

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Department of Neuroscience, Erasmus MC, Rotterdam
Project Title:	Unraveling the function of cerebellar nuclear circuits in sensorimotor processing
Abstract:	<p>Elucidating the strategies that brain circuits use for precise neural computation remains one of the fundamental questions in neuroscience. The cerebellar system is especially suited for approaching this question, given its highly organized neural circuitry, well-defined electrophysiological properties, possibilities for cell-specific genetic manipulation, and ability to process sensorimotor tasks that are particularly demanding in the temporal domain. It is the long-term goal of our laboratory to unravel the cellular encoding mechanisms underlying sensorimotor processing and learning in the cerebellar nuclei (CN), which form the main target of the cerebellar cortex and the main output structure of the cerebellum as a whole. For this project we will address two Key objectives: <u>1.</u> To characterize local CN circuits in vitro using state-of-the-art electrophysiological and optogenetic techniques and elucidate their cellular mechanisms that control the temporal integration of complex excitatory and inhibitory input patterns. <u>2.</u> To unravel the in vivo mechanisms underlying integration of sensorimotor inputs in the CN during eye-blink conditioning, the model of choice for studying learning-dependent timing. Together, these objectives should provide not only new insights into the mechanisms of temporal signal processing in the cerebellar system, but also a general understanding of how sub-cortical structures can read out and integrate converging inputs and feedback neural computations during timing-sensitive operations in the brain.</p>
Requirements of candidate:	<p>Background: We expect you to be motivated to study cerebellar networks. You are creative and intelligent and you are not afraid to try something new. Ideally, you have experience with biology, biotechnology, medicine, electrophysiology, computational neuroscience and/or biochemistry.</p> <p>Master degree: Yes IELTS Grade: 7.0 (<i>minimal 6.0 per component</i>) or TOEFL: 100 (<i>minimal 20 per component</i>)</p>

<p>Supervisor information:</p>	<p>Prof. dr. C.I. De Zeeuw c.dezeeuw@erasmusmc.nl www.neuro.nl</p> <p>Selection of recent publications</p> <p>Badura A, Schonewille M, Voges K, Galliano E, Renier N, Gao Z, Witter L, Hoebeek FE, Chedotal A, De Zeeuw CI (2013) Climbing fiber input shapes reciprocity of Purkinje cell firing. <i>Neuron</i></p> <p>Baudouin SJ, Gaudias J, Gerharz S, Hatstatt L, Zhou K, Punnakkal P, Tanaka KF, Spooren W, Hen R, De Zeeuw CI, Vogt K, Scheiffele P (2012) Shared synaptic pathophysiology in syndromic and nonsyndromic rodent models of autism. <i>Science</i></p> <p>Boele HJ, Koekkoek SK, De Zeeuw CI, Ruigrok TJ (2013) Axonal sprouting and formation of terminals in the adult cerebellum during associative motor learning. <i>J Neurosci</i></p> <p>Clopath C, Badura A, De Zeeuw CI, Brunel N (2014) A cerebellar learning model of vestibulo-ocular reflex adaptation in wild-type and mutant mice. <i>J Neurosci</i></p> <p>De Gruijl JR, Hoogland TM, De Zeeuw CI (2014a) Behavioral correlates of complex spike synchrony in cerebellar microzones. <i>J Neurosci</i></p> <p>De Gruijl JR, Sokol PA, Negrello M, De Zeeuw CI (2014b) Modulation of electrotonic coupling in the inferior olive by inhibitory and excitatory inputs: integration in the glomerulus. <i>Neuron</i></p> <p>Galliano E, Potters JW, Elgersma Y, Wisden W, Kushner SA, De Zeeuw CI, Hoebeek FE (2013a) Synaptic transmission and plasticity at inputs to murine cerebellar Purkinje cells are largely dispensable for standard nonmotor tasks. <i>J Neurosci</i></p> <p>Galliano E, Gao Z, Schonewille M, Todorov B, Simons E, Pop AS, D'Angelo E, van den Maagdenberg AM, Hoebeek FE, De Zeeuw CI (2013b) Silencing the majority of cerebellar granule cells uncovers their essential role in motor learning and consolidation. <i>Cell Reports</i></p> <p>Gao Z, van Beugen BJ, De Zeeuw CI (2012a) Distributed synergistic plasticity and cerebellar learning. <i>Nature Reviews Neurosci</i></p> <p>Gao Z, Todorov B, Barrett