

Case Summary & Final Proceedings of SSV on the Kundu-JBC case
28 April, 2007

In August 2006, SSV received a signed complaint from Prof. Sohan P. Modak, a retired professor from the Dept of Zoology, University of Pune, alleging that Dr. Gopal Kundu and his coworkers (Hema Rangaswami and Anuradha Bulbule) from the National Centre for Cell Science (NCCS), Pune, India, published some papers in the prestigious Journal of Biological Chemistry, by “fraudulent reuse of the Western Blot data”. The locus standi of Prof. Modak is that he had a close association with the institute since its inception, as the Principal Co-Investigator/Founder of the NFATCC (subsequently renamed as NCCS), the first Research Director of NFATCC and a former member of the Governing Council of NCCS. His complaint also mentioned that even though an internal committee of the institute indicted the authors, the Director appointed another external committee, which exonerated the authors of all the charges and suspected complicity by the second committee chaired by Prof. G.Padmanabhan. This committee had several prominent scientists from different parts of India as its members, such as Dr. Kanury Rao, Dr. Dinakar Salunke, Dr. Umesh Varshney, Dr. Anil Tyagi, Dr. Shekhar Mande and Dr. Islam Khan.

SSV’s queries revealed that the first internal committee comprising of scientists from NCCS apparently held the authors guilty and sought withdrawal of the JBC papers (though no official record of it has been made available to SSV despite repeated requests). Kundu even confessed in writing about the problems in those papers and agreed to their withdrawal, but retracted his confession soon thereafter to claim innocence and accuse the committee of extracting a confession from him under duress. The Director then appointed a second committee chaired by Prof. G. Padmanabhan (GP), which concluded that “there is no substance in the allegations” and accused the complainant of “malicious intent to spoil the reputation of NCCS”. On the basis of the findings of the GP committee, NCCS issued an office memorandum exonerating the authors of all the charges.

SSV Analysis: The following two papers of Dr. Kundu and his coworkers were examined:

Paper I: Rangaswami H, Bulbule A, Kundu GC.

Nuclear factor-inducing kinase plays a crucial role in osteopontin-induced MAPK/
IkappaBalpha kinase-dependent nuclear factor kappaB-mediated promatrix
Metalloproteinase-9 activation.
J Biol Chem. 2004 Sep 10;279 (37):38921-35. Epub 2004 Jul 7.

Paper II: Rangaswami H, Bulbule A, Kundu GC.

JNK1 differentially regulates osteopontin-induced nuclear factor-inducing kinase/
MEKK1-dependent activating protein-1-mediated promatrix metalloproteinase-9
activation.
J Biol Chem. 2005 May 13;280(19):19381-92. Epub 2005 Mar 9.

Many figures published in both papers contained photographic strips with identical appearance of not only the bands, but also background noise signals, which ought to have been random. There were several instances of the use of identical strips of Western blots both within and between the above two papers to depict different results, constituting a prima-facie case of falsification and fabrication of results, as detailed below:

1. The strips used in the lower panels of Fig. 1B of paper I and Fig. 1B in paper II are the same, but denote different proteins, NIK and MEKK1.
2. The strips used in the lower panels of Fig. 1A of paper I and Fig. 1A in paper II are the same, but denote different proteins, actin and MEKK1.
3. The same strip from Fig. 3 B (bottom panel from paper I) was also used for Fig. 1c and 1d in paper II, again denoting different proteins.
4. The strip in Fig. 3 B (top) are the same in both paper I and paper II.
5. The strips used in the lower panels of Fig 3 A&B in Paper I are flip-flops of each other, though they represent the same protein & one lane is missing. Eg: 2,3,4,5 vs. 5,4,3,2,1.
6. Both the strips in the figure 7C of Paper I have been reused in fig. 6A of paper II. While actin is common to the bottom panel in both above cases, in the top panel, the same strip was used to denote ERK in one case and MEKK in another case, with different values.
7. The top panels of Fig. 6A and 8A of paper II use the same strip to denote upa and c-jun.

