

Medical Data Analysis

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Medical Data Analysis
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nabios GmbH was founded in 1998 by Dr. Gerda Wiedenmann and Dr. Valentin Demmel, physicists trained at the Max-Planck institutes in Germany. Both have gained comprehensive experience in the analysis of biosignals during various research cooperations with clinics, pharmaceutical companies, and other research institutes.

CRO
biosignal analysis
medical data analysis

Services and Consulting

The company serves as a specialized contract research organization (CRO) for the pharmaceutical industry, providing customized data analysis in all areas of medical research. *nabios* has specialized in the analysis of electrocardiographic signals (short- and long-term ECGs) and data from ambulatory blood pressure monitoring (ABPM). *nabios* has also experience in the field of image analysis and the analysis of electric encephalograms. *nabios* provides not only raw data calculation services, but helps clients in developing successful strategies for the design and evaluation of their individual experiments.

Philosophy

nabios is an organization based upon evidence based clinical research. Through its relationships with major clinical research centers, leading physicians and researchers, and a successful history of working with sponsors and other CROs, *nabios* is able to provide a value added service to the medical community.

Partners

The cooperation with *Medifacts*, Ltd. and *M² Worldwide*, well-known service providers in the areas of ABPM, 12-lead, and Holter ECGs allows *nabios* to provide full service monitoring to the industry, worldwide.

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Clinical Background

Standard 12-lead resting or exercise ECGs are recorded under controlled clinical conditions. Various parameters are derived which are used for diagnosis and assessment of drug safety and efficacy:

- Identification of arrhythmias (e.g. AF, VES, VT)
- Heart rate (during sinus rhythm)
- Conduction velocities estimated from single heart cycles (e.g. PR- and QT-intervals and their dispersion)
- Deviations in morphological features of cardiac cycles (e.g. ST-segment changes, T-wave alternans)

In particular the measurement of the QT-interval has recently gained considerably importance for the assessment of drug safety.

Technical Background

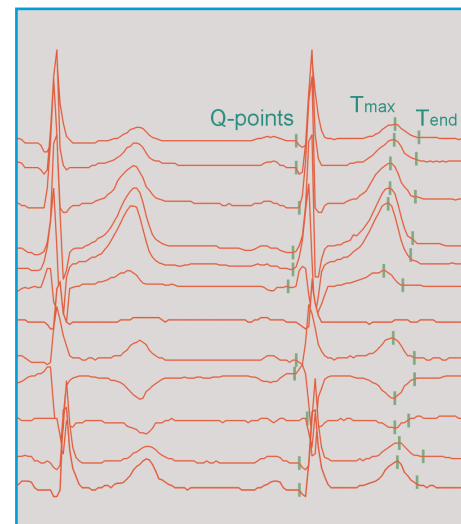
So far 12-lead ECGs are recorded and stored using hardcopy output from commercial ECG machines. Modern recording devices allow for digital assessment and storage of the signals at high sampling rates. From the hardcopy ECGs the relevant features are extracted manually using calipers or digitization boards. In case of digital recordings either electronic calipers or an algorithmic approach is used. In both cases it is necessary, however, to manually verify the results by experienced observers.

Services

nabios has developed flexible tools to assess ECGs from various digital ECG recording devices and from standard hardcopy ECGs. In the latter case the signals are digitized by applying novel algorithms to the scanned ECG images. Thus a standardization in the data preparation and handling is achieved. The digital ECGs are further processed using validated algorithms. The automatic feature detection is manually verified assuring high quality research results:

- Estimates of conduction velocities:
PR, QRS, QT, QTd, QTc, QTcd
- Heart rate
- Morphological features of single beats:
ST-segment changes, T-wave morphology
- Combinations of the above elements for customized solutions

ECG feature extraction



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Clinical Background

The ambulatory (Holter) ECG is a widely used noninvasive test to examine a patient over an extended period of time. The data are usually recorded from 24 hours up to 72 hours, covering one or more circadian cycles. The following derived parameters have been shown to be of clinical relevance:

- Arrhythmias (SVES, VES, AF, VT, etc.)
- Heart rate and its variability
- QT-interval duration
- ST-segment changes
- Other morphological features of cardiac cycles

In particular, the fluctuations of the beat-to-beat heart period (heart rate variability - HRV) has been used lately to study the (patho)physiology and pharmacology of the cardiovascular system.

Technical Background

The technological evolution during the past decade spawned analysis advances to examine various features of long-term ECGs in great detail. Since the data are collected in an ambulatory environment, however, they usually contain a considerable amount of noise. Thus it is necessary to build up sophisticated strategies for quality control covering every step during data processing and parameter calculation.

