ANNUAL REPORT 2012

Physics of Physiological Processes
Faculty of Physics, University of Vienna

STAFF

Group speaker:	Ao. Univ. Prof. Dr. Karl W. Kratky
Guest scientist:	Univ. Doz. Dr. Karl E. Kürten
Lecturers:	Mag. Werner Gruber, Univ. Doz. Dr. Karl E. Kürten, Mag. Dr. Hans Günter Löw
Volunteers:	Mag. Werner Gruber, Mag. Dr. Hans Günter Löw
Administration:	Andrea Hnizdo
Diploma students:	Matthias Fukac, Martina Hatzl, Jasmin Kölndorfer, Marvin Kovacs
PhD students:	Mag. Werner Gruber, Dr. Said Ibrahim, Rozhin Penjweini MSc

RESEARCH

The research group "Physics of Physiological Processes" deals with complex dynamical systems (chaos and systems research) in general and with the physics of the human body in particular. The following topics are considered: nonlinearity and feedback, chaos and fractals, self-organization and synchronization, neuronal and neural networks as well as cellular automata. These areas are interdisciplinary, connecting physics especially with biology, psychiatry/ medicine, economy and ecology. They are treated in various ways: from a fundamental point of view, studying computer experimental results and interpreting experimental data. The group's fields of research in more detail:

<u>Overview: Inter- and transdisciplinary aspects of the physics of physiological processes</u>

By means of studying complex dynamical systems, bridges to other sciences can be built, in research as well as in teaching. Attention is focused on biology and medicine. Among other things, it is investigated how chaos control is used by organisms to regulate their body functions efficiently. Furthermore, several therapies in complementary medicine are interpreted from the view-point of complex dynamical systems.

<u>Interconnected dynamical systems: From cellular automata to genetic and artificial neural network models</u>

Physical, biological, ecological and economical processes are treated using mathematical modeling and computer visualization. Topics:

- Pattern recognition, memorization and retrieval of information
- Self-organizing systems at the borderline between order and chaos
- Evolutionary economics and econophysics
- Neural network applications for computer-aided tomography

For details, see the project of K.E. Kürten and the diploma thesis of L. Geyrhofer.

<u>Neurophysics</u>

The aim of the research is to build up a programming environment to create better biological neuronal networks in order to verify medical and psychological theories of the brain. With this programming environment, it is possible to build up very complex simulations by use of few neurons in order to only of few neurons to describe synchronization of neurons as well as of complex neural systems just by few clicks. Thus, different problems of theoretical neuroscience, as cognitive learning, stammering or the perception of speech can be easily tackled.

The response of heart-rate variability (HRV) to various influences and stimuli

- Humans were exposed to light of different spectral composition and of different and varying intensity. In a further step, three kinds of sound were presented to humans. Data of biophysical parameters (e.g. ECG, EMG, breath) were acquired and then analyzed by nonlinear time series and other methods. Heart-rate variability (HRV) is a major aspect in these investigations.
- Calculating the breathing rate via HRV (utilizing the respiratory sinus arrhythmia) yields another interesting variable that makes new interpretations possible.
- This may be compared to direct measurements of the breathing rate, which also allows considering the breathing rate variability BRV, the counterpart of HRV. This is now under investigation.
- HRV (and BRV) are not only influenced by external stimuli, but also by internal ones, e.g., Hatha-yoga breathing techniques. For details, see the diploma thesis of M. Kovacs.

Biophysics and Medical Physics

- Biophysical investigations of photosensitization within mitotic cell cycle. Electromagnetically induced nonlinear dose-effect relations monitored by novel optical detection methods

For details, see the doctoral thesis of R. Penjweini.

In addition to the research, several courses are offered, e.g., "Complex dynamical systems", "Properties of biophysical systems in theoretical models and experiments", "Physics of physiological processes", "Complementary medicine" and "Theory of complex interconnected systems I & II".

