

## **Metabolic syndrome is associated with decreased heart rate variability in a sex-dependent manner: a comparison between 252 men and 249 women**

Impaired heart rate variability (HRV) is associated with increased risk of cardiovascular disease, but evidence regarding alterations of HRV in metabolic syndrome (MetS) remains elusive. In order to examine HRV in MetS, we subjected 501 volunteers without atherosclerosis, diabetes or antihypertensive medication, mean age 48 years, to passive head-up tilt. The subjects were divided to control men (n = 131), men with MetS (n = 121), control women (n = 191) and women with MetS (n = 58) according to the criteria by Alberti et al. (Circulation, 2009, 120, 1640). In unadjusted analyses (i) men and women with MetS had lower total power and high-frequency (HF) power of HRV than controls whether supine or upright (P<0.05 for all). (ii) Supine low-frequency (LF) power of HRV was lower in men (P = 0.012) but not in women (P = 0.064) with MetS than in controls, while men and women with MetS had lower upright LF power of HRV than controls (P <0.01 for both). (iii) The LF:HF ratio did not differ between subjects with and without MetS. After adjustment for age, smoking habits, alcohol intake, height, heart rate and breathing frequency, only the differences in upright total power and HF power of HRV between women with MetS and control women remained significant (P<0.05). In conclusion, reduced total and HF power of HRV in the upright position may partially explain why the relative increase in cardiovascular risk associated with MetS is greater in women than in men. Additionally, the present results emphasize that the confounding factors must be carefully taken into consideration when evaluating HRV.

### **General information**

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Contributors: Kangas, P., Tikkakoski, A., Uitto, M., Viik, J., Bouquin, H., Niemelä, O., Mustonen, J., Pörsti, I.

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Research output: [Contribution to journal](#) > [Article](#) > [Scientific](#) > [peer-review](#)

## **Disposable Microfluidic Sensor Based on Nanocellulose for Glucose Detection**

Point-of-care devices that are inexpensive, disposable, and environmentally friendly are becoming increasingly predominant in the field of biosensing and biodiagnostics. Here, microfluidics is a suitable option to endow portability and minimal reagent and material consumption. Nanocellulose is introduced to manufacture microfluidic channels and as a storage and immobilization compartment of glucose oxidase. Improved enzymatic activity retention is demonstrated in a simple and disposable point-of-care diagnostic unit that is able to detect glucose from fluid matrices at 0.1 mM concentration and in less than 10 min. It is concluded that the patterning and fluidic technologies that are possible with nanocellulose enable easily scalable multianalyte designs.

### **General information**

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Organisations: Faculty of Biomedical Sciences and Engineering, Research group: Nanoscale Phenomena and Measurements (NPM), Research group: Sensor Technology and Biomeasurements (STB)

Contributors: Uddin, K. M. A., Jokinen, V., Jahangiri, F., Franssila, S., Rojas, O. J., Tuukkanen, S.

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10.1002/gch2.201800079  
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<http://urn.fi/URN:NBN:fi:tty-201901111085>  
Source: RIS  
Source-ID: urn:5DCAE8AD3B0885AE0C73C44A3C1A3B43  
Research output: Contribution to journal > Article > Scientific > peer-review

### **Impact of Variable RNA-Sequencing Depth on Gene Expression Signatures and Target Compound Robustness: Case Study Examining Brain Tumor (Glioma) Disease Progression**

**Purpose:** Gene expression profiling can uncover biologic mechanisms underlying disease and is important in drug development. RNA sequencing (RNA-seq) is routinely used to assess gene expression, but costs remain high. Sample multiplexing reduces RNAseq costs; however, multiplexed samples have lower cDNA sequencing depth, which can hinder accurate differential gene expression detection. The impact of sequencing depth alteration on RNA-seq-based downstream analyses such as gene expression connectivity mapping is not known, where this method is used to identify potential therapeutic compounds for repurposing.

**Methods:** In this study, published RNA-seq profiles from patients with brain tumor (glioma) were assembled into two disease progression gene signature contrasts for astrocytoma. Available treatments for glioma have limited effectiveness, rendering this a disease of poor clinical outcome. Gene signatures were subsampled to simulate sequencing alterations and analyzed in connectivity mapping to investigate target compound robustness.

