

**Erasmus University Rotterdam, the Netherlands**  
**CSC PhD 2015 Project Description**

<b>School/Department:</b>	Department of Neuroscience, Erasmus MC, Rotterdam
<b>Project Title:</b>	<i>In vivo</i> imaging and optogenetic stimulation of the dynamic organization of neuronal network activity in the cerebellum
<b>Abstract:</b>	<p>The cerebellum integrates sensorimotor and cognitive information. Its neuronal circuitry topographically connects with the inferior olive forming well-organized modules, each of which acts as a functional unit. Recently, we showed that cerebellar modules differ in their intrinsic properties showing different firing frequencies (Zhou et al., 2014). For the current project we will investigate for each individual module in Crus I and II of the cerebellum which sensory input can modulate its activity and which motor output can be controlled by this activity. Using <i>in vivo</i> two-photon <math>\text{Ca}^{2+}</math> imaging we will record how different sensory inputs and behavioral tasks dynamically modulate the formation of neuronal ensembles in the cerebellar cortex. You will relate these findings to the anatomical connections of the recorded neurons, directly linking structure and function. In the second part of your project you will use optogenetic stimulation of the functional modules to further test the functional relevance for sensorimotor processing and cognition. More specifically, with our modern equipment we are able to stimulate specific spatiotemporal patterns of Purkinje cell activity, resembling the patterns that we can observe following the two-photon <math>\text{Ca}^{2+}</math> imaging described above. Thereby, we can elucidate to what extent the patterns of activity observed under the first part of the project will be sufficient to elicit the behavior they can be correlated with. By combining various fundamental approaches to shed light on current enigmas of cerebellar processing, we hope to clarify the role of the cerebellum in health and disease. Our lab is one of the most influential research groups for studying cerebellar function in the world. We have a strong expertise in multidisciplinary neuroscience ranging from molecular neurobiology, cell and systems physiology, and computational neuroscience up to behavior and clinical studies.</p>
<b>Requirements of candidate:</b>	<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 imaging, animal behavior and/or computer programming.</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><b>Supervisor information:</b></p>	<p>Prof. dr. C.I. De Zeeuw <a href="mailto:c.dezeeuw@erasmusmc.nl">c.dezeeuw@erasmusmc.nl</a> <a href="http://www.neuro.nl">www.neuro.nl</a></p> <p><b>Selection of recent publications</b></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 Ca<sup>2+</sup>-dependent K<sup>+</sup>-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>Raika 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, Neumeyer 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, Hugarir 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<sup>-</sup> 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, Vinueza-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, Winkelman BH, Heidenreich M, Frens MA, Chabbert C, de Zeeuw CI, Jentsch TJ (2013) Vestibular role of KCNQ4 and KCNQ5 K<sup>+</sup> 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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