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THE PAP SMEAR BENCHMARK

**INTELLIGENT AND NATURE-INSPIRED APPROACHES
IN PAP SMEAR DIAGNOSIS**

**Special Session Proceedings of the
NISIS – 2006 Symposium**

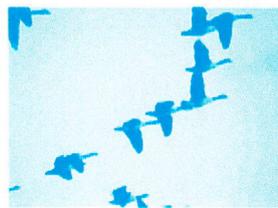
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EDITORIAL

Pap-smear diagnosis represents perhaps the most successful attempt of medical science and practice to face the threat of cancer in humans. George Papanikolaou through pioneer microscopic research is considered the founder of the related methodology since the first half of the 20th century. Since then, the examination of the uterus cervix and the analysis of the specimen through a microscope has become a standard practice for medical doctors worldwide. The even increasing number of people subjected periodically to this routine examination, renders the establishment of reliable automated techniques for cell classification and diagnosis an urgent need, as cyto-technicians face serious difficulties from continuously increased routine workload. The pap-smear database provides data and a baseline for comparing classification methods. The data base contains 917 images of pap-smear cells, classified carefully by cyto-technicians and doctors in the Herlev University Hospital, Denmark. Each cell is described by 20 numerical features, and the cells fall into 7 classes. Students and researchers can access the database on the Internet, and use it to test and compare their own classification methods.

The first aim of the current special session is to introduce a carefully selected set of data, representing images of cells, either normal or abnormal, in order to attract scientists from different disciplines who would like to implement reliable methods for data analysis and cell recognition and classification. Another aim of the session is related to the experimentation using nature-inspired intelligent techniques, in an attempt to gain credit from embedding them in more complex schemes of diagnosis, generalization and data classification. In this sense, different approaches are presented and discussed in the papers that follow, which belong to:

- a. standard (conventional) numerical data analysis techniques
- b. heuristic search algorithmic optimization methods
- c. computational intelligence techniques based on evolutionary optimization
- d. nature inspired techniques Brief characterization of the outcome (accurate, NI can serve as a good alternative to AI/CI in specific tasks like optimization)

In (b), (c), and (d), of the abovementioned approaches, the final classification task, is always performed through a variation of the typical nearest neighbor classification techniques, a fact which renders the proposed techniques as hybrid intelligent schemes for data classification. It is clear, that nature inspired techniques, can mainly perform adequately –if not greatly– the task of solving complex optimization problems, such as the feature subset selection problem, which is the case in this problem.

Nevertheless, a variety of previous intelligent approaches have been applied to an older database, consisting of similar type of data, also available from Herlev University Hospital, Denmark. Those data should be considered somewhat worse in quality of information representation, thus it was later decided to be substituted by the newer data collection. Among the methods applied to the old data set can be found the following approaches:

- Neuro-fuzzy approaches
- Second Order Neural Networks
- Genetic Programming
- Evolutionary Neural Logic Networks
- Nearest Neighbor Classification
- Hard and Fuzzy C-means classification

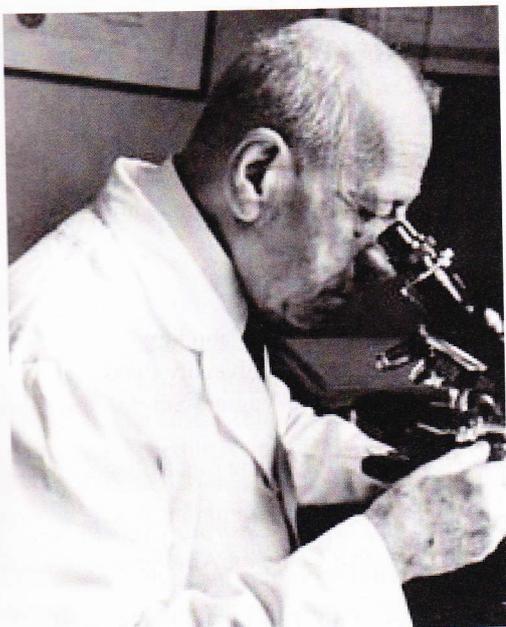
Due to this work previously elaborated by collaborative researchers on the problem of pap-smear diagnosis, detailed comparison and discussion has been included in the papers of this special session, regarding the performance of the new proposed approaches to the old data set. Results show that the proposed methods outperform all the previous ones, rendering this issue a useful standard basis for the application of future similar intelligent attempts for analyzing the new pap-smear database benchmark.

Data are available at www.fuzzy.iau.dtu.dk/download/smear2005

The electronic version of the special session proceedings as well as the related presentation slides will be available to download at <http://decision.fme.aegean.gr/pap-smear>, shortly after the symposium.

The special session organizers would like to express their thanks to NISIS Scientific Committee, for their funding support as well as for giving them the opportunity to organize this session, as part of the NISIS Annual Symposium, NISIS-2006, Puerto de la Cruz, Tenerife, Spain, 29 Nov. – 01 Dec. 2006.

PROF. GEORGIOS PAPANICOLAOU (MD) AND HIS PIONEER RESEARCH ON PAP-SMEAR DIAGNOSIS



George Nicholas Papanicolaou (or Georgios Papanikolaou) was born on the 13th of May 1883, in Kymi (or Coumi) of Evia Island, Greece, to Nicholas (a physician) and Mary Critsutas Papanicolaou. He received an M.D. degree from the University of Athens (1904) and a PhD in biological sciences and zoology from the University of Munich (1910). He got married to Andromachue (Mary) Mavroyeni in 1910. He initially worked as a physiologist for an expedition of the Oceanographic Institute of Monaco for one year. In 1912, he took part in the Balkan War, as an officer in the Greek army medical corps. He then moved to USA in 1913, where he worked initially as a salesman and as a violin player in restaurants. Soon he started working as an anatomy assistant at Cornell University, where he became a full professor in 1924. He was also occupied as a pathologist in New York Hospital (1913) and he became a USA citizen in 1927.