PUBLICATIONS

a-c. ARTICLES (contributions in scientific journals and books)

a. ALREADY ISSUED

- **R. Penjweini**, **H.G. Loew**, M.R. Hamblin and **K.W. Kratk**y, *Long-term monitoring of live cell proliferation in presence of PVP-Hypericin: a new strategy using ms pulses of LED and the fluorescent dye CFSE*. J. of Microscopy **145**$_1$ (2012) 100-108.

During fluorescent live cell imaging it is critical to keep excitation light dose as low as possible, especially in presence of photosensitizer drugs, which generate free radicals upon photobleaching. During fluorescent imaging, stress by excitation and free radicals induces serious cell damages that may arrest the cell cycle. This limits the usefulness of the technique for drug discovery, when prolonged live cell imaging is necessary. This paper presents a strategy to provide gentle experimental conditions for dynamic monitoring of the proliferation of human lung epithelial carcinoma cells (A549) in presence of the photosensitizer PVP-Hypericin (PVP: polyvinylpyrrolidone). The distinctive strategy of this paper is based on the stringent environmental control and optimizing the excitation light dose by i) using a low-power pulsed blue light-emitting diode (LED) with short pulse duration of 1.29 ms and ii) adding a non-toxic fluorescent dye called carboxyfluorescein-diacetate-succinimidyl-ester (CFSE) to improve the fluorescence signals. To demonstrate the usefulness of the strategy, fluorescence signals and proliferation of dual-marked cells, during 5-hour fluorescence imaging under pulsed excitation, were compared with those kept under continuous excitation and non-marked reference cells. The results demonstrated 3% cell division and 2% apoptosis due to pulsed excitation compared to no division and 85% apoptosis under the continuous irradiation. Therefore, our strategy allows live cell imaging to be performed over longer time scales than with conventional continuous excitation.

- **K.E. Kürten**, *Coexistence of opportunists, contrarians, and inconvincibles in binary opinion networks.* In: I. Spanulescu (ed.), Econophysics, New Economy and Complexity. Proceedings of the International Conference ENEC-012, 30 May - 1 June 2012, Bucharest, Victor Publishing House 2012 (pp.313-321).

We study a model for the emergence of collective decision making heuristics, consisting of four different classes of interacting agents, whose opinions are described by binary state variables. In particular, a subtle interplay between opportunist, contrarians and inconvincibles sticking stubbornly on their opinion, leads to phase transitions which abruptly can change the outcome of a public debate. At a critical density the inconvincibles reduce the fraction of an initial majority such that the initial minority can win the debate.

b. ACCEPTED

- **R. Penjweini**, **H.G. Loew**, M. Eisenbauer and **K.W. Kratky**, *Modifying excitation light dose of novel photosensitizer PVP-Hypericin for photodynamic diagnosis and therapy.* Journal of Photochemistry and Photobiology B: Biology **120** (2013) 120–129.

Conventional photodynamic diagnosis (PDD) and therapy (PDT) makes use of photosensitizers that are excited by continuous light irradiation of specific wavelengths. In the case of PDT, the overdose of continuous excitation may lead to an expansion of necrosis in cancer cells or morbidity in healthy surroundings. The present study deals with 5-hour fluorescence imaging of living human lung epithelial carcinoma cells (A549) in presence of a novel photosensitizer, PVP-Hypericin (PVP: polyvinylpyrrolidone) to optimize the excitation light doses for PDD and PDT. A number of timelapse imaging experiments were performed using a low-power blue LED operating in either continuous or pulsed mode. The irradiance I^* were 1.59, 6.34 and 14.27 mW/cm^2, the pulse lengths L being 0.127, 1.29, 13, 54.5, 131 and 60,000 ms. Then, the relation between irradiance, various exposure times, photobleaching and phototoxicity of PVP-Hyperycin was investigated. Results showed a nonlinear relationship between the amounts of excitation dose, cell viability and toxicity. For all experimental I^*, minimal phototoxicity and photobleaching was detected when cells were exposed to brief pulses of light ($L \leq 13$ ms). On the other hand, pulsed excitation with $I^* = 14.27$ mW/cm^2 and $L = 131$ ms induced high percentages of apoptosis comparable to the long exposures of $L = 60{,}000$ ms and the continuous excitation. Thus, replacement of continuous excitation by a pulsed one seems applicable for PDT.

