Meddelelser, v/Morten Frydenberg Institut for Biostatistik Aarhus Universietet BREV Ukonvoluteret

PP Danmark

Returneres ved varig adresseændring

Næste animmer af "MEDDELELSER" udkommer 2. juni 1998.

Bidrag til dette gammer skal være redaktøren i hænde senest

mandag den 25. maj 1998.

Bidrag bedes sendt til:

Meddelelser, v/Morten Frydenberg Institut for Biostatistik Hægh-Guldbergs Gade 10 8000 Århus C. eller med e-mail til: morten@biostat.aau.dk

Samme adresse bedes benyttet ved indmeldelse i DSTS og ved adresseændring.

Bidrag i elektronisk form ønskes helst i et af nedenstående formater: Word, LATEX, HTML, Postscript eller ASCII.

Anno neeringa f stillinger er pr. 1. Januar 1998 kr. 500 pr. side

# **MEDDELELSER**

Dansk Selskab for Teoretisk Statistik

## Department of Theoretical Statistics University of Aarhus

Tirsdag den 12. maj, kl. 14.15 i H2.28

Stefano Maria Iacus, Dipartimento di Scienze Statistiche, Università degli Stadi di Padova.

Title and abstract will later be announced on http://www.mi aau dk/events/

Torsdag den 14. maj, kl. 14.15 i H2.28

Elisa Nicolato, Dipartimento di Matematica Para e Applicata, Universita' di Padova:

A Bayesian Dynamic Programming Approach to Optimal Maintenance combined with Burn-in.

We consider a complex system consisting of N identical components that are expected to function properly during a given period (mission time). Due to the possibility of failure before completion of the passion time, one allows for Burn-in an order to cope with the problem of "infant mortality" as well as Maintenance (to reduce somehow to zero the age of the surviving components). But, as one can observe it various situations, after maintenance, the failure rate has a sudden increase, immediately followed by a period of relatively sharp decrease towards normal levels, from which it then starts to increase again due to ageing. This makes it convenient to let each moment of maintenance follow by a period of burn-in (maintenance induced burn-in). We present a two-level (Bayesian) Dynamic Programming approach to determine the optimal timing of the maintenance interventions and durations of burn-in, including maintenance-induced burn-in.

(Joint work with Wolfgang J. Ranggaldier

Organizer: Jens Ledet Jensen

### Selskabets bestyrelse:

Formand:		
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2200 København N		

Selskabets www-adresse: Http://www.dsts.dk.

Generiske e-mail-adresser i selskabet:

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Jyske anliggender: jysk, jyskeanl, jufland Indkøb: indk, indkoeber, suppl, supplier

Meddelelser: medd, meddelseler, newsl, newsletter

Bestyrelsen: best, bestyr, bestyrelse, board

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### Odense Universitet

Campusvej 55 DK-5230 Odense M Tlf. 6557 2387 Fax 6593 2691

Institut for Matematik og Datalogi

Til alle undervisere i matematiske fag ved AUC, AU, OU, KU, RUC, KVL.

> 22. april 1998 HJM/hjm

### NYT CENSORKORPS.

Pr. 1/4 1998 er der udpeget et nyt censorkorps i de matematiske fag, inklusive matematik-økonomi uddannelsen, matematisk statistik og forsikringsmatematik. Listerne kan beses via min hjemmeside http://www.imada.ou.dk/~hjm/censorliste.html

I forhold til den gamle liste er der gledet 49 navne ud, og der er kommet 59 nye navne til. Udskiftningen er dikteret af bekendtgørelsens krav om, at mindst 25 % af det gamle korps skal skiftes ud. Paa ovennævnte censorhjemmeside kan man iøvrigt ogsaa se en kort beskrivelse af, hvilke principper censorformandskabet har brugt ved udarbejdelsen af den nye liste.

I allersidste fase af proceduren sagde en del foreslåede personer nej tak, så det er tænkeligt, at der bliver behov for at supplere den nye liste med nogle flere navne, men her ved sommereksamen 1998 skulle man vel kunne klare sig i lyset af følgende:

Ved eksamen sommeren 1998 kan man anvende censorer fra både den gamle og den nye liste, men fra efteråret 1998 gælder kun den nye.

Med venlig hilsen,

Hans J. Murkholm, censorformand, matematik.