George Papanicolaou was associated with the Cornell University school of medicine for 48 years as a physician and researcher. While studying microscopic slides of cells that had been cast off (exfoliated) in body fluids of laboratory animals and humans, he recognized the presence of abnormal cancer cells. The discovery led to the famous test that bears the first syllable of his last name, the Pap test. He is recognized by his colleagues as the father of modern cytology. Papanicolaou's early work studied the role of chromosomes in sex determination. During these studies Papanicolaou noted cyclical changes in various vaginal discharges from test animals that Papanicolaou linked to the ovarian and uterine cycles. Specifically, at Cornell, Papanicolaou began working with microscope slides of vaginal secretions of guinea pigs, where he observed that changes in forms of the epithelial cells (the outer layer of the skin or of an organ) correspond with the animal's estrus or menstrual cycle. Using the changes as a measuring device, he was able to study sex hormones and the menstrual cycles of other laboratory animals. In 1923 in an attempt to test his theories in humans, Papanicolaou undertook a study of human vaginal smears. During his research Papanicolaou observed that smears from women who had been diagnosed with cervical cancer showed cellular abnormalities (enlarged, deformed, or hyperchromatic nuclei). Writing in the medical journal *Growth* in 1920, he outlined his theory that a microscopic smear of vaginal fluid could detect the presence of cancer cells in the uterus. For a decade he paid little attention to his research in this area, but after the encouragement of his colleagues at Cornell, continued his research on the matter and devoted full time to his research. Later in 1943, he published his findings showing smears of vaginal fluid which could indicate cervical and uterine cancer before symptoms appear. The "new cancer diagnosis," the Pap smear test, won acceptance and became a routine screening technique. During a pap-test, a scraping or smear is taken from the woman's cervix (the mouth of the uterus) or from the vagina, then is stained and examined under the microscope, where cells may appear normal, cancerous, or suspicious. It is a simple, painless, and effective means of early cancer detection. Papanicolaou's findings in fact meant that cervical cancer could be detected and treated before it could metastasize to other sites. The paper and the Pap test proved to be a fundamental milestone in the treatment of a deadly cancer in women. Papanicolaou won international recognition for his research findings. He spent much of his time promoting the test and trained thousands of students in the microscopic detection techniques. Once the test had been accepted, he began to apply the same principle of exfoliate cytology to cancers of the lung, stomach, and bladder. At Cornell he founded the Papanicolaou Research Center where he was working seven days a week peering at slides and looking for malignant cells. He was very rarely going on vacation stating that his work was extremely interesting and demanding. His wife worked with him for a long time as his research

assistant. Papanicolaou won twelve prestigious awards including the Borden award of the Association of Medical Colleges in 1940, the Lasker award of the Public Health Association in 1950, and the honor medal from the American Cancer Society in 1952. His native town of Kymi renamed their town square in his honor. He was the author of 4 books and 150 articles. Around 1961 he took over the Papanicolaou Cancer Institute in Miami. While he was planning for the further expansion of the institute he suffered a heart attack and died on February 19, 1962. He was buried in USA (Clinton, NJ). In 1992, the *Journal of the Florida Medical Association* issued a thirty year commemorative of his death, which states that because of his persistence, there has been a seventy-percent decrease in cervical and uterine cancer. His techniques are also being applied to other organs and systems in the use of fine needle aspiration.

Basic Bibliography and Related Sources

- The Papanicolaou Society of Cytopathology, <http://www.papsociety.org/drpap.html>
- http://ctct.essortment.com/uterinecancerp_ruxf.htm
- <http://www.teslasociety.com/pap.htm>
- <http://www.whonamedit.com/doctor.cfm/2402.html>
- <http://www.unmc.edu/Community/ruralmeded/facil/research/papanicolaou.htm>
- Papanicolaou G.N (1954): Atlas of Exfoliative Cytology, Harvard University Press
- Papanicolaou G.N, Traut H.F. Diagnosis of Uterine Cancer by the Vaginal Smear. New York, The Commonwealth Fund, 1943.
- Speert H. Obstetric and Gynecologic Milestones. New York, 1958, The MacMillan Company. Page 285-29
- G. N. Papanicolaou and C. R. Stockard: *The Existence of a Typical Oestrous Cycle in the Guinea Pig; with a Study of its histological and Physiological Changes*. American Journal of Anatomy, 1917, 22: 225-283.
- G. N. Papanicolaou: *New Cancer Diagnosis*. Proceedings of the Third Race Betterment Conference, January 2-6. 1928. 1928: 528-534.
- G. N. Papanicolaou and Herbert Traut: *The diagnostic value of vaginal smears in carcinoma of the uterus*. American Journal of Obstetrics and Gynecology, St. Louis, 1941, 42: 193-206.
- G. N. Papanicolaou: *Dedication of the Papanicolaou Cancer Research Institute*. Journal of the American Medical Association, 1962, 182: 556-559.
- D. E. Carmichael: *The Pap Smear: Life of George N. Papanicolaou*. Springfield, Illinois, 1973.