**Results:** Data loss to gene signatures led to the loss, gain, and consistent identification of significant connections. The most accurate gene signature contrast with consistent patient gene expression profiles was more resilient to data loss and identified robust target compounds. Target compounds lost included candidate compounds of potential clinical utility in glioma (eg, suramin, dasatinib). Lost connections may have been linked to low-abundance genes in the gene signature that closely characterized the disease phenotype. Consistently identified connections may have been related to highly expressed abundant genes that were ever-present in gene signatures, despite data reductions. Potential noise surrounding findings included false-positive connections that were gained as a result of gene signature modification with data loss.

**Conclusion:** Findings highlight the necessity for gene signature accuracy for connectivity mapping, which should improve the clinical utility of future target compound discoveries.

#### **General information**

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Organisations: Faculty of Biomedical Sciences and Engineering, Queen's University Belfast; Johns Hopkins University, Baltimore, MD., Queen's University of Belfast, Brain Tumour Research Centre, University of Bristol, Bristol, United Kingdom., Belfast Health and Social Care Trust, Belfast, United Kingdom., Tampere University of Technology, Korkeakoulunkatu 10, 33720 Tampere, Finland, Queen's University Belfast; Belfast Health and Social Care Trust, Belfast, United Kingdom.

Contributors: Stupnikov, A., O'Reilly, P. G., McInerney, C. E., Roddy, A. C., Dunne, P. D., Gilmore, A., Ellis, H. P., Flannery, T., Healy, E., McIntosh, S. A., Savage, K., Kurian, K. M., Emmert-Streib, F., Prise, K. M., Salto-Tellez, M., McArt, D. G.

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Peer-reviewed: Yes

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Volume: 2

ISSN (Print): 2473-4284

Original language: English

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### **Porous poly-L-lactide-co-1-caprolactone scaffold: A novel biomaterial for vaginal tissue engineering**

The surgical reconstruction of functional neovagina is challenging and susceptible to complications. Therefore, developing tissue engineering-based treatment methods for vaginal defects is important. Our aim was to develop and test a novel

supercritical carbon dioxide foamed poly-L-lactide-co-1-caprolactone (scPLCL) scaffold for vaginal reconstruction. The scaffolds were manufactured and characterized for porosity (65 + 4%), pore size (350 + 150  $\mu$ m) and elastic modulus (2.8 + 0.4 MPa). Vaginal epithelial (EC) and stromal cells (SC) were isolated, expanded and characterized with flow cytometry. Finally, cells were cultured with scPLCL scaffolds in separate and/or co-cultures. Their attachment, viability, proliferation and phenotype were analysed. Both cell types strongly expressed cell surface markers CD44, CD73 and CD166. Strong expression of CD326 was detected with ECs and CD90 and CD105 with SCs. Both ECs and SCs attached and maintained viability on scPLCL. Further, scPLCL supported the proliferation of especially ECs, which also maintained epithelial phenotype (cytokeratin expression) during 14-day assessment period. Interestingly, ECs expressed uroplakin (UP) Ia, UP Ib and UP III markers; further, UP Ia and UP III expression was significantly higher on ECs cultured on scPLCL than on cell culture plastic.

#### General information

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MoE publication type: A1 Journal article-refereed

Organisations: Faculty of Biomedical Sciences and Engineering, Research group: Biomaterials and Tissue Engineering Group, Research group: Computational Biophysics and Imaging Group, Tampere University Hospital

Contributors: Sartoneva, R., Kuismanen, K., Juntunen, M., Karjalainen, S., Hannula, M., Kyllönen, L., Hyttinen, J., Huhtala, H., Paakinaho, K., Miettinen, S.

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Peer-reviewed: Yes

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Scopus rating (2018): CiteScore 2.71 SJR 1.131 SNIP 1.058

Original language: English

ASJC Scopus subject areas: General

Keywords: Cell characterization, Neovagina, Poly-L-lactide-co-1-caprolactone, Vaginal epithelial cell, Vaginal stromal cell, Vaginal tissue engineering

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Source: Scopus

Source-ID: 85053196533

Research output: Contribution to journal › Article › Scientific › peer-review

#### Temperature-dependence of the single-cell variability in the kinetics of transcription activation in *Escherichia coli*

From in vivo single-cell, single-RNA measurements of the activation times and subsequent steady-state active transcription kinetics of a single-copy Lac-ara-1 promoter in *Escherichia coli*, we characterize the intake kinetics of the inducer (IPTG) from the media, following temperature shifts. For this, for temperature shifts of various degrees, we obtain the distributions of transcription activation times as well as the distributions of intervals between consecutive RNA productions following activation in individual cells. We then propose a novel methodology that makes use of deconvolution techniques to extract the mean and the variability of the distribution of intake times. We find that cells, following shifts to low temperatures have higher intake times, although, counter-intuitively, the cell-to-cell variability of these times is lower. We validate the results using a new methodology for direct estimation of mean intake times from measurements of activation times at various inducer concentrations. The results confirm that *E. coli*'s inducer intake times from the environment are significantly higher, following a shift to a sub-optimal temperature. Finally, we provide evidence that this is likely due to the emergence of additional rate-limiting steps in the intake process at low temperatures, explaining the reduced cell-to-cell variability in intake times.

