media having verifiable scattering and absorption can be constructed using mixtures of intralipid, India ink and water. Previous work in the group has also produced software to control a 2 Megapixel deformable mirror. This can create an arbitrarily wave front from an incoming plane wave and the propagation of this wave front in the medium can then be analysed. There are many open questions and the student is strongly encouraged to also formulate questions on his/her own when working with the project. Examples of questions are:

1. Phase conjugation in thick samples is limited by losses and leakage of light not hitting mirror/detector. How much can this be improved by encapsulating the sample with a thin reflecting film (R > 0.95) with only holes for input and output light?
2. How does the amount of light which can be transmitted through the medium depend on the scattering and absorption coefficients of the medium?
3. What is the success of focusing in different parts of the scattering medium? (For instance, focus in and off the line defined by input and output points)? How can this be measured?
4. Is there a difference in focusing fidelity when the phase conjugation is done in transmission mode and reflection mode? *Transmission mode*: input and output on different sides of sample of thickness 2*d,* deformable mirror on input side (Fig 1). *Reflection mode*: input and output on same side of sample of thickness *d,* deformable mirror on other side of sample (Fig 2).

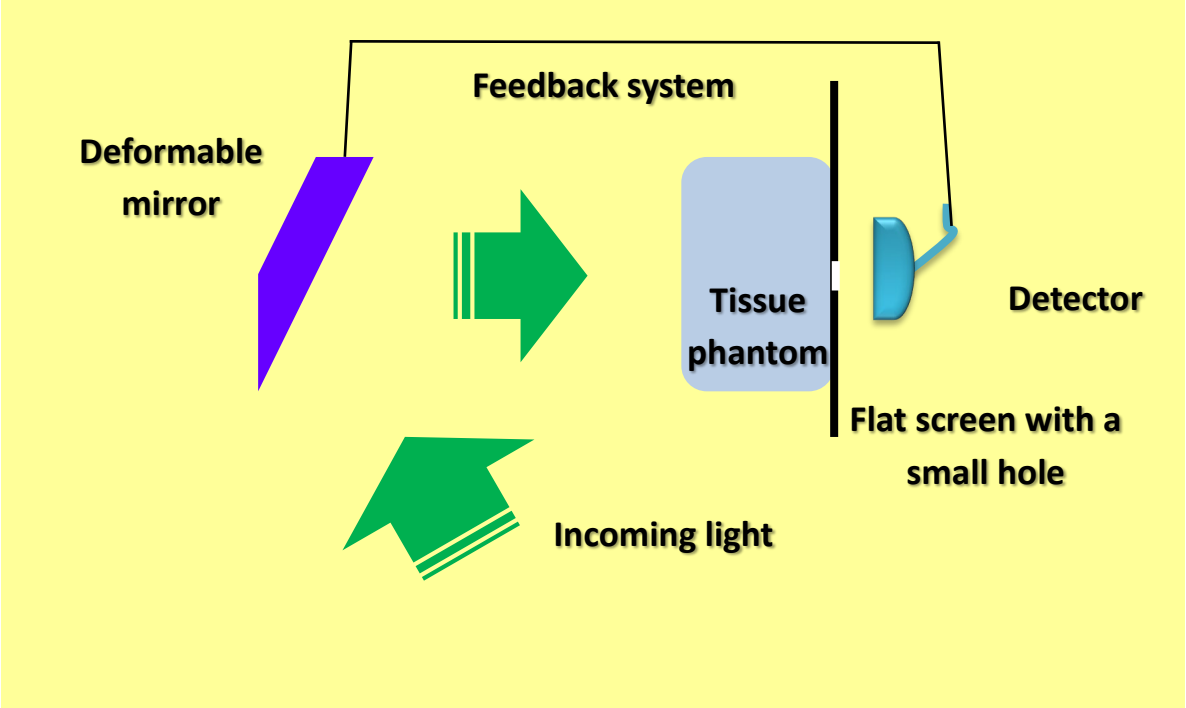

Fig 1. Incoming light with a plane wave front is reflected by a deformable mirror and enters a tissue phantom. A fraction of the light will be transmitted through a small hole in the flat screen and reach the detector. Using this signal a feedback system is employed to change the surface of the deformable mirror. This changes the wave front of the light going into the tissue phantom. In this way one can try to optimize the light through the hole.