c. SUBMITTED

- **R. Penjweini**, **H.G. Loew**, P. Breit and **K.W. Kratky**, *Optimizing the antitumor selectivity of PVP-Hypericin re A549 cancer cells and HLF normal cells through pulsed blue light* (submitted)

Photodynamic therapy (PDT) is based on the preferential accumulation of photosensitizer in cancer cells with subsequent cytotoxicity mediated by singlet oxygen production after light excitation. As photosensitizers accumulate also in the surrounding non-cancer cells, the risk of damaging them by photosensitization is a limitation of PDT. Thus, minimizing the side effects of PDT on normal cells is one of the challenging problems in medical practice. This paper studies the PDT side-effects of photosensitizer PVP-Hypericin (PVP: polyvinylpyrrolidone), excited with continuous or pulsed irradiation, on combined cell lines of human lung carcinoma epithelial cells (A549) and normal human lung fibroblast cells (HLF). In-vitro PDTs are performed using pulsed or continuous irradiation with light intensities $I^* = 1.59$, 6.34 and 14.27 mW/cm^2. The LED pulse lengths L are 0.127, 1.29, 13, 54.5 and 131 ms. Then fluorescence and phototoxicity of PVP-Hypericin in the A549 cancer cells are compared with those of HLF normal cells. Although, PVP-Hypericin accumulates more in A549 cancer cells, the results show that HLF cells produce dose-dependent photoreactions in the presence of photosensitizer. PVP-Hypericin induces the most optimized anticancer efficacy with moderate side-effects for $I^* = 14.27$ mW/cm^{2}and $L = 131$ ms.

- D.M. Forrester, F.V. Kusmartsev and **K.E. Kürten**, *Arrays of spontaneously generated orbital moments and dragonfly wing fractals* (submitted)

Groups of Josephson junction-rings that spontaneously generate a magnetisation exhibit a fractal structure in the spontaneous flux and energy characteristics. In this paper we shown that for different levels of coupling strength there is a fractal characteristic that is reminiscent of the Hofstadter butterfly. We call this the dragonfly wing fractal. Groups of π-rings are shown to be highly sensitive to low frequency magnetic fields.

- **K.E. Kürten** and C. Krattenthaler, *Fractal properties of one-dimensional chains of competing particles: an exactly solvable model* (submitted)

Problems in many areas of physics can be reduced to the study of two-dimensional mappings. In particular, conversion between Hamiltonian forms and two-dimensional mappings of the plane into itself have a wide application range in the theoretical analysis of dynamical systems. Examples range from problems of coupled oscillators subjected to an external force to coupled magnetic layered systems subjected to an external magnetic field and Josephson junction rings that spontaneously generate magnetizations. Since the type of solutions can sensitively depend on both, on the system parameters as well as on the initial conditions, stable as well as unstable periodic orbits play an important role inducing transitions from quasiperiodic to chaotic behaviour accompanied by fractal energy spectra.

d. ABSTRACTS IN CONFERENCE PROCEEDINGS

- **K.W. Kratky**, Vorurteilsfreie Erschließung aller Quellen medizinischen Wissens. In: Internationale Ganzheitsmedizinische Tage IGMEDT (4.-6.5.2012, Salzburg, Austria), Abstractband I, S.5.

e. BOOKS

- M. Puntigam, H. Oberhummer und **W. Gruber**, *Gedankenlesen durch Schneckenstreicheln: Was wir von Tieren über Physik lernen können***.** Carl Hanser Verlag, München 2012.