Note: Point no. 5 above indicates reuse of the same data within the same paper (Paper I) and point no. 7 indicates reuse within Paper II, whereas all the others indicate reuse of the same data from Paper I in Paper II. The results of the digital analysis of the above similarities using MATLAB software have been appended at the end of this report.

SSV's letter to the Secretary DBT dt. 25 Sept. 2006 with a list of similarities and our queries regarding both the enquiry committees was never answered. The Director, NCCS only sent a copy of the report of the 2nd enquiry committee, without any further comments or answers. Dr. Kundu has also been contacted and he denied these charges. SSV's own consultations with independent experts including a digital image analyst indicated that the similarities between the figures are too substantial to be dismissed as superficial. One immunologist has also asserted that it is just not possible to get too many such random similarities repeating so systematically between two independent sets of experiments, even if they were done by the same person using the same materials in the same lab.

In the meantime, JBC has announced the withdrawal of the second paper (paper II above) on its website in mid-Feb, 2007. Earlier, Dr. Kundu confirmed to SSV that JBC contacted him with certain queries regarding his papers and that he submitted all the requisite information to them. Even after the JBC withdrawal, he continued to maintain that he stood by his papers, indicating that he was not a party to the withdrawal. The JBC did not mention who withdrew the paper and on what basis, and did not respond to SSV queries in this regard. This forced SSV to contact ASBMB, the society that publishes JBC, which then clarified that the journal took its own decision based on its own independent investigation. It states "The paper that you refer to, and related documents including digitally analyzed figures, were carefully reviewed by the Publications Office, the Journal Editor and the Publications Committee of ASBMB. A brief statement from the author's Institution indicating that they found no problem with the paper was also available to the Committee. However, it was the unanimous conclusion of the Editors and the Committee that there was data in a second paper that was reproduced (without citation and with different labelling) from a previously published paper. We therefore notified the author and withdrew the paper." It is important to emphasise here that two independent, parallel investigations by JBC and SSV have come to the same conclusions regarding misconduct by the authors of the two papers.

The JBC also simultaneously published an editorial (mid Feb., 2007) against image manipulations, though no manipulated paper was specifically cited. Among other things, the JBC editorial states “Within the past year, we have, both during and after the review process, detected cases of fraud; re-use of figures from one paper to another for new purposes, re-use of control images within a single paper without explicitly noting the repetition, removal of “contaminating” bands from gel patterns, etc. After investigation of such cases, papers have been rejected or withdrawn and institutional officers notified of misconduct.”

Conclusions and recommendations: In view of the above, SSV has come to the following conclusions and recommendations regarding the issue:

Kundu and his coworkers: They are ALL guilty of misconduct for falsification/fabrication of data in their paper. As a corresponding author and head of the group who receives most of the laurels for the publications of his group (such as the Bhatnagar Prize), Dr. Kundu must also take most of the blame for this misconduct. The concerned authorities should seriously reconsider their position in this case and take appropriate and exemplary action on ALL the authors. Any disproportionate punishment of the students/post-docs while shielding the senior scientists will open up new issues of injustice.

The JBC and ASBMB: The journal must be appreciated for going through the painful process of its own investigation and withdrawal of a published paper. Even though JBC did not reveal the exact figures that were reused, the results of SSV’s own investigation indicate that the journal was correct in its conclusions as well as in its decision to withdraw the paper. However, there have been some deficiencies on the part of the journal. Firstly, the journal failed to detect misconduct both before and after publication, till it was alerted from outside. Secondly, JBC announced a withdrawal under the “additions and corrections” category and not the “retractions” category, and did not mention who withdrew and on what basis, as was done in the earlier cases, creating confusion. Thirdly, JBC editor did not respond to queries from SSV regarding who withdrew it and on what basis, raising questions of accountability of journals regarding their decisions. It was only after ASBMB intervened that SSV obtained a clear picture. SSV records its sincere appreciation to ASBMB for its cooperation and prompt response to our queries in this regard. In order to clear the clouds, the JBC should shift its statement of withdrawal to the “retractions” section and add a detailed note on who withdrew the paper and on what basis, in order to send the right signals to all concerned on either side of the research integrity line.

