

Curriculum Vitae



Name Jochen LANG
Birthdate 12.08.1957
Nationality German
Diplomas MD, "Approbation als Arzt" (*licence to work as physician*);
FMGEMS (eligible for application in the US);
privatdocent (Université de Genève, CH)
Current Position: Professeur (PU Classe Excellence), Université de Bordeaux 1

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1976 Humanistisches Abitur (Griechisch, Latein, Mathematik) *Gymnasium Marienstatt* (Rheinland-Pfalz, FRG)
1977-84 Fellow of the German University Foundation ([Studienstiftung](#))
1977-84 **Medical School** Würzburg, FRG (1977-1980); Paris V, Hôpital Cochin, Paris, France (1980-1981), Freiburg, FRG (1981-1984); Genève (1984)
Clerkships: Bella Coola Indian Reserve General Hospital, B.C., Canada (VIII-X/1979), Pennsylvania State University Medical School, USA (II-III/1983)
1984 **Federal exam and "Approbation als Arzt"**
Thesis "magna cum laude" (Inst. für Pharmakologie, U. Freiburg, Germany; Pr. K. Starke, Pr. H. Moehler)
1985 **FMGEMS**
1985-88 **Postdoctoral fellow, Max-Planck-Institut**, Abt. Neuropharmakologie, Martinsried/FRG (Prof. A. Herz)
1988-90 **Intern, Dept. de Médecine Interne, Hôpital Cantonal Universitaire de Genève, Genève (CH)** (Prof. A. Müller) and **Div. d'Endocrinologie** (Prof. A. Burger)
1990-91 **Research fellow, Division de Biochimie Clinique et Diabète Expérimentale**, Université de Genève, CH (Prof. C.B. Wollheim)
1991-97 **Maître-Assistant, Division de Biochimie Clinique et Diabète Expérimentale**, Université de Genève (Prof. C.B. Wollheim)
1997-2000 **Chef de Clinique Scientifique** and group leader, **Div. Biochimie Clinique et Diabète Expérimentale**, Université de Genève
2000 **Professor, Université de Bordeaux I, Group leader, UMR CNRS 5248**
Vice-director, Bordeaux University Doctoral School in Health and Life Sciences (since 2007)
Member elected, National Committee, French Research Council (CNRS), Section Cell Biology

RESEARCH FIELDS:

Cell Biology, Biochemistry, Electrophysiology; Biosensors, Diabetes, Pancreatic β -cells, Signal Transduction, Intracellular Transport (Exocytosis), Transmembrane proteins (function and structure).

EVALUATION ACTIVITIES:

PhD candidates (Doctoral School); Career Advancement (U. Glasgow, ICL UK; U. Singapore); Wellcome Trust, Project and Fellowship Grants, UK; Austrian Nat'l Science Foundation; FP6 and FP7 (RESEARCH Networks, Marie Curie Training Networks; rapporteur et moniteur); Ministério da Ciência et Ensino Superior, Portuguese Science and Technology Foundation; Comité National CNRS, section 23; CODDIM; AERES, Singapore Nat'l University.

AWARD:

1996, Prix Denber-Pinard de l'Université de Genève (best publication)