LECTURES, CONFERENCE CONTRIBUTIONS, POSTERS

a. LECTURES

K.W. Kratky

- *Sind wir alle gleich? Universale – typengerechte – personalisierte Medizin* (ärztliche Fortbildung im Krankenhaus der Barmherzigen Brüder, Wien, Austria), 9.2.2012
- *Komplementärmedizin* (Kombistudium Pflege Wien, Pflegeakademie – Schule für allgemeine Gesundheits- und Krankenpflege der Barmherzigen Brüder, Wien, Austria), 13., 16. & 20.2.2012
- *Weltbilder komplementärmedizinischer Richtungen* (Ringvorlesung "Komplementärmedizinische Methoden. Grundlagen und Praxis" an der Medizinischen Universität Wien, Austria), 14.3.2012
- *Komplementäre Medizinsysteme* (Weiterbildung "Energetische Modelle und Methoden – Therapeutische Berührung", Zentrum – Lebensenergie, Wien), 23.3.2012

K.E. Kürten

- Wealth-exchange – versus energy-exchange models revisited (Department of Molecular Cell Biology, Leuven, Belgium), 11.6.2012
- Wealth-exchange – versus energy-exchange models revisited (Department of Physics, Loughborough University, UK), 16.5.2012

b. CONFERENCE CONTRIBUTIONS

K.W. Kratky

- Vorurteilsfreie Erschließung aller Quellen medizinischen Wissens (eingeladener Vortrag beim Kongress "Internationale Ganzheitsmedizinische Tage" IGMEDT, 4.-6.5.2012, Salzburg, Austria), 4.5.2012

K.E. Kürten

- *Coexistence of opportunists, contrarians, and inconvincibles in binary opinion networks* (invited lecture, ENEC 2012. International Conference on Econophysics, New Economy and Complexity; May 30-June 1, 2012; Bucharest, Romania), 31.5.2012

DIPLOMA THESES – PHD THESES (Supervisor: **K.W. Kratky**)

a. CURRENT DIPLOMA THESES

- **M. Fukac,** *Simulation des menschlichen Sehsystems*
- **J. Kölndorfer,** *Klassifizierung von Sprache und Geräuschen mittels eines Biologischen Neuronalen Netzwerks von Integrate-and-Fire Oszillatoren*

b. COMPLETED DIPLOMA THESES

- **M. Hatzl,** *Die Wirkung von optischen und akustischen Reizen auf die Puls-Atem-Variablen: Auswertung und Interpretation von Experimenten.*

Einführung: Der menschliche Organismus wird tagtäglich mit den unterschiedlichsten optischen und akustischen Reizen konfrontiert. Die Heart-Rate-Variability, in der Folge kurz HRV genannt, gibt Aufschluss über den Regulationszustand des Herz-Kreislauf-Systems, sowie des vegetativen Nervensystems.
Methoden und Ziele: Als Grundlage dieser Arbeit gelten die Dissertation "Die Wirkung von Licht verschiedener spektraler Zusammensetzung auf die Variabilität der Herzfrequenz" von Axel Schäfer, sowie die beiden Diplomarbeiten "Wirkung von grünem Licht unterschiedlicher zeitlicher Variation auf die Heart-Rate-Variability" von Naciye Elagöz und "Auswirkung von akustischen Reizen auf die Heart Rate Variability - Eine zeitreihenanalytische Untersuchung" von David Diepold. Das Ziel ist eine Weiterentwicklung der statistischen Auswertung zum Zweck des direkten Vergleiches der verschiedenen Studien und zur Erlangung neuer Erkenntnisse hinsichtlich der Ergebnisse. In allen drei Arbeiten war die Durchführung der Experimente sehr ähnlich. 12 bzw. in einem Fall 8 Probanden wurden jeweils verschiedenen optischen und akustischen Reizen nach einer bestimmten zeitlichen Abfolge ausgesetzt. Untersucht wurden die HRV-Variablen der Time- und Frequency-Domain, sowie nichtlineare Variablen. Mittels der sogenannten respiratorischen Sinusarrhythmie kann aus der HRV auch der Puls-Atem-Quotient bzw. die Atemfrequenz ermittelt werden. In der vorliegenden Arbeit beschränkt sich die vergleichende Untersuchung auf die Puls-Atem-Variablen. Untersucht werden die Unterschiede zwischen den Ruhe- und Reizphasen mittels verschiedener statistischer Tests. Ein weiteres Augenmerk liegt auf der Auswertung der Artefaktkorrektur und der Trendbereinigung auf vorhandene Signifikanzen.
Ergebnisse: In allen drei untersuchten Arbeiten ergaben sich Unterschiede zwischen den Signifikanzen der artefaktkorrigierten und nicht-artefaktkorrigierten Daten. Auch die Trendbereinigung brachte zum Teil neue Ergebnisse.