The concerned Indian authorities: SSV regrets the lack of response of the Secretary, DBT to our queries for 6 months, and the failure of the director, NCCS to provide information to SSV regarding the findings of the first committee appointed by him, even though he readily sent the report of the second committee. It is extremely important for the authorities of NCCS and DBT to repair the damage to the reputation of Indian science caused by the JBC withdrawal and prove their commitment to research integrity and scientific values through their exemplary actions. The govt. of India should take serious cognisance of the earlier editorial in BMJ expressing concerns over the lack of proper response from the Indian government to queries regarding such cases. It is particularly significant to note that the JBC investigated and withdrew the paper of Kundu inspite of being informed in advance that the NCCS “found no problem with the paper”.

The Enquiry Committees: SSV is also constrained to comment on the second part of the complaint of possible complicity in the exoneration of the authors by the GP committee. It is

obvious that the results of SSV's own investigation (as well as that of JBC) do not agree with the conclusions of the Padmanabhan committee. However, SSV currently does not have any evidence to distinguish between willful complicity and a genuine error of judgment by the committee (assuming that their competence is beyond doubt) and would urge its Chairman and the members to reconsider their position in the light of JBC withdrawal and SSV's findings.

The Scientific Community: The SSV records its appreciation of the efforts of the complainant, Prof. Modak and all those who brought the issue into focus and helped us to bring this difficult case to conclusion. SSV also requests the scientific community to develop a rigorous, analytical and quantitative scientific method for detection of image manipulation beyond any doubt and make it widely available. As a preventive step, research institutions and journals may adopt the following policy on image handling pioneered by The Journal of Cell Biology that is being adopted in many countries, and is available online at the site: http://www.jcb.org/misc/ifora.shtml#image_acquisition

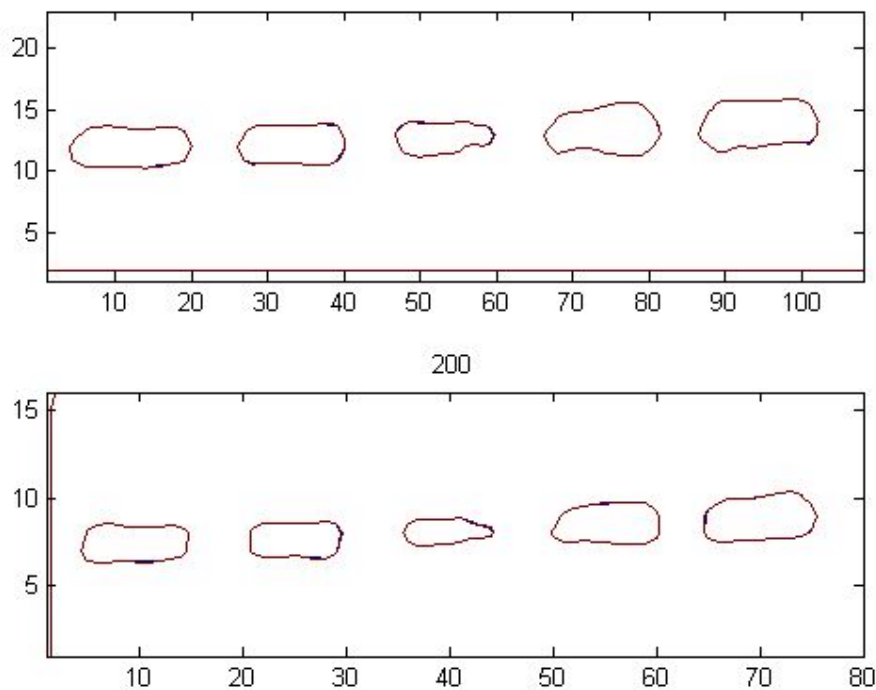
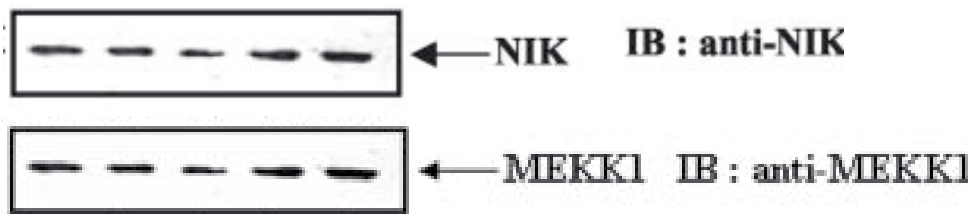
“No specific feature within an image may be enhanced, obscured, moved, removed, or introduced. The groupings of images from different parts of the same gel, or from different gels, fields or exposures must be made explicit by the arrangement of the figure (e.g. using dividing lines) and in the text of the figure legend. Adjustments of brightness, contrast, or color balance are acceptable if and as long as they do not obscure or eliminate any information present in the original. Nonlinear adjustments (e.g. changes to gamma settings) must be disclosed in the figure legend”