#### General information

Publication status: Published

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Organisations: Faculty of Biomedical Sciences and Engineering, Research group: Laboratory of Biosystem Dynamics-LBD

Contributors: Goncalves, N., Startceva, S., Palma, C., Bahrudeen, M., Oliveira, S., Ribeiro, A. S.

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Research output: Contribution to journal › Article › Scientific › peer-review

## Large-Scale Simulation of the Phenotypical Variability Induced by Loss-of-Function Long QT Mutations in Human Induced Pluripotent Stem Cell Cardiomyocytes

### General information

Publication status: Published

MoE publication type: A1 Journal article-refereed

Organisations: Faculty of Biomedical Sciences and Engineering, Research group: Computational Biophysics and Imaging Group, University of Bologna

Contributors: Paci, M., Casini, S., Bellin, M., Hyttinen, J., Severi, S.

Publication date: 2018

Peer-reviewed: Yes

### Publication information

Journal: International Journal of Molecular Sciences

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ISSN (Print): 1422-0067

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Scopus rating (2018): CiteScore 4.32 SJR 1.312 SNIP 1.224

Original language: English

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<http://urn.fi/URN:NBN:fi:tyy-201901071021>

Research output: Contribution to journal › Article › Scientific › peer-review

## Modeling and Engineering Promoters with Pre-defined RNA Production Dynamics in Escherichia Coli

Recent developments in live-cell time-lapse microscopy and signal processing methods for single-cell, single-RNA detection now allow characterizing the in vivo dynamics of RNA production of Escherichia coli promoters at the single event level. This dynamics is mostly controlled at the promoter region, which can be engineered with single nucleotide precision. Based on these developments, we propose a new strategy to engineer genes with predefined transcription dynamics (mean and standard deviation of the distribution of RNA numbers of a cell population). For this, we use stochastic modelling followed by genetic engineering, to design synthetic promoters whose rate-limiting steps kinetics allow achieving a desired RNA production kinetics. We present an example where, from a pre-defined kinetics, a stochastic model is first designed, from which a promoter is selected based on its rate-limiting steps kinetics. Next, we engineer mutant promoters and select the one that best fits the intended distribution of RNA numbers in a cell population. As the modelling strategies and databases of models, genetic constructs, and information on these constructs kinetics improve, we expect our strategy to be able to accommodate a wide variety of pre-defined RNA production kinetics.

### General information

Publication status: Published

MoE publication type: A4 Article in a conference publication

Organisations: Faculty of Biomedical Sciences and Engineering, Research group: Laboratory of Biosystem Dynamics-LBD, Research group: Computational Systems Biology

Contributors: Oliveira, S. M. D., Bahrudeen, M. N. M., Startceva, S., Kandavalli, V., Ribeiro, A. S.  
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Publication date: 2018

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Publisher: Springer Verlag  
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Volume: 11095 LNBI  
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ASJC Scopus subject areas: Theoretical Computer Science, Computer Science(all)  
Keywords: Gene engineering framework, Model of transcription initiation, Rate-limiting steps, Synthetic constructs  
DOIs:  
10.1007/978-3-319-99429-1\_1  
Source: Scopus  
Source-ID: 85053213051  
Research output: Chapter in Book/Report/Conference proceeding > Conference contribution > Scientific > peer-review

#### Effect of Implant Coating on Wireless Powering for Intracranial Pressure Monitoring System

A fully wireless implantable system can be used for long-term monitoring of intracranial pressure. In this type of system, an implant is placed under the skull and monitored pressure is transmitted wirelessly outside the skull. Moreover, the implant is powered through an inductive coupling. To avoid any infection and damage to the implant, the implant should be coated with biocompatible material. In this paper, we investigate the impact of coating on the maximum wireless link power efficiency through simulations in anatomical and layered tissue head models and present test results.