- **M. Kovacs,** *Die Auswirkung von Hathayoga-Atemtechniken auf Herzfrequenzvariabilität und Atemvariablen*

Die vorliegende Arbeit untersucht den Einfluss von drei Yoga-Atemtechniken auf Herzfrequenzvariabilität (heart rate variability, HRV) und Atemvariablen. Ziel war es, Effekte zu identifizieren, die im Laufe einer Messung auftraten, sowie den Einfluss verschiedener Gruppierungsmerkmale auszuwerten – z.B. Yoga-Lehrerfahrung und Alter. Bewertet wurden das Elektrokardiogramm (EKG) und die Atemkurven von 24 gesunden Männern und Frauen während einer per CD angeleiteten Pranayama-Trainingseinheit. Der Messablauf umfasste Ruhephasen in Rückenlage am Anfang und am Ende, sowie dazwischen abwechselnde Phasen entspannten Sitzens und des Übens der drei Atemtechniken Nadi Shodhana, Bhramari und Ujjayi – ebenfalls in sitzender Position.

Jeweils 3-minütige Messintervalle jeder dieser Phasen wurden mit Hilfe nicht-parametrischer statistischer Analyseverfahren nach zwei unterschiedlichen Betrachtungsweisen ausgewertet: Einerseits die Änderungen von HRV-Time-Domain- und Atemvariablen im Vergleich verschiedener Messintervalle, andererseits die Unterschiede zwischen Gruppen während jedes Messintervalls. Es wurden jeweils mehrere statistische Ansätze verfolgt, sodass neben altbewährten Testverfahren auch weniger verbreitete Analysemethoden Anwendung fanden. Diese resultierten in einem umfassenden Bild und ermöglichten eine fundierte Einschätzung der Signifikanz der Ergebnisse.

Letztlich konnten verschiedene Effekte identifiziert werden, wobei die Hauptergebnisse die folgenden waren: In der Liegephase am Ende der Trainingseinheit hatte die Herzfrequenz einen niedrigeren Wert als in jener zu Beginn. Während Ujjayi war die Herzfrequenz gegenüber den anderen Atemtechniken gesenkt, die Standardabweichung der Dauer aufeinanderfolgender Herzzyklen (SDNN) war hingegen erhöht. Bei Gruppierung nach verschiedenen Merkmalen wiesen Yoga-Lehrende einen niedrigeren Wert für SDNN auf als Übende. Gleiches ließ sich auch mit schwächerer Signifikanz für eine Gruppe älterer Personen gegenüber einer jüngeren Gruppe feststellen. Welcher der beiden Faktoren – Lehrerfahrung oder Alter – die größere Rolle spielt, konnte nicht endgültig geklärt werden.

c. CURRENT PHD THESES

- **W. Gruber**
  Synchronisationszustände des Gehirns und die Bedeutung für die Informationsverarbeitung
- **S. Ibrahim**
  Naturwissenschaftliche Grundlagen der medizinischen Systeme

d. COMPLETED PHD THESIS

- **R. Penjweini** (Co-Supervisor: **H.G. Löw**)
  Biophysical investigations of photosensitization within mitotic cell cycle. Electromagnetically induced nonlinear dose-effect relations monitored by novel optical detection methods

Photodynamic diagnosis and therapy (PDD and PDT) are known as techniques for the detection and treatment of cancer. PDD and PDT are based on the selective accumulation of a photosensitizer in cancer cells with subsequent fluorescence and reactive oxygen emission after photoexcitation. However, the prospect for using these techniques has been limited by lack of effective photoexcitation protocols.

The method of this thesis (I) regulates the photoexcitation of a novel photosensitizer PVP-Hypericin (PVP: polyvinylpyrrolidone) and (II) monitors the parameters relevant to the PDD and PDT effects.