Encl: **Results of the digital image analysis** (PTO)

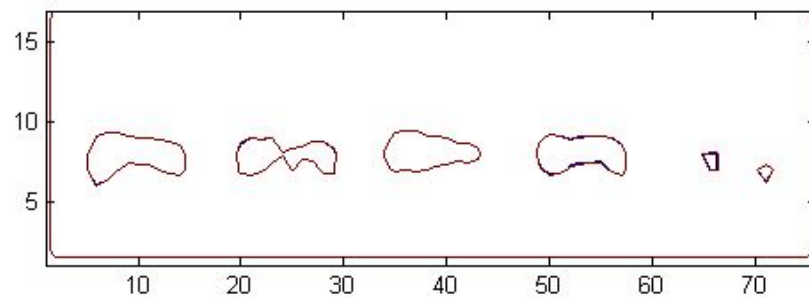
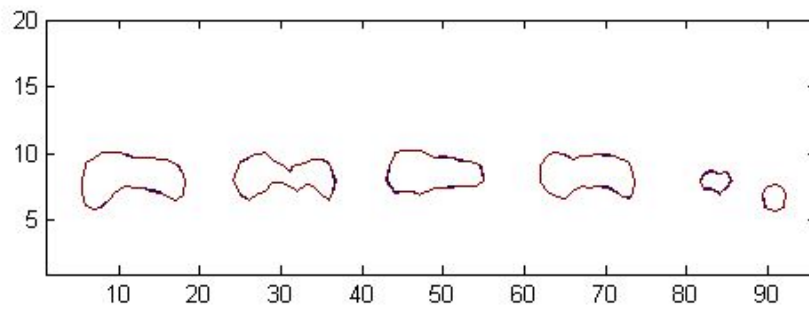
Digital analysis of the photographs

This was done by an IT faculty with research expertise on digital image analysis, using MATLAB software. The photographic images corresponding to the various similarities listed in the beginning of this report were extracted from the JBC website. The images were not encrypted and therefore the full resolution of the images could be extracted from the figures and were found to be good enough for the current analysis. Each set of images under comparison were visualized in several different ways and many sets of plots were generated, but only one or two representative plots are provided here for each set of figures that were compared.