LANGUAGES

Fluent: German, English, French; Basic knowledge : Italian, Romaunc

PUBLICATIONS

Original Contributions

46. Raoux, M., Bornat, Y., Quotb, A., Catargi, B., Renaud, S. and Lang, J. *Non-invasive long-term and real-time analysis of endocrine cells on micro-electrode arrays.* J. Physiol. **2012**, 590:1085-1092.
45. A. Quotb, Bornat Y, Raoux M, Lang J, Renaud S. *NeuroBetaMed: A re-configurable wavelet-based event detection circuit for in vitro biological signals.* 2012 IEEE International Symposium on Circuits and Systems (ISCAS), Seoul, Korea (South). **2012**.
44. Roger, B., J. Papin, P. Vacher, M. Raoux, A. Mulot, M. Dubois, B.H. Vanderwalle, F. Pattou, G. Charpentier, J.C. Jonas, N. Moustaid-44. Roger, B.*, J. Papin*, P. Vacher, M. Raoux, A. Mulot, M. Dubois, B.H. Vanderwalle, F. Pattou, G. Charpentier, J.C. Jonas, N. Moustaid-Moussa, and J. Lang, *Adenylyl cyclase 8 is central to glucagon-like peptide 1 signalling and effects of chronically elevated glucose in rat and human pancreatic beta cells.* Diabetologia, **in press**.
43. F. Boal, M. Laguerre, A. Milochau, J. Lang and P. A. Scotti. *A charged prominence in the linker domain of the cysteine-string protein CSP α mediates its regulated interaction with the calcium sensor synaptotagmin 9 during exocytosis.* FASEB J., **in press**.
42. Yassine, W., A. Milochau, S. Buchoux, J. Lang, B. Desbat, and R. Oda, Effect of monolayer lipid charges on the structure and orientation of protein VAMP1 at the air-water interface. Biochem. Biophys. Acta – Biomembranes, **2010**, 1798:928-937.
41. Bornat, Y.; Raoux, M.; Boutaib, Y.; Morin, F. O.; Charpentier, G.; Lang, J.; Renaud, S. *Detection of electrical activity of pancreatic β -cells using micro-electrode arrays.* Proceedings 5th IEEE Int. Symposium on Electronic Design, Test & Applications, **in press**.
40. Yassine, W., Taib, N., Federman, S., Milochau, A., Castano, S., Sbi, W., Manigand, C., Laguerre, M., Desbat, B., Oda, R. and J. Lang, *Reversible transition between α -helix and β -sheet conformation of a transmembrane domain.* Biochem. Biophys. Acta – Biomembranes, **2009**, 1788:1722-1730.
39. Karaca, M., Castel, J., Tourrel-Cuzin, C., Brun, M., Geant, A., Dubois, M., Catesson, S., Rodriguez, M., Luquet, S., Cattan, P., Lockhart, B., Lang, J., Ktorza A., Magnan, C. and C. Kargar, *Exploring Functional β -Cell Heterogeneity In Vivo Using PSA-NCAM as a Specific Marker.* PLoS ONE, **2009**, 4: e5555
38. Grise, F., N. Taib, C. Monterrat, V. Lagr e, and J. Lang, *Distinct roles of the C₂A and the C₂B domain of the vesicular Ca²⁺ sensor synaptotagmin 9 in endocrine β -cells.* Biochem. J., **2007**, 403: p. 483-492.
37. Monterrat, C., F. Grise, A. H mar, and J. Lang, *The calcium-sensing protein synaptotagmin 7 is expressed on different endosomal compartments in pancreatic β -cells and in neurons but not on large dense core vesicles.* Histochem. Cell Biol., **2007**, 127: 625-632.
36. Boal, F., S. Le Pevelen, C. Cziepluch, P. Scotti, and J. Lang, *Cysteine-string protein isoform beta (Csp β) is targeted to the trans-Golgi network as a non-palmitoylated CSP in clonal β -cells.* Biochim. Biophys. Acta - Mol. Cell Res., **2007**. 1773: p. 109-119.
35. Dubois, M., P. Vacher, B. Roger, D. Huyghe, B. Vandewalle, J. Kerr-Conte, F. Pattou, N. Moustaid Moussa, and J. Lang, *Glucotoxicity inhibits late steps of insulin exocytosis.* Endocrinology, **2007**. 148: p.1605-1614.