#### General information

Publication status: Published  
MoE publication type: A4 Article in a conference publication  
Organisations: Faculty of Biomedical Sciences and Engineering, Research group: Wireless Identification and Sensing Systems Research Group  
Contributors: Khan, W., Rizwan, M., Behfar, M., Sydänheimo, L., Björninen, T., Ukkonen, L.  
Number of pages: 2  
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#### Host publication information

Title of host publication: Proceedings of 2017 IEEE AP-S/URSI  
Publisher: IEEE  
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Name: Digest of the IEEE Antennas and Propagation Society International Symposium  
ISSN (Electronic): 1947-1491  
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APS2017  
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10.1109/APUSNCURSINRSM.2017.8072237  
URLs:  
<http://urn.fi/URN:NBN:fi:tty-201801091041>  
Research output: Chapter in Book/Report/Conference proceeding > Conference contribution > Scientific > peer-review

#### Glass and Glass-Ceramic Scaffolds: Manufacturing Methods and the Impact of Crystallization on In-Vitro Dissolution

#### General information

Publication status: Published  
MoE publication type: A3 Part of a book or another research book  
Organisations: Faculty of Biomedical Sciences and Engineering, Research group: Biomaterials and Tissue Engineering Group  
Contributors: Nommets-Nomm, A., Massera, J.

Number of pages: 19  
Publication date: 2017

#### Host publication information

Title of host publication: Scaffolds in Tissue Engineering - Materials, Technologies and Clinical Applications  
Publisher: InTech Open Access Publisher  
ISBN (Electronic): 978-953-51-3642-2  
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10.5772/intechopen.70242

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<http://urn.fi/URN:NBN:fi:tty-201801091057>

Research output: Chapter in Book/Report/Conference proceeding › Chapter › Scientific › peer-review

#### Nonlinear Effects of Winter Swimming and Sauna Recreational Activities on the Heart Rate Variability

Sauna sessions and winter swimming are traditional and popular recreational activities in certain countries. Their positive effects on health and relaxation, both as separate and combined activities, are commonly reported. However, systematic studies of these effects are relatively scarce, especially regarding the nonlinear analysis of the physiological measurements of the heart activity. We performed Multi-Scale Entropy (MSE) and Detrended Fluctuation (DFA) analyses on the inter-beat time series (about 72 h long) of 21 healthy volunteers studied in three distinct contexts: winter swimming combined with sauna bathing (W), sauna bathing alone (S), and control (C) with no related activities. We confirmed that the scaling exponents (DFA) and complexity indices (determined from MSE) stay within the variation observed for healthy individuals as compared to public data sets. Next, we showed that S and W interventions have uncorrelated effects on the whole time series complexity in each individual. Additionally, the long-range scaling properties of S and W groups are not correlated as determined by DFA. Thus, we speculate that winter swimming combined with sauna bathing and sauna bathing alone might have different physiological responses.

#### General information

Publication status: Published

MoE publication type: A1 Journal article-refereed

Organisations: Physics, Faculty of Biomedical Sciences and Engineering, Tampere Univ Technol, Tampere University of Technology, Lund Univ, Lund University

Contributors: Potapov, I., Haverinen, S., Smolander, J., Viik, J., Räsänen, E.

Number of pages: 4

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Scopus rating (2017): CiteScore 0.53 SJR 0.191 SNIP 0.361

Original language: English

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#### Bibliographical note

EXT="Smolander, Juhani"

Research output: Contribution to journal › Article › Scientific › peer-review

#### Short- and Long-Range Correlations in Beat Rate Variability of Human Pluripotent-Stem-Cell-Derived Cardiomyocytes

A healthy heart exhibits fractal, i.e., long-range correlated fluctuations in heart rate variability (HRV). It is recently shown that fractal dynamics is also an intrinsic feature of human-induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs). In this study, we investigate short- and long-range correlations in beat rate variability (BRV) of hiPSC-CMs, obtained from a healthy subject and symptomatic and asymptomatic long QT syndrome patients. It is shown that it is important to distinguish correlation properties in short and long time scales, as the scaling exponents are significantly different and also behave differently in the acute exposure to pharmacological compounds that modulate  $\beta$ 1-adrenoreceptors and cardiac ion channel generating delayed, outwardly rectifying K<sup>+</sup> current (IKs). While long-range scaling is sensitive to the drug exposure, short-range scaling is barely affected.