Tele on 557 2309

E-mai/hjm@imada.ou.dk

### SEMINAR I MATEMATISK STATISTIK OG SANDSYNLIGHEDSREGNING

Afdeling for Teoretisk Statistik, Københavns Universitet

Seminarerne afholdes kl. 15:15 præcis i auditorium 10 på H.C.Ørsted Instituttet.

Der serveres te i lokale E325 kl. 15:00.

(Michael Sørensen)

Onsdag den 6. maj: Bent Jørgensen (University of British Columbia and OdenseUniversity):

### Basu's Theorem and Generalizations.

Abstract: Se Meddelelser nr. 2.

Onsdag den 13. maj: Stefano Iacus (Le Mans):

# The van Trees inequality for small dispersion diffusions with application to semiparametric models.

We will derive the van Trees inequality for diffusion processes with small dispersion asymptotics. This inequality is a Bayesian version of the Cramér-Rao device and concerns a lower bound on the quadratic risk. The peculiarity of this inequality is that the lower bound does not depend on the properties of the estimators (i.e. bias) and can be easily used in non-parametric and semiparametric models.

We will show how to construct an asymptotic lower bound that does not depend on the prior distribution and an alternative proof of classical semiparametric local minimax lower bounds based on the van Trees inequality. This approach, altough applicable only for the quadratic loss functions, is powerful and a simpler one and does not require LAN properties of the models involved as in traditional proofs based on the Hájek-Le Cam inequality.

Onsdag den 20. maj: Inge Henningsen (ATS-KU):

### Lægevidenskab og køn

En analyse af det lægevidenskabelige område på Københavns Universitet med henblik på en kortlægning af kvindernes placering blandt de videnskabeligt ansatte.

### STUDIEGRUPPE I STATISTISK INFERENS FOR STOKASTISKE PROCESSER.

Afdeling for Teoretisk Statistik, Københavns Universitet

Studiegruppen, som samler deltagere fra hele Hovedstadsområdet, mødes ca. 1 gang om måneden. Yderligere information om studiegruppen og dens hidtidige arbejde kan findes på www-siden http://www.math.ku.dk/~michael/studiegruppe, hvor man også kan se, hvordan man tilmelder sig studiegruppens mailing list.

Kommende møder:

Mandag den 27. april kl. 14:15-16:00: Ernst Hansen (ATS-KU): **Pulse dimension estimation**. Sted: A 107 på HCØ.

Torsdag den 28. maj: Ulrike Putschke (Humboldt-Universität zu Berlin): Asymptotic properties of the MLE for the 2-dimensionalOrnstein-Uhlenbeck process. Klokkeslet og lokale meddeles senere på www-siden.

### **SEMINAR**

Afdeling for Matematik, Aalborg Universitet
Frederiks Bajers vej 7E.
Alle er velkomne
(Martin Bøgsted Hansen)

Torsdag den 7. maj 1998 kl. 14 i lokale E3-109

Tail asymptotics for M/G/1 type queueing processes with subexponential increments
Jakob R. Møller, Department of Mathematical Statistics, Lund University;}

Bivariate regenerative Markov modulated queueing processes  $\{I_n, L_n\}$  are described.  $\{I_n\}$  is the phase-process and  $\{L_n\}$  is the level--process. Increments in the level process have subexponential distributions. A general boundary behavior at the level 0 is allowed. The asymptotic tail of the cycle maximum  $M_{C'''''}$  during a regenerative cycle C''''''' and the asymptotic tail of the stationary random variable  $L_{\infty}$ , respectively, of the level process are given and shown to be subexponential, with  $L_{\infty}$  having the heavier tail.

Vært: Bjarne Højgaard

### SEMINAR I ANVENDT STATISTIK

Biostatistisk afdeling, Københavns Universitet
Seminarerne afholdes kl. 15.15, Panum Instituttet, Blegdamsvej 3.

(Indgangen Nørre Alle 20 kan benyttes).

Der serveres te i Biostatistisk Afdeling på gangarealet (33.4.11) kl.14.45.

(Thomas Scheike)

Mandag d. 11. Maj 1998, lokale 31.01.4a

# An application of shared frailty models to the failure time analysis of total hip protheses

Guido Schwarzer, Center for Data Analysis and Model Building, University of Freiburg, Germany.

