Overall, the Journal Club article by Jan Kaminski does a very good job of highlighting key features of our model of Hebbian synaptic working memory (WM) and puts it in the appropriate context of recent experimental work (i.e. Lundqvist et al., 2016; Rose et al., 2016), demonstrating the need for better memory models that are mechanistically different from the now embattled concept of persistent activity as a prime mechanism of WM maintenance. It is probably fair to say that our model exemplifies a recent shift in neuroscience from the desire to study WM in isolation to the realization that there is something akin to intermediate-term memory, and often neglected interactions with LTM (Fuster, 2009) (and further needed differentiations we will address in a bit). Less reductive and more extensive experimental work is needed to integrate memory mechanisms across anatomical and temporal scales. The reviewers own recent work on recording MTL and frontal areas (Kaminski et al., 2017) certainly contributes to that effort.

However, we strongly feel that the intent of our model is more radical than what this somewhat inclusive portrayal as an additional intermediate timescale memory process might suggest. The reviewer rightly points out that our Hebbian synaptic WM model can encode novel items and also explains recent evidence on activity-silent WM (D'Esposito and Postle, 2015; Stokes, 2015; Rose et al., 2016). It further reproduces load dependent brief gamma bursts as observed in brain areas such as MTL (Axmacher et al., 2007) or PFC (Lundqvist et al., 2016). Such transient activity is not necessarily found or properly described by studies that instead sample recorded neurons for selectivity based on a premise of persistent activity which often involves intra-trial and/or inter-trial averaging. Instead, we interpret evidence of persistent activity as signs of attended memory (as is usually the case in any single-item DMS task, or multi-item tasks with retro-cues that control internal focus) rather than a maintenance mechanism in itself. So instead of distinguishing declarative memory neatly into WM (persistent spiking)-ITM-LTM, we find it more useful to pose that virtually all WM is synaptic and involves ITM and LTM recruitment and that experimentally observed persistent activity in analogy with LTM is a sign of memory readout during attention and selective focus rather than a mechanism for temporary storage of information.

More broadly, we think recent evidence is pointing out that we need to differentiate more clearly when we are talking about memory. Dividing it along the anatomical and temporal axes into PFC-MTL, WM-LTM, is not good enough because there are massive observable differences between single and multi-item memory, attended and unattended memory, goal-directed and incidental encoding, activity-decodable and activity-silent memory, DMS tasks and cued or free recall, etc.

Greetings from Stockholm, Sweden

\Florian Fiebig & Anders Lansner