

ACTION PLANN CUM STATUS REPORT OF THE ACTIVITIES OF CENTER OF EXCELLANCE ON SYSTEMS BIOLOGY AND BIOMEDICAL ENGINEERING – UNIVERSITY OF CALCUTTA

The Center of Excellence on Systems Biology and Biomedical Engineering at University of Calcutta has several research work groups under the leaderships of different faculty members. Currently, the Systems Biology work is led by **Prof. Anjan Dasgupta and Dr. Sudip Kundu**. On the other hand, the biomedical engineering works has three components: (i) developing computer aided diagnosis systems led by **Dr. Nabendu Chaki and Dr. Amlan Chakraborti**, (ii) optical methods for non-invasive diagnosis led by **Prof. Ajay Ghosh and Dr. Kallol Bhattacharya** (iii) development of microfluidics chip led by **Dr. Sanatan Chattopadhyay**. The ultimate aim is to collate the knowledge and expertise gained from these different groups to a particular focus. The center has also aimed to start an M. Tech Course in “Medical Instrumentation”.

We would first describe the salient features of our progress as also recognized by the expert committee and then our shortcomings we observed or / and pointed out by the experts and the steps we have taken to overcome our shortcomings.

Area of Systems Biology:

Group Performance:

The group made significant progress in construction of first genome scale metabolic network of photosynthetic leaf as is evident from very good publication (also mentioned in expert's comments), developed web-based tools to analyze the post-transcriptional data and also to curate the metabolic data.

A non-equilibrium thermodynamic model has been proposed that explains the entropy enthalpy compensation. The larger fluctuation tolerance of smaller organisms has been explained in terms of this model.

Work in progress:

As mentioned previously and in the expert's comment, we have already made good progress. To continue we are currently pursuing the following works.

- The work on the energetics and interactions of photorespiration (generally considered as wasteful process and demand for extensive analysis) and identifying the chlorophyll (the light harvesting pigment) biosynthesis process are in adequate progress and would be continued.
- We have almost completed the genome scale metabolic model of *Oryza sativa indica*, which is on its way to be communicated very soon.
- We have started incorporating the transcriptomic and proteomics data to understand the cellular response in stressed conditions.
- A clustering approach has been employed to describe evolutionary interactions between ‘workers’ and ‘cheaters’ (terms borrowed using game theoretical approaches in biology). The approach attempts to model optimal prescription of pro-biotic dose, pro-biotics behaving analogous to cheaters.

Major Concerns / Recommendations and steps taken by the group:

The expert committee has made no recommendation in this area, thus we continued our research in the defined area we mentioned earlier.

Area of computer aided diagnosis systems:

Group Performance:

Good progress has been achieved in computerized evaluation of Spine Deformity using image processing techniques. Our proposed technique for Cobb Angle measurement for Scoliotic spine using Digital X-Ray images gave excellent results. Research progress has also been made in the automated evaluation of Lumbolumbar (LL) angle of the vertebral column (common cause of back pain) from digital CT images. Our proposed technique involves automatic segmentation and feature selection for quantification of the LL angle.

Apart from the above mentioned research works new research activities have been initiated in the areas of automated detection of lung nodules/tumours from digital X-ray/CT images, Tooth Segmentation from CT images for orthodontic surgery and treatment, fusion of CT/MRI images, inductive sensing for health monitoring of metallic implants and custom hardware design for bio-medical signal processing.

Collaborations with industries have been achieved in the areas of android application development for data capture from portable diagnostic unit TD 2138 and related data visualization and report generation. This work has been done in collaboration with Pracsol Technologies Kolkata. Communications are in process with GE Bangalore for research collaboration in the areas of computer aided diagnosis for lung and liver cancer detection. One of the research scholars of CoE is presently interning at GE in the area of digital X ray image analysis.

Work in progress:

As mentioned previously and in the expert's comment, we have already made good progress. To continue we are currently pursuing the following works.