Joint work with Martin Schumacher, Institute of Medical Biometry and Medical Informatics, University of Freiburg, Germany.

In a specialized hospital in the Freiburg neighbourhood, data on total hip protheses has been documented prospectively during the last 14 years. The data comprises 869 patients/1018 hip protheses with complete information on time to revision, time to death, stem type and size, and various patient-specific variables. The main aim of the analysis was the identification of potential risk factors responsible for failure of the hip prothesis due to aseptic loosening of the stem. Proportional hazard regression models were used in a competing risk framework in order to account for concurrent mortality. To ensure independence of observational units we considered only the failure time of the first implanted hip prothesis. However, this approach does not use the complete failure time information available.

In a subsequent analysis, we utilized shared Gamma frailty models to account for possible dependencies in the failure times of patients with bilateral protheses. Our results indicate that the failure times of bilateral hip protheses could be treated as if they behave independent. This conclusion could be confirmed in a simulation study which was aligned to the specific design of our data set. Furthermore, we observed that the variability of the estimated frailty parameter depends markedly on the number of patients with bilateral protheses and events observed for both protheses.

Mandag d. 18. maj 1998, lokale 31.01.4a

# Models for survival data based on multivariate frailty distributions.

Philip Hougaard (Novo Nordisk)

For many purposes, the standard "shared" frailty model for multivariate survival data is not satisfactory. Some cases, where extension could be desired are

1. More complicated dependence structures for data with more than two observations (like father - mother - child or whole biological/adoptive families).

- Simultaneous handling of data with varying degrees of dependence (like monozy-gotic and dizygotic twins).
- 3. Center by treatment interaction in drug trials.
- Alternating models (with transitions back and forth between states like healthy and diseased).
- 5. For giving a better fit to bivariate data.
- To avoid (reduce?) identifiability problems in gamma frailty models with covari-ates acting by proportional hazards.
- 7. Short-term dependence (that is, frailty changing over time).
- 8. Hidden cause of death model (that is, even though the actual cause of death is un-known we might get a different dependence structure by assuming a different frailty for each cause of death).

I will introduce multivariate frailty models using two different approaches to derive such distributions, and discuss in which cases, it makes a real and important extension. Two major applications considered are survival of twins, and recurrent episodes of bleeding for postmenopausal women, receiving hormone replacement therapy.

Mandag d. 25 maj 1998, kl 11.15, lokale 1.2.65

### How many people can the earth support?

Cohen, Joel E. (Rockefeller University and Columbia University New York, USA)

The human population of the Earth has multiplied 1,000-fold in the last 10,000 years, and 90 percent of this growth has occurred within the last 350 years. Now at nearly 6 billion, the population is expected to grow by additional billions in coming decades. Can the Earth support billions of additional people, or the people it has now, at present levels of living or better? How many people can the Earth support?

The Earth's capacity to support people is determined both by natural constraints and by hman choices (past, present and future) concerning population, economics, environment, and culture (including values and politics). Human carrying capacity is therefore dynamic and uncertain. Published numerical estimates of Earth's "human carrying capacity" range from fewer than one billion to more than one trillion. The estimates make different assumptions about both natural constraints and future human choices.

The Earth's capacities to provide inputs and absorb outputs of human material activities are not infinite. In the coming half century, we and our children are less likely to face absolute limits than difficult trade-offs -- trade-offs among population size and economic well-being and environmental quality and dearly held values.

To make the coming trade-offs easier, the "bigger pie" school says: develop more technology. The "fewer forks" school says: slow population growth and reduce consumption. The "better manners" school says: improve people's interactions (for example, by defining property rights to open-access resources, by increasing equality, and by improving governance). All these approaches have value.

Mandag d. 25. maj 1998, lokale 31.01.4a

### **Limiting Dilution Assays**

Lise Brøndsted (Biostatistisk Afdeling, Københavns Universitet)
Lars Vindeløv og Charlotte A. Russell (Hæmatologisk Klinik II, Rigshospitalet)

Ved knoglemarvstransplantation er der risiko for graft-versus-host disease, som opstår ved at donorceller reagerer imod patienten (de såkaldte alloreaktive T-celler fra donoren reagerer mod antigener fra patienten). Af behandlingshensyn skal frekvensen af alloreaktive T-celler estimeres, og dette kan gøres ved at måle koncentrationen af et stoffet IL-2 i fortyndinger af varierende styrke (et varierende antal donorceller tilsættes et fast antal patientceller). Eksistensen af én alloreaktiv T-celle i en fortynding antages at give en koncentration af stoffet over støjniveau (single-hit modellen), og en sådan fortynding kaldes positiv.

