Applied Nonlinear Statistical Methods, 6th of October 2014, University of Tampere

Name of the course: Applied Nonlinear Statistical Methods

Course Overview:

Researchers often recognize that nonlinear regression models are more applicable for modelling their physical and medical processes than are linear ones for several important reasons. Nonlinear models usually fit their data well and often in a more parsimonious manner (typically with far fewer model parameters). Also, nonlinear models and the corresponding model parameters are usually more scientifically meaningful. But selecting an efficient experimental design; choosing, fitting and interpreting an appropriate nonlinear model; and deriving and interpreting confidence intervals for key model parameters can present practitioners with fundamental and important challenges.

This course first reviews the essentials of linear regression, and subsequently introduces and illustrates generalized linear models (such as logistic regression), Gaussian nonlinear models, and generalized nonlinear models, focusing on applications. Illustrations are given from the domains of bioassay, relative potency and drug or similar compound synergy useful in biomedical and environmental sciences. Caveats are discussed regarding convergence, diagnostics, and the inadequacy of standard (Wald) confidence intervals – which are the intervals provided by most software packages. Extensions to bivariate situations (such as those focusing on both efficacy and safety of drugs) and censored (survival) analysis are also provided, as are implications for experimental design. Implementation using the SAS® and R statistical software packages will be discussed, but references will be made to other packages (such as SPSS and STATA) as well.

Course Outline:

I. Brief review of simple and multiple linear regression; two-sample t-tests, ANOVA, ANOCOV (analysis of covariance); diagnostics and model checking; logistic regression.
II. Introduction to Gaussian nonlinear models; practical concerns (choosing a model, starting values); nonlinear contrasted with linear models and with generalized linear models; applications (substance dissolution and enzyme kinetics); confidence regions, intervals, and the impact of curvature (nonlinearity, asymmetry).
III. Diagnostics and model checking; examples involving ELISA's (and other assays) and pharmacokinetics; extensions of classical methods including modelling variance functions and correlated responses; mixed and hierarchical nonlinear models.
IV. Generalized nonlinear models and applications in bioassay, relative potency, and drug/similar compound synergy modelling; usefulness and limitations of the IML and NLMIXED SAS® procedures, and the NLS R procedure.
V. Experimental design strategies including benefits and limitations of optimal designs; robust 'optimal' design strategies; geometric designs.
VI. Extensions to (multivariate) bivariate Gaussian and binomial responses and to censored data in the context of the detection of drug/similar compound synergy.

Teaching methods: Lecture and practical.

Passing the course: Active participation to lectures and practicals.

Lecturer: Professor **Timothy E. O'Brien,** Department of Mathematics and Statistics, Loyola University of Chicago.

Coordinator: Professor Tapio Nummi (tapio.nummi@uta.fi).

Language and extent: Teaching language English, extent 2 ECTS.

Target group: doctoral students in health sciences, doctoral students in other relevant fields, students in statistics, biostatisticians.

Limited access: Maximum 35 participants, doctoral students in health sciences and members of the Finnish society of biostatistics will be priorized.

Time: 6.10.2014
Place: Linna, Kalevantie 5
Enrolment: sihteeri@biostatistiikanseura.org At the latest 26.9.2014.

SCHEDULE

	Date	**Time**	**Place**
Lecture:			
Monday	6 October	9-16	LINNA, LS K108
Practicals:			
Monday	6 October	16-18	LINNA, ML51

Software in practicals: R (free software, http://www.r-project.org)