#### General information

Publication status: Published

MoE publication type: A4 Article in a conference publication  
Organisations: Physics, Research area: Computational Physics, Research group: Quantum Control and Dynamics, Institute of Biomedical Technology and BioMediTech, Heart Group, BioMediTech Institute and Faculty of Medicine and Life Science, University of Tampere, The Heart Center, Tampere University Hospital  
Contributors: Kim, J., Kuusela, J., Aalto-Setälä, K., Räsänen, E.  
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10.22489/CinC.2017.207-155

#### Bibliographical note

DUPL=42741204

Research output: Chapter in Book/Report/Conference proceeding › Conference contribution › Scientific › peer-review

### The impact of acquisition dose on quantitative breast density estimation with digital mammography: results from ACRIN PA 4006

#### General information

Publication status: Published  
MoE publication type: A1 Journal article-refereed  
Organisations: University of Pennsylvania  
Contributors: Chen, L., Ray, S., Keller, B., Pertuz, S., McDonald, E., Conant, E., Kontos, D.  
Publication date: Sep 2016  
Peer-reviewed: Yes

#### Publication information

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Volume: 280  
Issue number: 3  
ISSN (Print): 0033-8419  
Ratings:  
Scopus rating (2016): CiteScore 5.67 SJR 3.56 SNIP 2.816  
Original language: English  
DOIs:  
10.1148/radiol.2016151749  
Research output: Contribution to journal › Article › Scientific › peer-review

### Fully-automated quantitative estimation of volumetric breast density from digital breast tomosynthesis images

#### General information

Publication status: Published  
MoE publication type: A1 Journal article-refereed  
Organisations: Former organisation of the author  
Contributors: Pertuz, S., McDonald, E., Weinstein, S., Conant, E., Kontos, D.  
Pages: 65-74  
Publication date: Apr 2016  
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Journal: Radiology  
Volume: 279  
Issue number: 1  
ISSN (Print): 0033-8419  
Ratings:  
Scopus rating (2016): CiteScore 5.67 SJR 3.56 SNIP 2.816  
Original language: English

DOIs:

10.1148/radiol.2015150277

Research output: Contribution to journal › Article › Scientific › peer-review

### **Levosimendan alone and in combination with valsartan prevents stroke in Dahl salt-sensitive rats**

The effects of levosimendan on cerebrovascular lesions and mortality were investigated in models of primary and secondary stroke. We aimed to determine whether the effects of levosimendan are comparable to and/or cumulative with those of valsartan, and to investigate whether levosimendan-induced vasodilation has a role in its effects on stroke. In a primary stroke Dahl/Rapp rat model, mortality rates were 70% and 5% for vehicle and levosimendan, respectively. Both stroke incidence (85% vs. 10%,  $P<0.001$ ) and stroke-associated behavioral deficits (7-point neuroscore: 4.59 vs. 5.96,  $P<0.001$ ) were worse for vehicle compared to levosimendan. In a secondary stroke model in which levosimendan treatment was started after cerebrovascular incidences were already detected, mean survival times were 15 days with vehicle, 20 days with levosimendan ( $P=0.025$ , vs. vehicle), 22 days with valsartan ( $P=0.001$ , vs. vehicle), and 31 days with levosimendan plus valsartan ( $P<0.001$ , vs. vehicle). The respective survivals were 0%, 16%, 20% and 59%, and the respective incidences of severe lesions were 50%, 67%, 50% and 11%. In this rat model, levosimendan increased blood volume of the cerebral vessels, with significant effects in the microvessels of the cortex ( $\Delta R=3.5\pm 0.15$  vs.  $2.7\pm 0.17$  ml for vehicle;  $P=0.001$ ) and hemisphere ( $\Delta R=3.2\pm 0.23$  vs.  $2.6\pm 0.14$  ml for vehicle;  $P=0.018$ ). Overall, levosimendan significantly reduced stroke-induced mortality and morbidity, both alone and with valsartan, with apparent cumulative effects, an activity in which the vasodilatory effects of levosimendan have a role.

### **General information**

Publication status: Published

MoE publication type: A1 Journal article-refereed

Organisations: Department of Signal Processing, Tampere University of Technology

Contributors: Levijoki, J., Kivikko, M., Pollesello, P., Sallinen, J., Hyttilä-Hopponen, M., Kuoppamäki, M., Haasio, K., Gröhn, O., Miettinen, R., Puoliväli, J., Tähtivaara, L., Yrjänheikki, J., Haapalinna, A.

Number of pages: 9

Pages: 132-40

Publication date: 5 Mar 2015

Peer-reviewed: Yes

### **Publication information**

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Volume: 750

ISSN (Print): 0014-2999

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Scopus rating (2015): CiteScore 2.93 SJR 1.122 SNIP 1.016

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DOIs:

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### **Bibliographical note**

INT=sgn,"Miettinen, Riitta"

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