Der udføres en fortyndingsrække (limiting dilution assay), der typisk består af 10 forskellige fortyndinger og 24 replikater (brønde) for hver fortynding, og brøndene inddeles i positive og negative svarende til koncentrationen af stoffet. Ud fra en Poissonmodel for antallet af alloraktive T-celler i hver brønd estimeres frekvensen af alloreaktive T-celler ved maksimum likelihood metoden, og et konfidensinterval for frekvensen af alloreaktive T-celler konstrueres symmetrisk på logaritmeskala. Modellens forudsætninger kontrolleres ved sammenligning med double-hit modellen, hvor det antages at der skal mindst to alloreaktive T-celler i en fortynding for at få en koncentration af stoffet over støjniveau.

Der er et begrænset antal patientceller til rådighed, og under denne begrænsning udføres et simulationsstudium for at undersøge effekten af designet på den estimerede frekvens af allreaktive T-celler.

# Center for Registerforskning Statistiker

Til centerets registerbaserede forskningsprojekter indenfor sociologi, socialmedicin og epidemiologi søges en videnskabelig medarbejder med statistisk uddannelse. Medarbejderen skal også medvirke ved centerets informations- og rådgivningsvirksomhed. Den helt rigtige ansøger har...

- interesse for statistisk analyse af forløbsdata inden for sundheds- og samfundsvidenskaberne
- relevant akademisk uddannelse, fx statistiker eller matematikøkonom
- interesse for empirisk forskning og gerne erfaring med anvendelse af registerdata
- betydelig erfaring med edb, herunder erfaring med SAS

... men vi hører også gerne fra ansøgere som ikke opfylder alle disse krav.

Ansættelsens varighed er to år, med mulighed for forlængelse. Løn svarende til overenskomst mellem den pågældendes faglige organisation og Staten, herunder forskertillæg. Centeret tilbyder et tværfagligt og inspirerende miljø med gode faglige udviklingsmuligheder for en person med interesse for anvendt statistik.

Yderligere oplysninger kan fås ved henvendelse til centerleder Henrik Møller på tlf. 39 17 38 55. Ansøgning sendes til Center for Registerforskning, Sejrøgade 11, 2100 København Ø. senest den 15/6 1998.

Center for Registerforskning er et forskningscenter, oprettet i 1995 af Danmarks Grundforskningsfond. Centeret har til huse i lejede lokaler i Danmarks Statistiks bygning på Østerbro i København. Centeret beskæftiger sig med oplysnings- og uddannelsesvirksomhed om registre og registerforskning, og yder praktisk hjælp til forskningsprojekter. Centeret driver selv forskning indenfor bl.a. epidemiologi, demografi, samfundsmedicin og sociologi.

### **INSERM**

INSTITUT NATIONAL DE SANTÉ ET DE LA RECHERCHE MEDICALE

### ATELIER INSERM 100 MODELES MULTI-ETATS EN EPIDEMIOLOGIE

18-19 June 1998 - Phase ... I Le Vésinet(Paris),France 8-9 October 1998 Phase ... II Bordeaux, France

# ATELIER INSERM ON MULTI-STATE MODELS IN EPIDEMIOLOGY"

### General information

Scientific committee: Daniel Commenges, INSERM U330, Bordeaux; Per K Andersen, Statistical Research Unit, Copenhague; Sylvia Richardson, INSERM U170, Paris.

