HOMOPHONIC SUBSTITUTION

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Presented by CID B. DEARAÚJO

Historically most of the secret-key cryptographic systems that have been broken were broken by exploiting the deviation of the statistics of the clear-text from that of a completely random sequence. *Homophonic substitution* is a venerable technique for converting a clear-text sequence into a random sequence. In 1988 Günther introduced an important generalization of homophonic substitution called *variable-length homophonic substitution*.

The purpose of this presentation is first to review the information-theoretic treatment of Günther's homophonic substitution and then show how to implement it with a finite memory, considering clear-text symbol probabilities which are rational numbers. Shannon's concept of a *strongly-ideal* cipher system will be reviewed in order to provide the motivation for using any kind of homophonic substitution. The precise definition of variable-length homophonic substitution is presented together with the necessary and sufficient condition for such a substitution to be perfect, i.e., to create a completely random sequence. By employing binary coding, perfect homophonic substitution can be achieved with the introduction of less than 2 bits of entropy in each encoded source letter, and can be implemented using less than 4 random bits per coded letter. Some properties of the geometric series, resulting from the base 2 expansion of the clear-text symbol probabilities, are presented and are used to establish an accurate lower bound for the redundancy in homophonic substitution. — (*May 24, 2002*) .

POLYANILINE-SILICON HETEROJUNCTIONS AS A SENSING DEVICE

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Presented by GILBERTO F. DESÁ

Increasing concern with environmental and personal protection together with widespread requirements for more accurate process control has created a need for new or improved sensors for measuring both physical and chemical parameters. This need for better sensors is strongly influenced by the increasing use of intelligent microelectronics for monitoring and control.

Among several sensing devices developed for a wide range of gases, from organic or inorganic pollutants which must be measured at parts per millions level or lower, the conducting polymer or more specifically polyaniline have been considered as a prominent new materials for the development of chemical sensors. The very great interest for these polymers is the relative ease of syntheses by chemical or electrochemical oxidative polymerizations of the monomers, and by the fact that the π-conjugated polymer behaves as a synthetic metal when simultaneously is in the doped and oxidized state. The combination of these two doping processes allows one to develop a material with interesting electronic, electrochemical, magnetic or optical properties.

In the last decade our group has been concentrated with the development of new synthetic routes to prepare conducting polymer to improve its solubility and processability, also we have been involved with the development of sensor for glucose (1-2), ammonia (3), salinity measurements (4), radiation detection (5) using polyaniline as a active support. In this meeting we will present the recent development of semiconductor-polymer heterojunction to be applied as a gamma radiation detection and as a gas-sensing device. — (*May 24, 2002*) .

NATURAL RADIOACTIVITY: OCCURRENCE AND APPLICATIONS ON ENVIRONMENTAL STUDIES

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Although the radioactivity concept has been intrinsically bounded to its weapon applications or to nuclear disasters, as that of Chernobyl, we should not forget that radioactivity is a natural phenomenon and there are radioactive substances in the air we breathe, in the food we eat and even in our clothes.

Natural radionuclides cover a large variety of chemical elements that allows several applications on environmental studies. One of the most known is dating, not only with ^{14}C but, also, with other radionuclides. The so-called radioactive disequilibrium of the uranium and the thorium series could be applied on the study of geochemical processes as water mixing, residence times and siltation rates.

The present talk aims, initially, to refresh the concept of radioactivity as natural phenomena, including natural

radionuclides origin and abundance on different environmental matrices. Following, potential applications on environmental studies will be presented, and, finally, results obtained on several project developed by the Instituto de Radioproteção e Dosimetria/Comissão Nacional de Energia Nuclear (IRD/CNEN/MCT) and by the Chemistry Department of PUC-Rio. — (*May 24, 2002*) .

CLINICAL STUDIES – GENERIC MEDICINES

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Presented by HELIO B. COUTINHO

Clinical testing is not the only way to discover drug effects on people. That is the reason controlled clinical trials are the only legal basis for central regulatory agencies in each country, such as FDA, to conclude that a new drug has clinical effectiveness for a drug or biologic. Before clinical testing begins, researchers analyze the drug's main physical and chemical properties in the laboratory and study its pharmacological and toxic effects in laboratory animals. On the other hand, bioequivalence studies are the clinical test used, most often, when a sponsor proposes manufacture a generic version of an approved off-patent product. The law 9.787 (1999), established the legal basis for the institution of generic drugs in Brazil. Our research group started clinical trial and bioequivalence studies, with collaboration of the Public Pharmaceutical Laboratory of Pernambuco State (LAFEPE), the Brazilian official company to pioneer the development of medicines for AIDS and herperviruses treatment, between 1995 to 1998, even before the establishment of generic policy in Brazil. In 1997 and 1998, LAFEPE was ranked in 21st market position vs. all public and private pharmaceutical laboratories in Brazil. The Aids medicines at a low cost increased the production and sales, and were the main reason of such inedited result.

As a result of the studies developed, the following medicines were introduced to the Brazilian market by LAFEPE: stavudine and zidovudine (AZT) capsules, ganciclovir injectable, lamivudine + AZT, didanosine, lamivudine, and zalcitabine tablets. The result showed bioequivalence for lamivudine tablets (RT) as the 90% CI for both Cmax (99,7) and AUC0-12 (96,7) geom. mean ratios lie within the 80-125% interval. On AZT + DDI therapy the plasma HIV RNA levels decreased $> 0,5$ log after 30 days. The ganciclovir clinical study showed similar results in reference product by the control of retinitis in Aids patients infected with CMV. The stavudine and zalcitabine clinical study demonstrated no adverse effects reported and biochemical parameters remained unchanged and within the reference range. The pharmacokinetics parameters found for AZT + Lamivudine tablet were: AUC0-12 (8975 e 12.189ng.h/ml); Cmax (7.330 e 3.610 ng/ml) respectively, similar to the reference medicine. — (*May 24, 2002*) .

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BACTERIOLOGICAL LARVICIDES OF DIPTERAN DISEASE VECTORS

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The bacteria *Bacillus sphaericus* (*Bs*) and *B. thuringiensis* serovar. *israelensis* (*Bti*), display toxic action on mosquitoes and black flies, important vectors of man disease, acting as per os larvicides. These sporulating bacteria show a major advantage over synthetic insecticides: selectivity due to the specific mode of action. *Bs* is toxic against some species of Culicidae while *Bti* is also highly toxic against Simuliidae.

Both bacteria produce, during the sporulation, crystals, which contain protoxins. *Bti* crystals contain four polypeptides of 123-, 135-, 72- and 28-kDa, respectively called Cry4A, Cry4B, Cry11A and CytA. For *Bs*, crystals contain a toxin (Bin) made of two polypeptides of 42- and 51-kDa, called BinA and BinB, respectively. The mode of action of these proteins on larvae involves the ingestion of crystals and spores in suspension in water. Inside the midgut lumen, under the action of the alkaline pH and proteinases, protoxins in the crystals are solubilized and activated. Released toxins bind to apical microvilli of midgut cells, then cytopathological alterations are observed in midgut cells, leading to the death of larvae. Those toxins need to act in synergy to display the full toxicity and also bind to specific receptors in the larval midgut. Recently, the receptor of the Bin toxin of *Bs* in *C. pipiens* larvae was identified as being an α-glucosidase of 60 kDa.

Bti and *Bs* based larvicides have been produced and successfully used in vector control programs throughout the world. *Bti* has been mostly used to control species