Fig. 1B of paper I and Fig. 1B in paper II (lower panels): Slice analysis



**Fig. 1A of paper I and Fig. 1A in paper II (lower panels): Slice Analysis
Analysis Set 1**



 ← **Actin** IB : anti-actin

 ← **MEKK1** IB : anti-MEKK1

Analysis Set 2

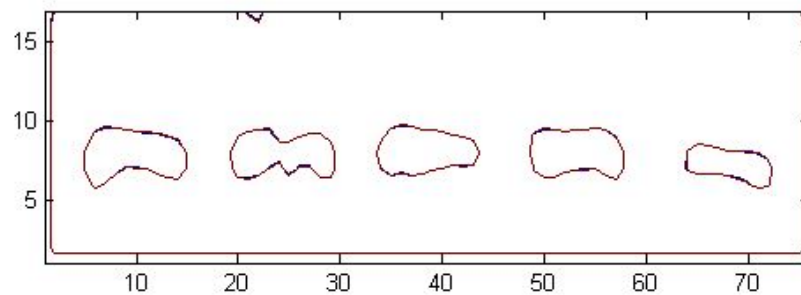
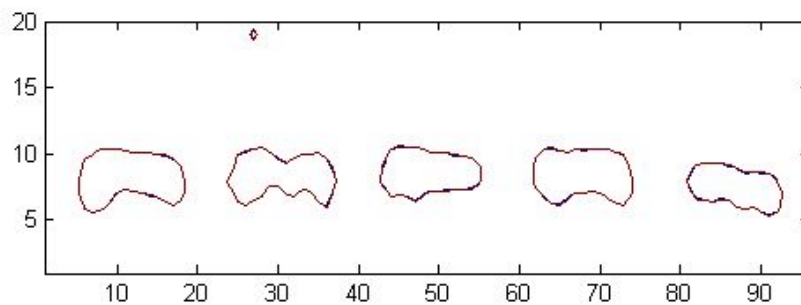
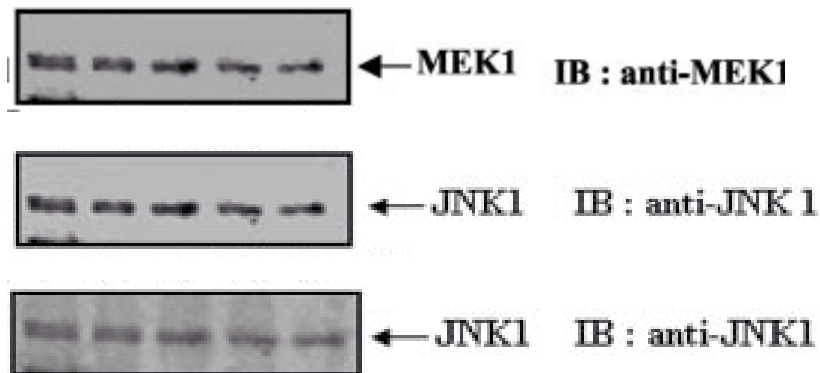