### Organising committee:

Atelier de formation INSERM(France). 101, rue de Tolbiac - 75654 Paris cedex 13;

**Telephone:** (33) 44 23 62 05/06/07 - **Fax**- (33)44 23 62 93

Email:ateliers@tolbiac.inserm.fr http://www.u-bordeaux2.fr/Actu/Congres/INSERM100

### Objective

The objective is to present the modern approaches to multi-state models and their applications to longitudinal data especially in the field of chronic diseases. For such diseases, it is often rewarding to distinguish several states of evolution. This allows to analyze more finely this evolution and to use more information because the whole information from the start to the end of the disease process is not available for all patients. There are more and more data from cohort studies which lend themselves to such analyzes. Alzheimer's disease and AIDS are two important examples of application of this approach. The "illness-death" models are particularly useful to study chronic diseases in aged people; in order to modelize the evolution of HIV positive subjects, one generally defines a larger number of states based either on clinical or biological criteria. The aim of this workshop is to give tools for analyzing such data to epidemiologists and to present the state of the art of this approach to more theoretically oriented biostatisticians.

**Audience**: Biostatisticians, epidemiologists having a good level in biostatistics and working on the analysis of cohort data.

### STATE OF THE ART... PHASE I

Number of participants:70.

Dates: June 1998.

### Objective:

The objective of this workshop is to illustrate modern approaches to multi-states models and applications to cohort studies of chronic diseases.

### Main Topics:

- Generalities: a)multi-state models, Markov and semi-Markov models; b)schemes of observation: continuous observation, interval censored data, truncation.
- Parametric approach: a) homogeneous Markov models; b) application to AIDS; c) non-homogeneous models and semi-Markov models.
- Non-parametric approach: non-homogeneous models and semi-Markov models with application to AIDS.
- Approach by counting processes: a) counting processes and application to survival data; b)
   Markov models: competing risks and the illness-death model; estimation of transition probabilities; c) semi-Markov models.
- Application to dementia: the illness-death model.
- Application to cancer.
- Application to public health.

### Speakers:

Alioum Ahmadou, Bordeaux, INSERM
Per K Andersen, Copenhague, Universite of Copenhagen
Daniel Commenges, Bordeaux, INSERM
Frank Gauzere, Bordeaux, INSERM
Niels Keiding, Copenhague, Universite of Copenhagen
Sylvia Richardson, Paris, INSERM
Martin Schumacher, Feiburg, Germany
Gabi Schulgen, Feiburg, Germany

### PRACTICAL COURSE... PHASE II

**Training program:** To confirm knowledge acquired in Phase I. To enter into the details of the methods by using data brought by participants. Four problems proposed by participants will be selectionned and analyzed. The use of conventional software as well as more specialized software will be studied. Selection: A maximum of 12 participants will be selected on their motivation and ability of treating real data with the multi-state approach.

### PROGRAMME OF PHASE I

### First day:

- 1. Survival analysis; problems of incomplete observations (censoring, truncation) (Per K
- 2. Multi-state models (MSM):definition and usual patterns In particular the different possibilities with 2 or 3 states will be considered: the survival, reversible, competing risk, progressive, illness-death models(Daniel Commenges)
- 3. Assumptions that can be made for a MSM Time-homogeneity: semi-Markov assumption: choice of the time scale; homogeneity versus frailty; censoring; covariates (Daniel Commenges)
- 4. Relevant quantities to estimate in a MSM: intensities, probability of being in one state at time t, incidence and prevalence of a disease (Per K Andersen) Lunch

- 5. Probability of events and likelihood Two cases: observations in continuous time; observation in discrete (arbitrary) times (Martin Schumacher)
- 6. Non-parametric estimation with continuous observation (simple case) (Niels Keiding)
- 7. Non-parametric estimation with continuous observation (with covariates) (Niels Keiding)
- 8. Non-parametric methods for interval censoring (Frank Gauzère)

### Second day:

1

- 9. Markov models with piecewise-constant intensities for continuous-time observations. The intensities are constant or piecewise constant and rates can be computed similarly as in the person-years and Poisson regression methods (Per K Andersen)
- 10. Homogeneous Markov model with discrete observation times; application to AIDS (Sylvia
- 11. Application of the Illness-death model to dementia (Daniel Commenges)
- 12. Application of MSM to duration of hospitalization (Gaby Schulgen, Martin Schumacher) Lunch
- 13. Application to bone-marrow transplant (Niels Keiding)
- 14. Other Application to cancer (Gaby Schulgen, Martin Schumacher)
- 15. Methods for treating problems with interval censoring and covariates A non-parametric method has been proposed by Kim. De Gruttola and Lagakos. Biometrics 49, 13-22, for a progressive model (Alioum Ahamadou)
- 16.Methods for treating problems with interval censoring and covariates: the penalized likelihood approach. This problem can be treated by generalizing the approach proposed in Joly, Commenges and Letenneur, Biometrics, in press (Daniel Commenges)

