

Bio-medical laser physics in development

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Optics, spectroscopy and laser applications are suitable high-tech fields for the promotion of physical research in developing countries, since the associated technology is affordable and connects to real-world applications. This is particularly true for diode laser-based research. A developmental programme, mostly for African universities, was pursued from the Lund University with support from the International Programme in Physical Sciences (IPPS), Uppsala and the Abdus Salaam International Centre for Theoretical Physics (ICTP) in Trieste. Our experience started with lecturing at the ICTP and at schools and conferences in Africa. Two 1-month workshops were arranged in Lund focusing on diode laser spectroscopy and applications; the first one in 1996 and the second one in 2001. In both workshops equipment was integrated in Lund and each group could bring a full set-up back to the home university, to be used in advanced teaching and research. Thus, in the 1996 smaller workshop, participants from Cape Coast (Ghana), Dakar (Senegal), Khartoum (Sudan) and Nairobi (Kenya) built experimental set-ups, primarily for diode laser spectroscopy on rubidium vapour. Resonance cells with separated Rb⁸⁵ and Rb⁸⁷ isotopes were used, and ground state hyperfine structure, isotopic shifts and Doppler broadening of free atoms could be studied. Using saturation spectroscopy even Doppler-free signals could be observed, and upper-state hyperfine structure be studied. As a follow-up of the workshop, a Lund graduate student, Peter Kauranen, toured the four African sites and helped to bring the equipment into high performance at each location.

The Lund Workshop "Laser Spectroscopy in Development"

The 2001 spring workshop had participants from the same sites but also from three additional universities, in Harare (Zimbabwe), Tunis (Tunisia) and Quito (Equador). The groups were generally composed by a senior researcher and a student from each location, working together on their own equipment. Lund graduate students Sara Pålsson, Mikael Sjöholm and Gabriel Somesfalean assisted in the workshop. Practical laboratory work was combined

with extensive lecturing on relevant topics, and study visits to different Lund research laboratories and to the Lund University Hospital. The main focus of the workshop was to build a compact fibre-optics fluorosensor, based on a Nichia violet diode laser and an integrated spectrometer. A prototype had previously been developed in Lund and successfully applied to vegetation monitoring and skin cancer detection. The Lund group has a long experience

in both these fields, which have relevance also to developing countries. The fact, that the hardware for these cutting-edge technology devices costs only 10,000 Euro, including a powerful lap-top computer for experiment control and data collection, made it a very realistic project. The six instruments are now being used in different research projects at the home universities. E.g., a controlled fluorescence study of the growth development of different species of cowpea was recently performed by the group in Cape Coast.

The 2001 workshop also dealt with high-resolution diode laser spectroscopy on free atomic and molecular gases. The Harare group got their own rubidium spectrometer, similar to the ones already in place at the other African sites and this project provided a good update for all. A special grant for the Zimbabwean university from SIDA/SAREC also allowed the integration of an instrumentation for Gas in Scattering Media Absorption Spectroscopy (GASMAS). The first paper on this new technique, where free gas, e.g., molecular oxygen, present in pores in scattering media is studied, had actually been published only 3 months before the 2001 workshop. The equipment is again affordable and allows studies of gas and gas diffusion in natural and synthetic materials such as wood, fruits, polystyrene foam, ceramics etc. A Ghanaese graduate student, Benjamin Anderson, stayed 6 months in Lund working with GASMAS. After some time back in Ghana he went on a 4-week research visit to Harare and performed very successful GASMAS experiments together with the local Zimbabwean team on their GASMAS equipment.

The experience from the diode laser spectroscopy project has been described in a recent EPN article, where also the GASMAS principles are presented. The present article focuses on some recent

developments in biomedical applications, in particular on the introduction of medical fluorescence diagnostics and photodynamic therapy (PDT) of cancer tumours in Dakar (Senegal). This field is particularly suited for cross-disciplinary interaction between physicists and physicians, and again, the techniques are affordable.



▲ Fig. 2: Participants from Senegal, A. Konte and A. Wagué, build and integrate a diode laser based fluorosensor during the 2001 workshop at Lund University. Conferring with them is K. Wangai.



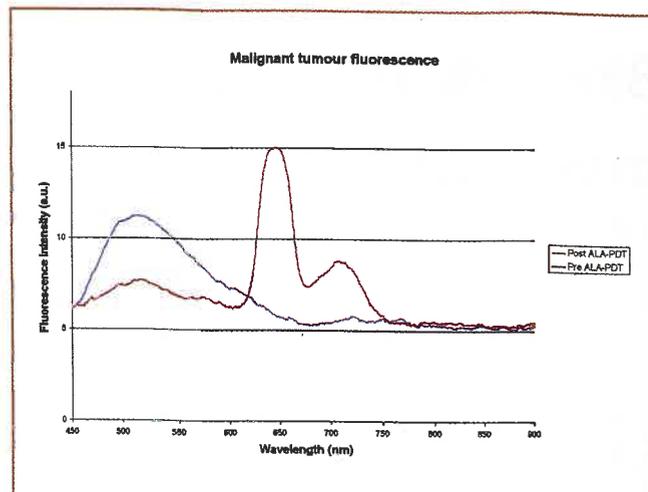
◀ Fig. 1: A group from the 2001 workshop in Lund photographed together at the Oncology Department of the Lund University Hospital for a training session with laser based fluorosensors. From left to right M. Diop, S. Pålsson, A. Abdalla, K. Kaduki, A. Konte, K. Dzinavatonga, J. Nejmedinne, A. Wagué, S. Svanberg, N. Ndlovu, M. Mathuthu, K. Svanberg and N. Bendsoe.