Fig. 3 B (bottom panel) from paper I and Fig. 1c and 1d in paper II



Slice analysis of the top and middle strips

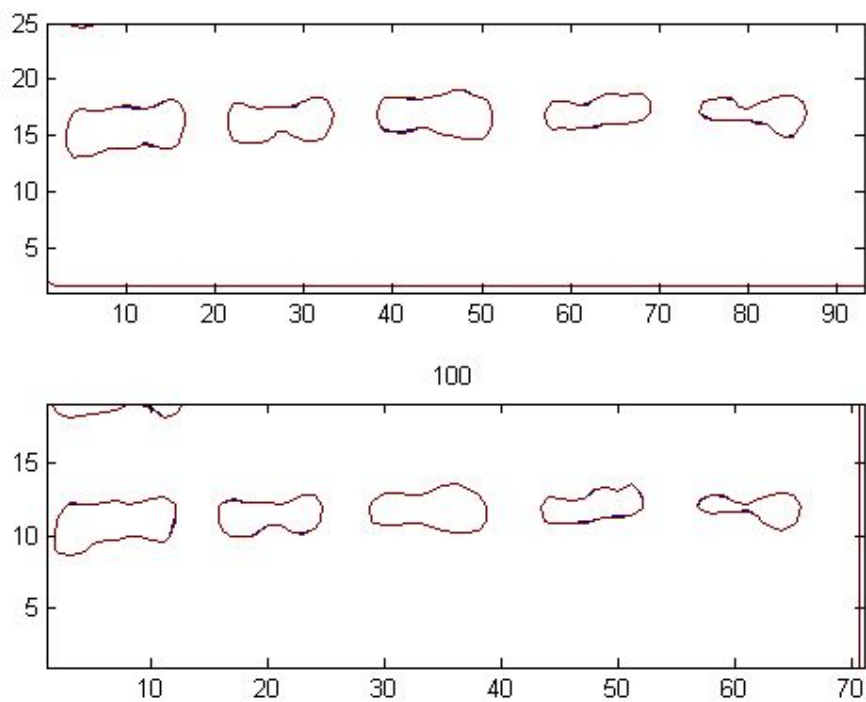


Fig. 3B (top strip) in papers I & II. Profiles of the raw image and rescaled, realigned image