# Kalender

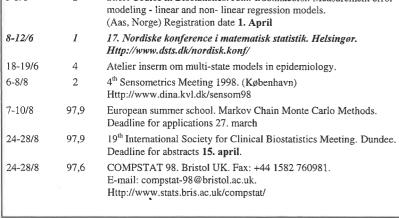
(arrangementer annonceret i MEDDELELSER)

Dato	Med. nr.	Aktivitet
4/5	3	Seminar. Robert V. Wells. The Mortality Transition in Schenectady, New York, 1880-1930.(OU)
4/5	3	Halvdags mode om Confounding/colinearitet.
5/5	3	Seminar. Bent Jørgensen. Dispersion Models and Longitudinal Data Analysis. (Biostatistik, KU)
6/5	2	Seminar. Bent Jørgensen. Basu's Theorem and Generalizations. (ATS,KU)
7/5	4	Seminar. Jakob R. Møller. Tail asymptotics for M/G/1 type queueing processes with subexponential increments.(Aalborg)
11/5	4	Seminar. Guido Schwarzer. An application of shared frailty models to the failure time analysis of tatal hip protheses. (Biostatistik, KU)
12/5	4	Seminar. Stefano Maria Iacus, title and abstract will later be announced on http://www.mi.aau.dk/events/. (ATS, AU).
13/5	4	Seminar. Stefano Iacus. The van Trees inequality for small dispersion diffusions with application to semiparametric models. (ATS, KU)
14/5	4	Seminar. Elisa Nicolato. A Bayesian Dynamic Programming Approach to Optimal Maintenance combined with Burn-in.(ATS, AU)
18/5	3	Seminar, Shariar Yousefi. A Socio-spatial Description of Interacting Population Dynamics. (OU)
20/5	4	Seminar, Inge Henningsen. Lægevidenskab og køn. (ATS, KU)
25/5	4	Seminar. Joel E. Chohen. How many people can the earth support. (Biostatistik, KU)
25/5	4	Seminar. Lise Brøndsted, Lars Vindeløv og Charlotte A. Russell. Limiting Dilution Assays (Biostatistik, KU)
25-29/5	3	Advanced Course: An Introduction to Malliavian Calculus with Applications to Finance. (MaPhySto, ÅU). Reg. før 1. april
28/5	4	Møde. Ernst Hansen. Pulse dimension estimation
29/5	4	$\label{eq:model} \mbox{Møde. Ulrike Putschke. Asymptotic properties of the MLE for the 2-dimensional Ornstein-Uhlenbeck process.}$

Dato	Med. nr.	Aktivitet
3-5/6	2	Short Course in Biostatistics. John Buonnacorsi. Measurement error modeling - linear and non- linear regression models. (Aas, Norge) Registration date 1. April
8-12/6	1	17. Nordiske konference i matematisk statistik. Helsingør. Http://www.dsts.dk/nordisk.konf/
18-19/6	4	Atelier inserm om multi-state models in epidemiology.
6-8/8	2	4 <sup>th</sup> Sensometrics Meeting 1998. (København) Http://www.dina.kvl.dk/sensom98
7-10/8	97,9	European summer school. Markov Chain Monte Carlo Methods. Deadline for applications 27. march
24-28/8	97,9	19 <sup>th</sup> International Society for Clinical Biostatistics Meeting. Dundee. Deadline for abstracts <b>15. april</b> .
24-28/8	97,6	COMPSTAT 98. Bristol UK. Fax: +44 1582 760981. E-mail: compstat-98@bristol.ac.uk. Http://www.stats.bris.ac.uk/compstat/

### Deadlines i 1998

#### Frist for indlevering af bidrag: MEDDELELSER udkommer: 2. juni 1998 25. maj 1998 24. juli 1998 3. august 1998 24. august 1998 1. september 1998 22. september 1998 1. oktober 1998 26. oktober 1998 2. november 1998 24. november 1998 1. december 1998



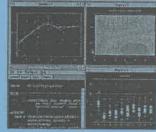
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