Fluorescence Diagnostics and Photodynamic Therapy

Certain organic molecules have a combination of interesting medical properties: they accumulate in cancer tumours, they mark the presence of a tumour by strong and specific laser-induced fluorescence, and upon tissue irradiation with red light, they mediate the conversion of ground-state molecular oxygen into toxic singlet oxygen. A selective release of this agent in tumour cells leads to specific necrosis and tumour eradication. The Lund group has been working in this field for almost 20 years. During recent year, the introduction of δ -amino levulinic acid (ALA) for PDT has greatly facilitated the application of the techniques. In contrast to most other sensitizers, which are suitable only for intravenous administration, ALA can be given orally, or applied topically as a cream on skin lesions. ALA enters the natural human haem cycle, where the tumour sensitizer Protoporphyrin IX is formed as an intermediate state before the red blood pigment is formed by iron incorporation in a final step. Enzymatic differences lead to the selective production of the strongly fluorescent and photodynamically active protoporphyrin in tumours.

During the International Commission on Optics Conference on Sustainable Development, Dakar, in April 2000, a lecture on the topic was given and there was also an opportunity to visit the Ear-Nose-Throat Clinic in Dakar and together with Prof. Malick Diop discuss the possibility to use PDT in Africa. The 2001 Lund workshop had fluorescence diagnostics and PDT as important aspects, with Dr. Diop and also Dr. Ntkomo Ndlovu, Radiation Therapy Unit, Harare, present together with their local physicist partners. Figure 1 shows part of the school participants together with the local hosts during a training session at the Lund University Oncological Department, where practical acquaintance with the medical laser techniques was obtained. Figure 2 illustrates the integration in Lund of a diode-based fluorosensor by the Dakar group. It is similar to the one described in the paper listed at the end of this article.

In January 2003 Lund researchers went to Dakar with the double purpose of lecturing at the Preparatory School on Biophotonics, arranged by the Cheik Anta Diop University, and to introduce medical fluorescence diagnostics and PDT in work with patients at the Oto-Rhino-Laryngology and Dermatology departments of the Artside le Dantec University Hospital. The Lund team brought a PDT treatment illumination source based on red light emitting diodes, ALA powder and relevant disposables. The laser fluorosensor shown in Figure 2 was already in place! Three patient were treated in a demonstration session, where the



▲ **Fig. 4:** Selective uptake of Protoporphyrin IX in a malignant tumour prior to PDT (red curve), and complete photobleaching of the sensitizer in the tumour after treatment (blue curve) as evidenced with the compact Dakar fluorosensor being integrated in Figure 2. (Courtesy: A.S. Ndao and A. Wagué, Dakar.)

Dakar physicists and physicians collaborated. In Figure 3, Prof. Diop and one of the authors prepare the treatment of an aggressive basal cell carcinoma in a Mauritanian patient. Laser-induced fluorescence recordings on a further Dakar patient taken with by the local physicists using their fluorosensor, are shown in Figure 4. The sharp Protoporphyrin peaks at 635 and 705 nm obtained on tumour tissue are shown. The completion of the PDT session using light-emitting diode light peaking at 635 nm, is evidenced from the total bleaching of the sensitizer in the irradiated region.

The different topics introduced at the African sites—high-resolution laser spectroscopy of free atoms, molecular gas monitoring in natural scattering media, environmental and medical laser-induced fluorescence, and finally, photodynamic therapy of malignant tumours, are all based on the use of diode lasers. The cutting edge technology, while being affordable, provides applications which make a lot of sense also to local governments, and can thus hopefully well serve in the promotion of the physical and medical sciences in developing countries.

Further reading

- S. Svanberg Laser Spectroscopy in Development *EPN* March/April 2002 pages 52-53
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- U. Gustafsson, S. Pålsson, and S. Svanberg Compact Fibre-optic Fluorosensor using a Continuous-wave Violet Diode Laser, *Rev. Sci. Instr.* 71 (2000) 3004
- I. Wang, N. Bendsoe, C. af Klinteberg, A.M.K. Enejder, S. Andersson-Engels, S. Svanberg and K. Svanberg, Photodynamic Therapy versus Cryosurgery of Basal Cell Carcinomas; Results of a Phase III Clinical Trial, *Br. J. Dermatology* 144 (2001) 832
- K. Svanberg, I. Wang, S. Colleen, I. Idvall, C. Ingvar, R. Rydell, D. Jocham, H. Diddens, S. Bown, G. Gregory, S. Montán, S. Andersson-Engels and S. Svanberg, Clinical Multi-Colour Fluorescence Imaging of Malignant Tumours - Initial Experience, *Acta Radiologica* 39 (1998) 2
- M. Sjöholm, G. Somesfalean, S. Andersson-Engels and S. Svanberg Analysis of Gas Dispersed in Scattering Solids and Liquids, *Optics Letters* 26 (2001) 16



▲ **Fig. 3:** Prof. Malick Diop and Katarina Svanberg prepare the PDT treatment in Dakar of a Mauritanian "Blue-men" tribe member, suffering from an aggressive basal cell carcinoma.