34. Lajus, S. and J. Lang, *Splice variant 3, but not 2 of receptor protein-tyrosine phosphatase sigma can mediate stimulation of insulin-secretion by alpha-latrotoxin.* J. Cell Biochem., **2006**. 98: p. 1552-1559.
33. Lajus, S., P. Vacher, D. Huber, M. Dubois, M.N. Benassy, Y. Ushkaryov, and J. Lang, *Alpha-latrotoxin induces exocytosis by inhibition of voltage-dependent K⁺ channels and by stimulation of L-type Ca²⁺ channels via latrophilin in β -cells.* J. Biol. Chem., **2006**. 281: p. 5522-5531.
32. Monterrat, C., F. Boal, F. Grise, A. Hemar, and J. Lang, *Synaptotagmin 8 is expressed both as a calcium-insensitive soluble and membrane protein in neurons, neuroendocrine and endocrine cells.* Biochem. Biophys. Acta - Mol. Cell Res., **2006**. 1763: p. 73-81.
31. Boal, F., H. Zhang, C. Tessier, P. Scotti, and J. Lang, *The variable C-terminus of cysteine string proteins modulates exocytosis and protein-protein interactions.* Biochemistry, **2004**. 43: p. 16212-16223
30. Zhang, H., K.W. Peters, F. Sun, C.R. Marino, J. Lang, R.D. Burgoyne, and R.A. Frizzell, *Cysteine string protein interacts with and modulates the maturation of the cystic fibrosis transmembrane conductance regulator.* J. Biol. Chem., **2002**. 277: p. 28948-28958.
29. Gut, A., C.E. Kiraly, M. Fukuda, K. Mikoshiba, C.B. Wollheim, and J. Lang, *Expression and localisation of synaptotagmin isoforms in endocrine beta-cells: their function in insulin exocytosis.* J. Cell Sci., **2001**. 114: p. 1709-1716.
28. Hashimoto, Y., T. Niikura, H. Tajima, T. Yasukawa, H. Sudo, Y. Ito, Y. Kita, M. Kawasumi, K. Kouyama, M. Doyu, G. Sobue, T. Koide, S. Tsuji, J. Lang, K. Kurokawa, and I. Nishimoto, *A rescue factor abolishing neuronal cell death by a wide spectrum of familial Alzheimer's disease genes and A β .* Proc. Nat'l Acad. Sci. U S A, **2001**. 98: p. 6336-6341.
27. Zhang, H., W.L. Kelley, L.H. Chamberlain, R.D. Burgoyne, and J. Lang, *Mutational analysis of cysteine-string protein function in insulin exocytosis.* J. Cell Sci., **1999**. 112: p. 1345-1351.
26. Lang, J., Y. Ushkaryov, A. Grasso, and C.B. Wollheim, *Ca²⁺-independent insulin exocytosis induced by α -latrotoxin requires latrophilin, a G protein-coupled receptor.* EMBO J., **1998**. 17: p. 648-657.
25. Zhang, H., W.L. Kelley, L.H. Chamberlain, R.D. Burgoyne, C.B. Wollheim, and J. Lang, *Cysteine-string proteins regulate exocytosis of insulin independent from transmembrane ion fluxes.* FEBS Lett., **1998**. 437: p. 267-272.
24. Zhang, H., H. Yasrebi-Nejad, and J. Lang, *G-protein β g-binding domains regulate insulin exocytosis in clonal pancreatic β -cells.* FEBS Lett., **1998**. 424: p. 202-206.
23. Lang, J., M. Fukuda, H. Zhang, K. Mikoshiba, and C.B. Wollheim, *The first C2 domain of synaptotagmin is required for exocytosis of insulin from pancreatic beta-cells: action of synaptotagmin at low micromolar calcium.* EMBO J., **1997**. 16: p. 5837-5846.
22. Lang, J., H. Zhang, V.V. Vaidyanathan, K. Sadoul, H. Niemann, and C.B. Wollheim, *Transient expression of botulinum neurotoxin C1 light chain differentially inhibits calcium and glucose induced insulin secretion in clonal β -cells.* FEBS Lett., **1997**. 419: p. 13-17.
21. Mohlig, M., S. Wolter, P. Mayer, J. Lang, M. Osterhoff, P.A. Horn, H. Schatz, and A. Pfeiffer, *Insulinoma cells contain an isoform of Ca²⁺/calmodulin-dependent protein kinase II delta associated with insulin secretion vesicles.* Endocrinology, **1997**. 138: p. 2577-2584.

