**Neurometabolic Coupling in premature Infants   
assessed by means of Transfer Entropy**

**Dries Hendrikxa,b**, Liesbeth Thewissenc,d, Anne Smitsc,d, Gunnar Naulaersc,d,   
Karel Allegaertc,e,f, Sabine Van Huffela,b, and Alexander Caicedoa,b

*a Department of Electrical Engineering, KU Leuven, Belgium*

*b imec, Leuven, Belgium*

*c Department of Development and Regeneration, KU Leuven, Belgium*

*d Department of Neonatology, UZ Leuven, Belgium*

*e Department of Pediatric Surgery and Intensive Care, Erasmus MC-Sophia Children’s Hospital, Rotterdam, The Netherlands*

*f Department of Neonatology, Erasmus MC-Sophia Children’s Hospital, Rotterdam, The Netherlands*

*Corresponding author e-mail address: dries.hendrikx@esat.kuleuven.be*

**Abstract:** Neurometabolic coupling (NMC) is a regulation mechanism that helps the brain to maintain an appropriate energy flow to the neural tissue under conditions of increased neuronal activity. It is however not yet clear to which extent this mechanism is present in the premature brain. In this study, we explore the use of transfer entropy (TE) in order to compute the nonlinear coupling between changes in brain function, assessed by means of EEG, and changes in brain oxygenation, assessed by means of near-infrared spectroscopy (NIRS). In a previous study, we have measured the coupling between both variables using a linear model to compute TE. The results indicated that changes in brain oxygenation were likely to precede changes in EEG activity. However, using a nonlinear and nonparametric approach to compute TE, the results indicate an opposite directionality of this coupling. The source of the different results provided by the linear and nonlinear TE is unclear and needs further research. We present the results from a cohort of 21 premature neonates, which are stratified in two groups, based on the presence of brain abnormalities observed on routine ultrasound (US) scans. Results indicate that TE values computed using the nonlinear approach are able to discriminate neonates with brain abnormalities from healthy neonates, indicating a possibly less functional NMC in neonates with brain abnormalities.

I prefer:  