CF, van Dorp S, Ferrari MD, van den Maagdenberg AM, De Zeeuw CI, Hoebeek FE (2012b) Cerebellar ataxia by enhanced Ca(V)2.1 currents is alleviated by Ca²⁺-dependent K⁺-channel activators in Cacna1a(S218L) mutant mice. <i>J Neurosci</i></p> <p>Gutierrez-Castellanos N, Winkelman BH, Tolosa-Rodriguez L, Devenney B, Reeves RH, De Zeeuw CI (2013) Size does not always matter: Ts65Dn Down syndrome mice show cerebellum-dependent motor learning deficits that cannot be rescued by postnatal SAG treatment. <i>J Neurosci</i></p> <p>Heck DH, De Zeeuw CI, Jaeger D, Khodakhah K, Person AL (2013) The neuronal code(s) of the cerebellum. <i>J Neurosci</i></p> <p>Jaarsma D, van den Berg R, Wulf PS, van Erp S, Keijzer N, Schlager MA, de Graaff E, De Zeeuw CI, Pasterkamp RJ, Akhmanova A, Hoogenraad CC (2014) A role for Bicaudal-D2 in radial cerebellar granule cell migration. <i>Nature Comm</i></p> <p>Ly R, Bouvier G, Schonewille M, Arabo A, Rondi-Reig L, Lena C, Casado M, De Zeeuw CI, Feltz A (2013) T-type channel blockade impairs long-term</p>
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	<p>potentiation at the parallel fiber-Purkinje cell synapse and cerebellar learning. PNAS</p> <p>Rahmati N, Owens CB, Bosman LW, Spanke JK, Lindeman S, Gong W, Potters JW, Romano V, Voges K, Moscato L, Koekkoek SK, Negrello M, De Zeeuw CI (2014) Cerebellar potentiation and learning a whisker-based object localization task with a time response window. J Neurosci</p> <p>Raikes RS, Weisz C, Hoebeek FE, Terzi MC, De Zeeuw CI, van den Maagdenberg AM, Jinnah HA, Hess EJ (2013) Stress, caffeine and ethanol trigger transient neurological dysfunction through shared mechanisms in a mouse calcium channelopathy. Neurobiol of Disease</p> <p>Saab AS, Neumeier A, Jahn HM, Cupido A, Simek AA, Boele HJ, Scheller A, Le Meur K, Gotz M, Monyer H, Sprengel R, Rubio ME, Deitmer JW, De Zeeuw CI, Kirchhoff F (2012) Bergmann glial AMPA receptors are required for fine motor coordination. Science</p> <p>Schonewille M, Belmeguenai A, Koekkoek SK, Houtman SH, Boele HJ, van Beugen BJ, Gao Z, Badura A, Ohtsuki G, Amerika WE, Hosy E, Hoebeek FE, Elgersma Y, Hansel C, De Zeeuw CI (2010) Purkinje cell-specific knockout of the protein phosphatase PP2B impairs potentiation and cerebellar motor learning. Neuron</p> <p>Schonewille M, Gao Z, Boele HJ, Veloz MF, Amerika WE, Simek AA, De Jeu MT, Steinberg JP, Takamiya K, Hoebeek FE, Linden DJ, Haganir RL, De Zeeuw CI (2011) Reevaluating the role of LTD in cerebellar motor learning. Neuron</p> <p>Seja P, Schonewille M, Spitzmaul G, Badura A, Klein I, Rudhard Y, Wisden W, Hubner CA, De Zeeuw CI, Jentsch TJ (2012) Raising cytosolic Cl⁻ in cerebellar granule cells affects their excitability and vestibulo-ocular learning. EMBO J</p> <p>Sepulveda-Falla D, Barrera-Ocampo A, Hagel C, Korwitz A, Vinuesa-Veloz MF, Zhou K, Schonewille M, Zhou H, Velazquez-Perez L, Rodriguez-Labrada R, Villegas A, Ferrer I, Lopera F, Langer T, De Zeeuw CI, Glatzel M (2014) Familial Alzheimer's disease-associated presenilin-1 alters cerebellar activity and calcium homeostasis. J Clin Invest</p> <p>Spitzmaul G, Tolosa L, Winkelmann BH, Heidenreich M, Frens MA, Chabbert C, de Zeeuw CI, Jentsch TJ (2013) Vestibular role of KCNQ4 and KCNQ5 K⁺ channels revealed by mouse models. J Biol Chem</p> <p>van Dorp S, De Zeeuw CI (2014) Variable timing of synaptic transmission in cerebellar unipolar brush cells. PNAS</p> <p>van Versendaal D, Rajendran R, Saiepour MH, Klooster J, Smit-Rigter L, Sommeijer JP, De Zeeuw CI, Hofer SB, Heimel JA, Levelt CN (2012) Elimination of inhibitory synapses is a major component of adult ocular dominance plasticity. Neuron</p> <p>Zariwala HA, Borghuis BG, Hoogland TM, Madisen L, Tian L, De Zeeuw CI, Zeng H, Looger LL, Svoboda K, Chen TW (2012) A Cre-dependent GCaMP3 reporter mouse for neuronal imaging in vivo. J Neurosci</p> <p>Zhou H, Lin Z, Voges K, Ju C, Gao Z, Bosman LW, Ruigrok TJ, Hoebeek FE, De Zeeuw CI, Schonewille M (2014a) Cerebellar modules operate at different frequencies. eLife</p> <p>Zhou K, Wolpert DM, De Zeeuw CI (2014b) Motor systems: reaching out and grasping the molecular tools. Current Biol</p>
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