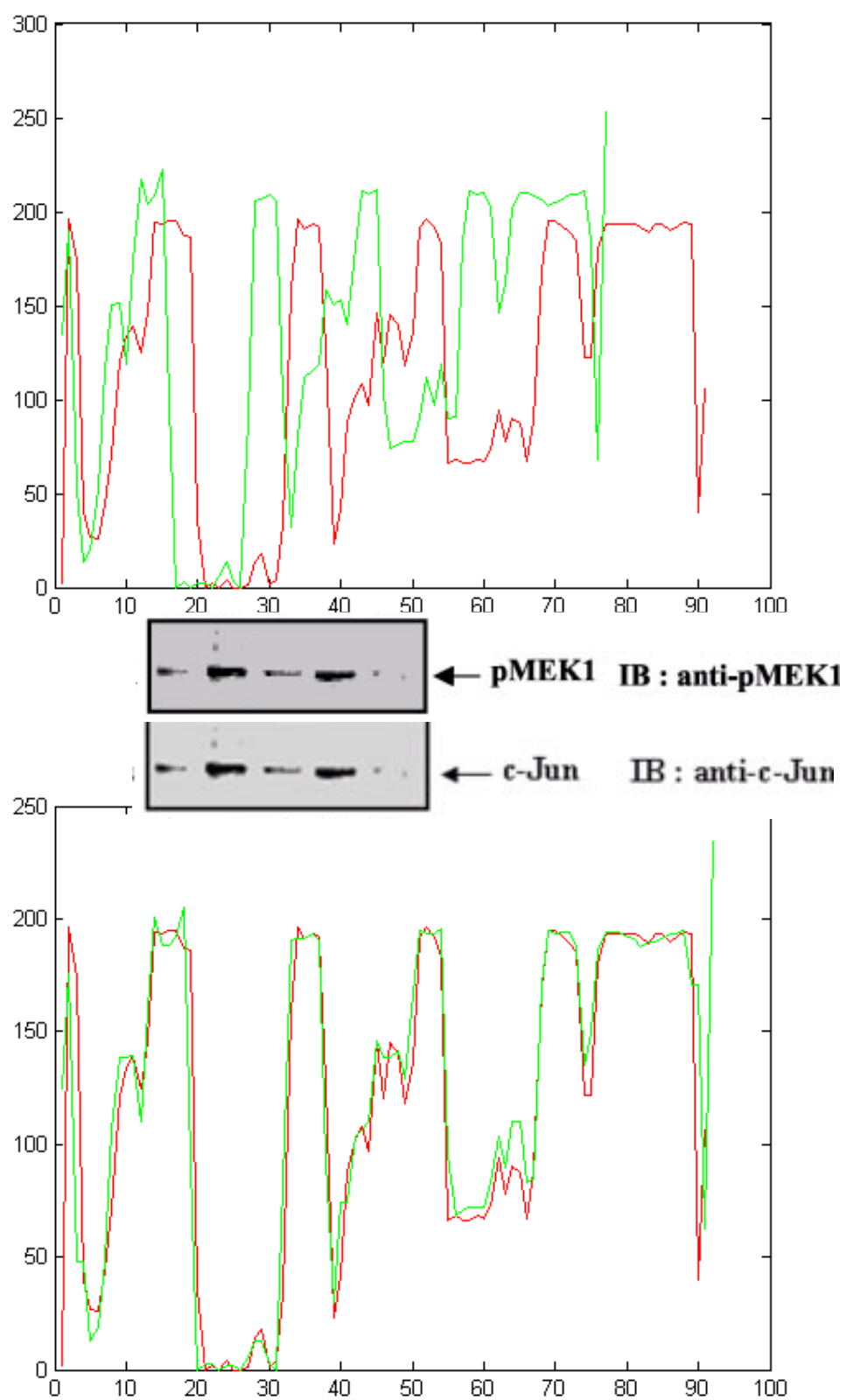


Fig. 3 A&B (lower strip) as flip-flops. Profiles of stretched & aligned images- not rescaled.