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18. Lang, J., I. Nishimoto, T. Okamoto, R. Regazzi, C. Kiraly, U. Weller, and C.B. Wollheim, *Direct control of exocytosis by receptor-mediated activation of the heterotrimeric GTPases G_i and G_o or by the expression of their active G alpha subunits*. [EMBO J.](#), **1995**. 14: p. 3635-3644.
17. Regazzi, R., C.B. Wollheim, J. Lang, J.M. Theler, O. Rossetto, C. Montecucco, K. Sadoul, U. Weller, M. Palmer, and B. Thorens, *VAMP-2 and cellubrevin are expressed in pancreatic beta-cells and are essential for Ca²⁺-but not for GTP gamma S-induced insulin secretion*. [EMBO J.](#), **1995**. 14: p. 2723-2730.
16. Sadoul, K., J. Lang, C. Montecucco, U. Weller, R. Regazzi, S. Catsicas, C.B. Wollheim, and P.A. Halban, *SNAP-25 is expressed in islets of Langerhans and is involved in insulin release*. [J. Cell Biol.](#), **1995**. 128: p. 1019-1028.
15. Juge-Aubry, C.E., H. Liang, J. Lang, J.W. Barlow, and A.G. Burger, *Synthesis and characterization of anti-idiotypic anti-T4 antibodies*. [Eur. J. Endocrinol.](#), **1994**. 130: p. 107-112.
14. Kiss, J.Z., C. Wang, S. Olive, G. Rougon, J. Lang, D. Baetens, D. Harry, and W.F. Pralong, *Activity-dependent mobilization of the adhesion molecule polysialic NCAM to the cell surface of neurons and endocrine cells*. [EMBO J.](#), **1994**. 13: p. 5284-5292.
13. Lang, J., F. Boulay, P. Parker, P. Gierschik, and C.B. Wollheim, *Regulation of cytosolic calcium and insulin secretion by galanin and ATP receptors: interactions of pertussis-toxin-sensitive and -insensitive signalling pathways*. [Biochem. J.](#), **1994**. 303 (Pt 3): p. 885-891.
12. Lang, J., F. Boulay, G. Li, and C.B. Wollheim, *Conserved transducer coupling but different effector linkage upon expression of the myeloid fMet-Leu-Phe receptor in insulin secreting cells*. [EMBO J.](#), **1993**. 12: p. 2671-2679.
11. Ammer, H., L. Nice, J. Lang, and R. Schulz, *Regulation of G proteins by chronic opiate and clonidine treatment in the guinea pig myenteric plexus*. [J. Pharmacol. Exp. Ther.](#), **1991**. 258: p. 790-796.
10. Costa, T., J. Lang, C. Gless, and A. Herz, *Spontaneous association between opioid receptors and GTP-binding regulatory proteins in native membranes: specific regulation by antagonists and sodium ions*. [Mol. Pharmacol.](#), **1990**. 37: p. 383-394.
9. Lang, J., *Purification and characterization of subforms of the guanine-nucleotide-binding proteins G alpha i and G alpha o*. [Eur. J. Biochem.](#), **1989**. 183: p. 687-692.
8. Lang, J. and T. Costa, *Chronic exposure of NG 108-15 cells to opiate agonists does not alter the amount of the guanine nucleotide-binding proteins Gi and Go*. [J. Neurochem.](#), **1989**. 53: p. 1500-1506.
7. Lang, J. and T. Costa, *Chronic naloxone treatment of NG 108-15 cells alters the function but not the amount of pertussis toxin substrates*. [Adv. Biosci.](#), **1989**. 75: p. 703-706.
6. Lang, J. and R. Schulz, *Chronic opiate receptor activation in vivo alters the level of G-protein subunits in guinea-pig myenteric plexus*. [Neuroscience](#), **1989**. 32: p. 503-510.
5. Lang, J. and T. Costa, *Distribution of the alpha-subunit of the guanine nucleotide-binding protein Gi2 and its comparison to G alpha o*. [J. Recept. Res.](#), **1989**. 9: p. 313-329.
4. Toselli, M., J. Lang, T. Costa, and H.D. Lux, *Direct modulation of voltage-dependent calcium channels by muscarinic activation of a pertussis toxin-sensitive G-protein in hippocampal neurons*. [Pflugers Arch.](#), **1989**. 415: p. 255-261.
3. Lang, J. and T. Costa, *Antisera against the 3-17 sequence of rat G alpha i recognize only a 40 kDa G-protein in brain*. [Biochem. Biophys. Res. Commun.](#), **1987**. 148: p. 838-848.
2. Przewlocki, R., T. Costa, J. Lang, and A. Herz, *Pertussis toxin abolishes the antinociception mediated by opioid receptors in rat spinal cord*. [Eur. J. Pharmacol.](#), **1987**. 144: p. 91-95.
1. Starke, K., L. Spath, J.D. Lang, and C. Adlung, *Further functional in vitro comparison of pre- and postsynaptic dopamine receptors in the rabbit caudate nucleus*. [Naunyn Schmiedebergs Arch Pharmacol](#), **1983**. 323: p. 298-306.

