Forgetting GluA3. The Discovery of GluA3 Plasticity and Its Role in Alzheimer's Disease
N.R. Reinders
Virtually all brain functions, including the formation of new memories, require communication between brain cells via their specialized contacts called ‘synapses’. Synapses use various AMPA receptors to facilitate the communication between brain cells, such as GluA1 or GluA3 AMPA receptors. Impaired synapse function can lead to cognitive decline like in Alzheimer’s disease, where the accumulation of amyloid beta (\(\alpha\beta\)) damages synapses. This thesis is dedicated to the question of how \(\alpha\beta\) accumulation affects synapses and how this can be prevented.

**Chapter 1:** Demonstrates that GluA3 deficiency effectively protects against the negative effects of \(\alpha\beta\) on synapses, memory and life expectancy of Alzheimer mouse models.

**Chapter 2:** Synaptic GluA3 AMPA-receptors exist in active and in-activated states. Activation of GluA3 AMPA-receptors regulates synaptic strength, constituting synaptic plasticity. GluA3 AMPA-receptors can be activated by a noradrenaline induced rise in cAMP.

**Chapter 3:** Preventing the \(\alpha\beta\) induced removal of synaptic GluA3 AMPA-receptors, protects synapses against the effects of \(\alpha\beta\).

**Chapter 4:** Sindbis-virus induced protein expression is a valid tool to study the physiology of living neurons (type of brain-cell).

The research described in thesis reveals a biochemical process which, when targeted by therapies, can help protect against cognitive symptoms in Alzheimer disease. One such therapy could involve reducing synaptic GluA3 with frequent behavioural and cognitive exercises or medication.