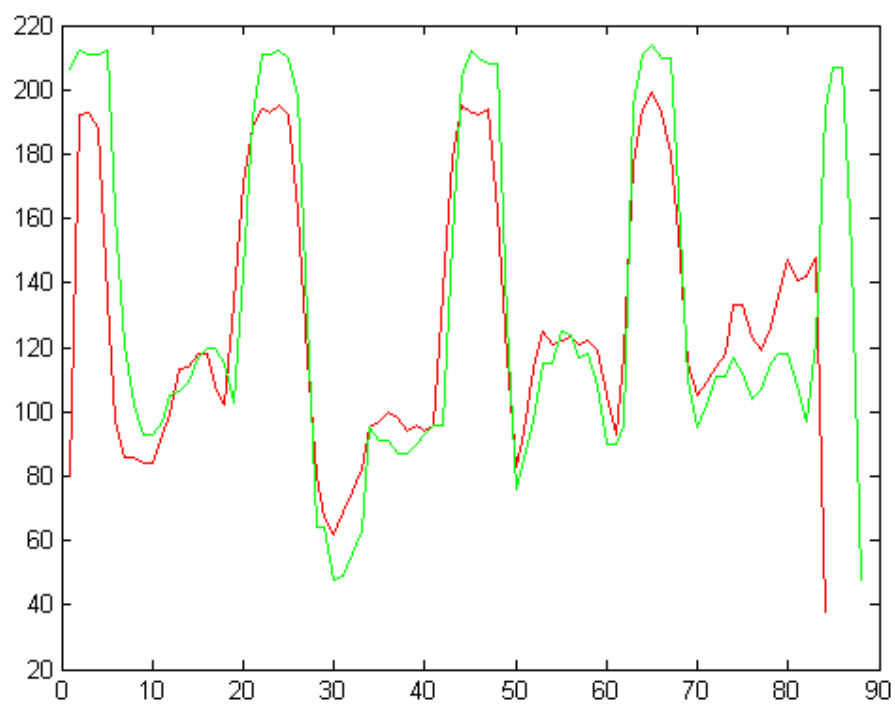
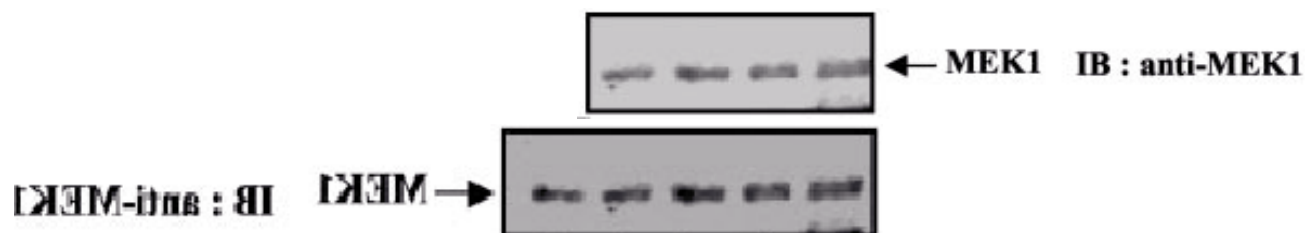
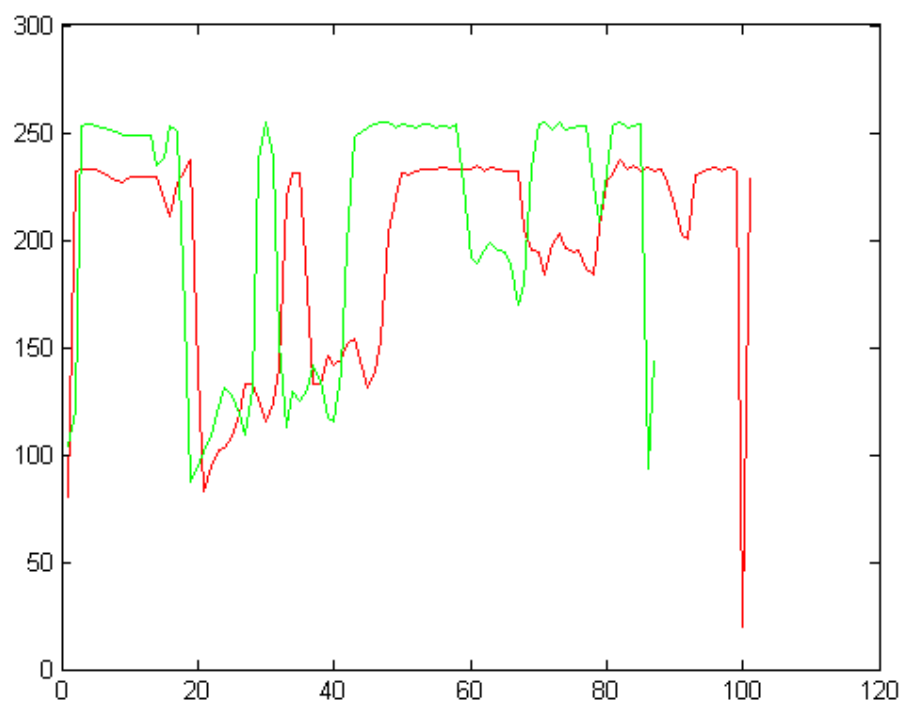
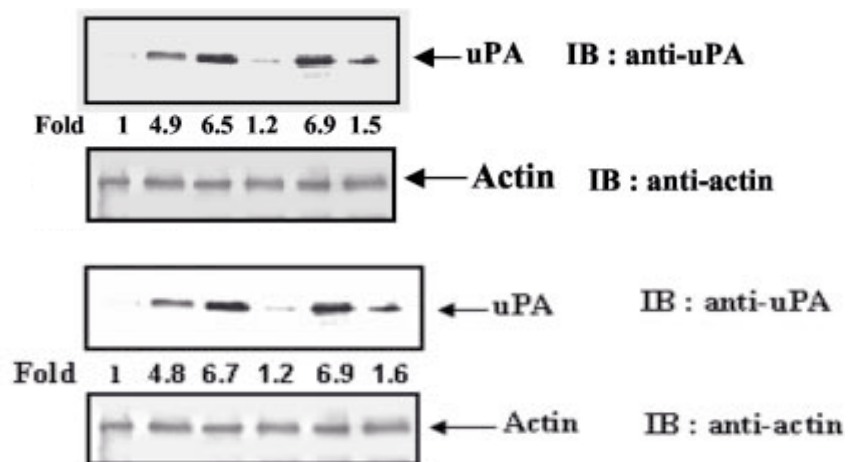


Fig. 7C (both strips) in papers I & Fig. 6A in paper II. Raw Profiles



Contour plots of the top strips of Fig. 6A and 8A in paper II.