Services

nabios uses a modular setup of validated computer programs which enables large data sets to be processed in a fast and flexible way. A special quality control scheme monitors all data calculation steps assuring reproducible research quality results. *nabios* offers data analysis and calculation for all clinically relevant parameters:

- Arrhythmia assessment:
Lown & Wolf classification, frequency of SVES, VES, Bigeminy, VT, AF
- Heart rate variability (following NASPE and ESC guidelines):
time and frequency domain
- Newly derived nonlinear parameters:
dimension analysis, entropy measures, geometrical descriptors of RR-interval scatterplots
- QT-intervals (beat-by-beat)
- Determination of other morphological changes:
PR-intervals, QRS-duration, T-wave alterations

Holter ECG analysis

HRV

QT



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Clinical Background

Similar to the Holter recording technique for electrocardiographic signals, ambulatory blood pressure data are used to capture the time-varying blood pressure signal through a 24h cycle. The analysis of blood pressure data as assessed with ABPM has become a major research tool in the investigation of hypertension diagnosis and therapy control. Research topics include prognosis for the development of cardiovascular diseases (e.g. target organ damage or stroke) and assessment of effects of antihypertensives agents.

Technical Background

Beside the standard mean values calculated during various periods different algorithms have been proposed for the analysis of ABPM data. These approaches can be divided in two main categories:

- Phenomenological description:
The data are characterized by different statistics, e.g. standard deviation of systolic blood pressure during day, the excess over a certain threshold (load), etc.
- Data modeling approach:
Predefined functions (e.g. a periodic Fourier function) are fitted to the data and the respective parameters are used as quantitative descriptors of the blood pressure signal.

Services

nabios offers all standard analyses for the determination of the various proposed data reduction methods:

- Mean blood pressure values during different periods of observation:
fixed times, electronic diary evaluation, individual day/night cycles using square wave fitting
- Variability of the blood pressure:
standard deviation, interquartile ranges, coefficient of variation, etc.
- Data modeling approach:
Fourier series, piecewise linear functions, splines

These methods can be combined and extended to provide tailored solutions according to the clients' needs.

ABPM analysis Model fitting



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Technical Background

Technological progress has large impact on medical knowledge generation. Many of the used clinical parameters are based on physical measurements which nowadays can be collected not only at single instances but during different periods of time and at high sampling rates. This growing amount of data has to be organized and requires extensive scientific investigations to explore the diverse clinically relevant parameters. The main toolbox for this data processing is provided by the mathematical, physical and information sciences.

Services

nabios has specialized in the analysis and interpretation of medical data. Through long-term research cooperations with clinical partners and sponsors *nabios* is able to bridge the gap between the analysis sciences and medicine. In scientific cooperations *nabios* has built up databases containing clinical parameters as well as parameters derived from ECG and ABPM for various patient populations and healthy normals. Based on these experiences sponsors can be provided with a complete consulting and analysis package for a successful realization of individual experiments and trials.

Customized services include:

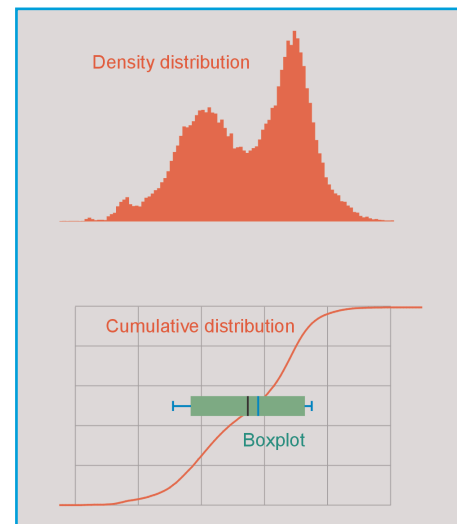
- Selection of appropriate recording and analysis techniques
- Synchronization of long-term ECG and ABPM measurements with occasionally sampled clinical parameters (e.g. QT-interval dependencies on drug plasma concentrations)
- Comparisons with similar patient groups and healthy volunteers

Standard services comprise:

- Development of statistical analysis plans
- Biometrical analysis
- Statistical (SAS) programming
- Graphics programming
- Database programming
- Report writing
- Presentation and publication

All derived parameters and results can be stored electronically using different ASCII and binary formats including SAS, SPSS, EXCEL, and ACCESS. For documentation purposes it is also possible to provide hardcopies or electronical images (e.g. tif, gif, jpeg, pdf, ps) of any data.

Consulting
Statistics
Evidence based medicine



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