Reviews

6. Rigalleau, V., J. Lang, and H. Gin, *Etiologie et physiopathologie du diabète de type 2*. [Encyclopédie Médico-chirurgicale](#), **2007**, in press.
5. Lang, J., *Seconds messagers et exocytose*. [Médecine Clinique - Endocrinologie et Diabète](#), **2006**. Nov 2006: p. 15-21.
4. Lang, J., *PIPs and pools in insulin secretion*. [Trends Endocrinol. Metab.](#), **2003**. 14: p. 297-299.
3. Lang, J., *Molecular mechanisms and regulation of insulin exocytosis as a paradigm of endocrine secretion*. [Eur. J. Biochem.](#), **1999**. 259: p. 3-17.
2. Wollheim, C.B., J. Lang, and R. Regazzi, *Regulation of exocytosis by Ca²⁺ and G-proteins*. [Diabetes Rev.](#), **1996**. 4: p. 277-297.
1. Wollheim, C.B. and J. Lang, *A game plan for exocytosis*. [Trends Cell Biol.](#), **1994**. 4: p. 339-341.

Book Chapters

- 3) Raoux, M.; Bontorin, G.; Bornat, Y.; Lang, J. and Sylvie Renaud. Bioelectronic sensing of insulin demand. In: *Biohybrid Systems*. Wiley-VCH. In press.
- 2) Lang, J., Regazzi, R. and C.B. Wollheim. 1997. Clostridial toxins and endocrine secretion: their use in insulin-secreting cells. In *Bacterial Toxins*, K. Aktories, editor. Chapman and Hall, p. 217-240.
- 1) Lang, J., 1990. Guanine nucleotide binding proteins and their coupling to opioid receptors. In *Neurobiology of Opioids*. O. F. X. Almeida and T. S. Shippenberg, editors. Springer, Heidelberg. pp 121-140.

Patents

13/01/2010; No FR 10/20502 ; titel "Capteur pour la mesure des besoins d'insuline d'un patient et procédé de fabrication de celui-ci" (M. Raoux, G. Charpentier, B. Catargi, S. Renaud, J. Lang)

PHD STUDENTS (no co-direction, except for co-tutelle)

Cathérine **Kiraly-Borry** (1995-98) «*Role of cytosolic factors in insulin exocytosis*», Université de Genève

Zhang **Hui** (1997-2000) «*Mutational analysis of CSP function in exocytosis*», Université de Genève

Carole **Monterrat** (2000-04) «*Les synaptotagmines et le transport vésiculaire dans les cellules β pancréatiques : une isoforme pour chaque étape ?* »

Sébastien **Tauzin** (2004-08); cotutelle Université Genève ; co-directeur D. Hoessli) «*Association oncogénique de Lyn et PAG dans les rafts de lymphomes B non-Hodgkiniens*

Sophie **Lajus** (2001-2005) « *α -latrotoxine, expression et trafic de son récepteur, la latrophiline, et sécrétion de l'insuline* »

Frédéric **Boal** (2002-06) «*La Cysteine-string protein : étude de ses interactions protéiques dans la sécrétion d'insuline* »

Florence **Grise** (2004-07) «*Recherche des senseurs calciques de la sécrétion d'insuline dans les cellules β -pancréatiques : Etude des synaptotagmines*»

Julien **Papin** (2006-09) «*Bases moléculaires des défauts sécrétoires des cellules β -pancréatiques lors de la glucotoxicité*»

Benoît **Hastoy** (2008-2011) «*Rôles de domaines transmembranaires de protéines SNARES dans l'exocytose de l'insuline* »

Fanny **Lebreton** (2011-2014) «*Investigation des ilots à l'aide des arrays à multi-électrodes* »

TEACHING (COURSES AND SEMINARS)

Co-director, Master Cell Biology and Physiopathology (Universités Bordeaux 1 et 2)

Biochemistry, 2nd year biology students, 30h/yr

Cell Biology, 2nd year biology students, 40h/yr

Cell Biology, 3rd year biology students, 15h/yr

Protein structure and cellular function, Master students (M1, biology), 15h/yr

Cellular Physiology and Pathophysiology, Master students (M1, biology), 10h/yr

Selected Topics in Transport and Secretion, Master students (M2, biology) 10h /yr