- The work on the detection of Spinal Deformity is now extended in 3D domain using CT images.
- Extension of the work on image denoising is going on for automatic detection of noise parameters from a given digital X-Ray/CT image, which will help in better denoisation of images.
- We have achieved good results for custom hardware design for real-time video processing using FPGA and this has good application for video based diagnostics.
- In regards to inductive sensing we have found that the sensing coil provided by Texas Instruments with their DAQ captures signal only within proximity of 8mm, which in our opinion is an extremely short distance and might not sense metallic implants under human tissue. Hence, we are designing our own PCB for inductive coil sensor and it will be then interfaced with the Texas Instruments DAQ.
- Automated analysis of microscopic images of peripheral blood smears for diagnosis of malaria, via use of digital image analysis techniques.

Major Concerns / Recommendations and steps taken by the group:

The expert committee has recommended more association of with hospitals and medical experts in our activity for obtaining clinical data as well as validation of our results.

We are in the process of finalising official formalities with Peerless Hospital, Kolkata in regards to obtaining of CT and Digital X-Ray images for lung cancer detection. We have also received consent from medical experts of Peerless Hospital in providing their expertise for verification and validation of our results. Talks with the medical personnel of NRS medical college, Kolkata have also been initiated.

Area of Optical methods for non-invasive diagnosis:

Group Performance:

The group has made some progress in the field of 3D Imaging of microstructures using novel configurations in interference microscopy with the target of fabricating a polarization OCT. Realizing that one of the main problems of interference microscopy involves the use of matching microscope objectives in both the sample and the reference arms of the interferometer resulting in a costly and complicated optical configuration besides the fact the matched objectives are difficult to obtain. To eliminate this difficulty, the optical alignment is so modified that the two interfering beams now pass through the same objective resulting in a clear image with superposed interference patterns. The 3D structure of the micro-sample is derived either by Fourier transformation or through the combination of four or more phase shifted interferograms.

Work in Progress:

- The transition from 3D analysis of inanimate microscopic objects to biological samples is in progress. This involves preparation of unstained biological phase samples.
- An in-line 3D phase microscopic system is being tested for 3D structures of erythrocytes.
- A full field birefringence microscope is being developed.
- Finalization of the optical configuration of polarization OCT based on results obtained so far.

Major Concerns / Recommendations and steps taken by the group:

The expert committee has made no recommendation in this area, thus we continued our research in the defined area mentioned earlier.

Area of development of microfluidics chip:

Group Performance:

The target of this work group is to develop a prototype which will be able to carry liquid droplets of L or nL volume in a controlled way by the application of controlled voltage sequences. The voltage sequence will correspond to a particular pathological or analytical method. In this context, an electrode array needs to be fabricated where voltages will be applied. The electrode array will be covered by an insulating layer followed by a hydrophobic layer coverage.

In the last few months the work in microfluidics area has been progressed significantly as recognised by the expert committee. The initial target of these last few months was to develop some prototype which can prove the concept that by applying some voltage the droplet of few micro-litres size can be moved. This initial goal has been reached. The progress is summarised below:

- By developing the process recipe, the prototype with single pair of gate electrodes, oxide layer and spin coated hydrophobic layer has been complete.
- Voltage has been applied and the movement of droplet is recorded.

Work in progress:

As mentioned previously and in the expert's comment, we have already made good progress. To continue we are currently pursuing the following works.

- We are currently designing the application oriented chip where the spacing and size are very crucial. Optimization of the layer thicknesses for insulating and hydrophobic layers is under progress.
- The droplet has been moved by applying voltage difference between the pair of electrodes. Now we are focusing to develop a multi-channel electrode system so that a sustained movement of the droplet can be achieved.
- For creating the sustained movement, the voltage sequence should be automatically applied to the consecutive electrodes. Such sequence will be generated from an appropriate hardware. Presently, we are focusing to develop such voltage sequence program.
- Once voltage sequence will be generated, it will be interfaced with the electrodes.

Major Concerns / Recommendations and steps taken by the group:

The expert committee has made no recommendation in this area, thus we continued our research

in the defined area we mentioned earlier.

Summary:

The expert committee has pointed out the research progress made by four major different groups. While they, in most of the cases, appreciated our progress (“Good progress made” in the comment); they have also made some recommendations in few cases to improve our research works. In particular, they have suggested to collect more patient data through collaboration with hospitals, to prepare a better datab base for clinical validation.

Major Concerns / Recommendations and steps taken by the COE:

The expert committee has recommended more association of with hospitals and medical experts in our activity for obtaining clinical data as well as validation of our results.

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