The strategy is based on the dynamic imaging of living human lung cancer cells and normal human lung fibroblast cells in the presence of PVP-Hypericin. Then, the relation between different light intensities, various exposure times, photobleaching and photocytotoxicity of PVP-Hypericin is studied. Based on the results, a specific irradiation protocol is developed, which can selectively destroy the cancer cells with relatively mild side-effects.

PRESENCE IN THE MEDIA

W. Gruber

- He features on all relevant media – as print, radio and television – in Austria, Germany and Switzerland.

MISCELLANEOUS

K.W. Kratky

- Member of the Editorial Board of the "Journal of Alternative Medicine Research" and of the Scientific Board of the journals "Systeme" and "lebensweise".
- Member of the Scientific Board of the Viennese International Academy of Holistic Medicine as well as the Institute of Ethno-music Therapy, Gföhl, Austria.
- Member of the team of the Interuniversity College for Health and Development, Graz / Castle of Seggau, Austria. There, also lecturer at the European Master's Degree Program for Integrated Health Sciences.

- Member of the "Beirat für Traditionelle Asiatische Medizin im Bundesministerium für Gesundheit" (Vienna, Austria).
- Member of the Scientific Committee of the 2nd Jerusalem International Conference on Integrative Medicine, May 13-15, 2012, Jerusalem, Israel.

K.E. Kürten

- Guest Scientist and Lecturer.
- Visiting professor (Loughborough University, UK)

W. Gruber

- Volunteer and Lecturer
- General Editor at CISCI (Cinema and Science), an EU-Project for teaching physics.
- Lecturer at various adult evening classes ("Wiener Volkshochschulen") within the context of the project "University meets public".
- Member of the "ScienceBusters".
- Vorstandsmitglied der VHS Meidling, Wien, Austria.
- Wissenschaftlicher Beirat der KPH Krems, Austria.

H.G. Löw

- Volunteer and Lecturer.
- Co-supervisor of the PhD thesis "Biophysical investigations of photosensitization within mitotic cell cycle. Electromagnetically induced nonlinear dose-effect relations monitored by novel optical detection methods" of R. Penjweini

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COURSES IN THE ACADEMIC YEAR 2011/12

K.W. Kratky

WS:	Physik Physiologischer Prozesse		VO, 2h
WS:	Spezialisierungsmodul Umwelt- und Biophysik	(als Mitveranstalter)	PR, 10h
SS:	Physik Physiologischer Prozesse		SE, 2h
SS:	Spezialisierungsmodul Umwelt- und Biophysik	(als Mitveranstalter)	PR, 10h
SS:	Facetten naturwissenschaftlichen Denkens (Ringvorlesung)	(als Mitveranstalter)	VO, 2h
SS:	Gemeinsamkeiten komplementärmedizinischer Methoden – aus naturwissenschaftlicher und interkultureller Sicht		VO, 2h

K.E. Kürten

WS:	Einführung in die Theorie vernetzter Systeme I - Vom zellulären Automaten zu genetischen und neuronalen Netzwerkmodellen		VO, 2h
WS:	Neuere Entwicklungen in der Theorie vernetzter Systeme		SE, 2h
SS:	Einführung in die Theorie vernetzter Systeme II - Vom zellulären Automaten zu genetischen und neuronalen Netzwerkmodellen		VO, 2h
SS:	Spezielle Anwendungen in der Theorie vernetzter Systeme II		SE, 2h

H.G. Löw

WS:	Biophysikalisches Praktikum für Vorgeschrittene, Vertiefung und Ergänzungen (als Mitveranstalter)		PR, 1h

W. Gruber

WS:	Biophysikalisches Praktikum für Vorgeschrittene	(als Mitveranstalter)	PR, 5h
WS:	Fachdidaktische Vertiefung – Methoden der Physikdidaktik	(als Mitveranstalter)	SE, 1h
SS:	Praktikum für Schulversuche II	(als Mitveranstalter)	PR, 6h

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