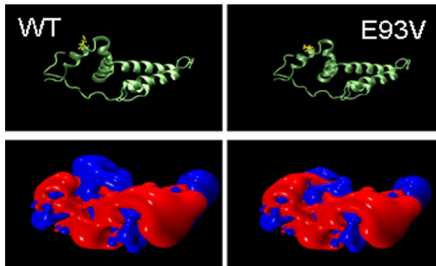
Islet Physiology, ENS-Lyon, Master students (M2, biology) 4h/yr

TEAM AND CURRENT RESEARCH PROJECTS

My current group consists of 2 Assistant professors, one clinical professor (diabetologist), 1 engineer, 1 technician, 2 postdoc, 1 PhD student and Master (diploma) students. Our group is part of the LABEX Amadeus.

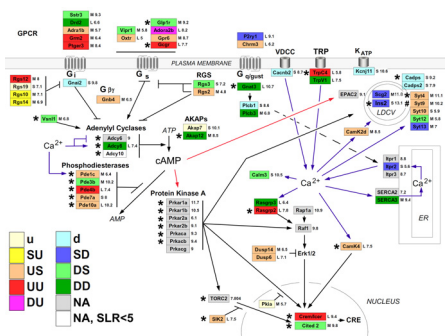
We have a long going expertise in β -cell biology (molecular cell biology and electrophysiology). Whereas in the past we have worked mostly on vesicular traffic in pancreatic beta-cells, our research interest has expanded recently and covers currently the following three main topics (more details can be found on the web-site, see above):

Traffic and exocytosis of insulin in pancreatic beta-cells



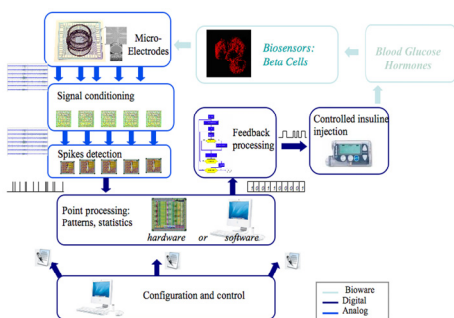
In collaboration with modellers and physical chemists we have shown the unprecedented dynamics of SNARE protein transmembrane dynamics using synthetic peptides and recombinant proteins. We are currently examining the biological role of these dynamics in live cells using classical approaches of cell biology (secretion assays in transiently knock-down cells and reconstitution with wild-type or point mutants) as well as TIRF and electrochemical (amperometry) and electrophysiological approaches (capacitance). *This project is funded by the ANR (French National Research Agency).*

Regulation of insulin exocytosis and diabetes



Our previous work established a model of glucotoxicity imitating in a very simple (and simplified) manner the effects of elevated levels of glucose as found in diabetes (Ref. 38). Transcriptome analysis revealed marked down-regulation of a signal transduction component expressed at low levels, adenylyl cyclase 8 (ADCY8) and re-expression of this component restored GLP-1 signalling. Moreover ADCY8 is tightly linked to the regulation of exocytosis (44). Further analysis revealed a stringent role of ADCY8 in glucose signalling itself and our transgenic knock-out mice are glucose-intolerant.

Beta-cells and bio-electronic hybrid sensors for screening and therapy



Online, long-term screening of beta- or islet cells is cumbersome and uses probes or genetic alterations that alter the cell behaviour. Moreover, glucose sensors currently in use are based on electrochemical detections and have certain drawbacks (no closed loop, single parameter detection, poor adaptation to everyday life events, risk of hypoglycaemia). We therefore set out to use beta-cells coupled to microelectronics as hybrid sensors for screening and, in the very long term, for therapy in conjunction with insulin pumps. This approach takes advantage of the beta cell shaped during evolution for recognizing and integrating signals.

Alterations in the membrane potential are the first integrative signal present in beta cells and represent the input of nutrients and of hormones. Although this can be measured by patch-clamp, the technique is complex, applicable to few cells and characterized by rapid run down. Recording of action potentials by micro-electrode arrays have been performed since years in neurons or cardiomyocytes, cells that depolarize to considerable positive potentials, but never tried in beta-cells that depolarize just to 0 millivolts. We have succeeded to establish this approach permitting long-term, non-invasive recordings and are currently developing this application in collaboration with a microelectronics group in Bordeaux and the University technical transfer office.