Suggestion of a preliminary time plan of project (total 20 weeks):

1. Literature study and definition of scope (4 weeks)
2. Building the experimental setup (1 week)

3. Learn how to make phantoms (1 week)
4. Learning how to program the HoloEye deformable mirror (1 week)
5. Initial tests and evaluation (2 weeks)
6. Plan new experiments, discuss with the people at the EE dept (2 weeks)
7. Carry out the new experiments (4 weeks)
8. Writing, documentation and presentation of work (5 weeks)
   For a 60 hp MSc project the experimental time would be extended and it would be possible to carry out more extensive comparisons with the theoretical calculations at the EE department.

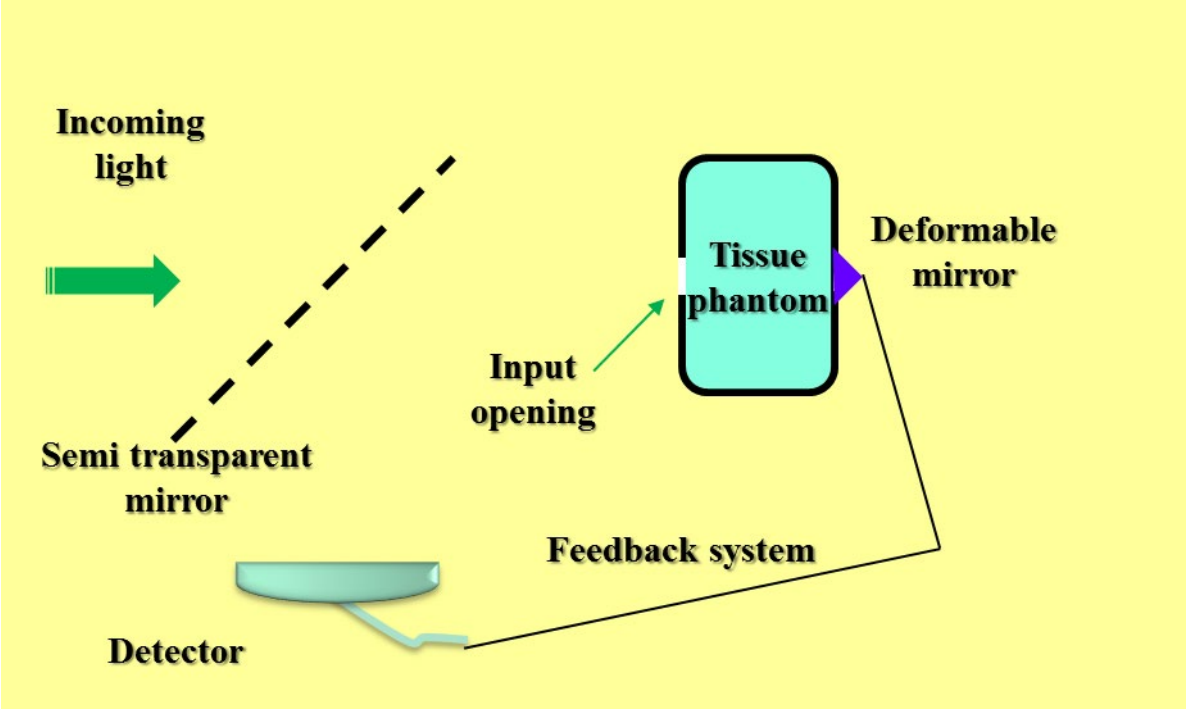

Fig 2. Similar to Fig. 1, but the tissue phantom is enclosed in a container with reflecting surfaces, the deformable mirror is replaced by a semi-transparent mirror, the detector is replaced by the deformable mirror and moved such that it picks up the light reflected by the semi-transparent mirror.

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