Christian Keysers - selected references

1 Keysers, C. & Gazzola, V. (2014). Hebbian learning and predictive mirror neurons for actions, sensations and emotions. *Philos.Trans.R.Soc.Lond B Biol.Sci., 369,* 20130175.
Notes: Spike-timing-dependent plasticity is considered the neurophysiological basis of Hebbian learning and has been shown to be sensitive to both contingency and contiguity between pre- and postsynaptic activity. Here, we will examine how applying this Hebbian learning rule to a system of interconnected neurons in the presence of direct or indirect re-afference (e.g. seeing/hearing one's own actions) predicts the emergence of mirror neurons with predictive properties. In this framework, we analyse how mirror neurons become a dynamic system that performs active inferences about the actions of others and allows joint actions despite sensorimotor delays. We explore how this system performs a projection of the self onto others, with egocentric biases to contribute to mind-reading. Finally, we argue that Hebbian learning predicts mirror-like neurons for sensations and emotions and review evidence for the presence of such vicarious activations outside the motor system

2 Keysers, C. & Gazzola, V. (2014). Dissociating the ability and propensity for empathy. *Trends in Cognitive Sciences, 18,* 163-166.
Notes: Neuroimaging suggests psychopaths have reduced vicarious activations when simply witnessing pain but less so when asked to empathize. This inspired us to distinguish the ability from the propensity to empathize. We argue that (i) this ability-propensity distinction is crucial to characterizing empathy in psychiatric disorders such as psychopathy and autism, (ii) that costly helping might be best predicted by the propensity for empathy, and (iii) suggest how social neuroscientists can start exploring this distinction

3 Keysers, C., Perrett, D. I., & Gazzola, V. (2014). Hebbian Learning is about contingency, not contiguity, and explains the emergence of predictive mirror neurons. *Behavioral and Brain Sciences, 37,* 205-206.
Notes: Hebbian Learning should not be reduced to contiguity, as it detects contingency and causality. Hebbian Learning accounts of mirror neurons make predictions that differ from associative learning: Through Hebbian Learning, mirror neurons become dynamic networks that calculate predictions and prediction errors and relate to ideomotor theories. The social force of imitation is important for mirror neuron emergence and suggests canalization

4 Hasson, U., Ghazanfar, A. A., Galantucci, B., Garrod, S., & Keysers, C. (2012). Brain-to-brain coupling: a mechanism for creating and sharing a social world. *Trends in Cognitive Sciences, 16,* 114-121.
Notes: Cognition materializes in an interpersonal space. The emergence of complex behaviors requires the coordination of actions among individuals according to a shared set of rules. Despite the central role of other individuals

in shaping one's mind, most cognitive studies focus on processes that occur within a single individual. We call for a shift from a single-brain to a multi-brain frame of reference. We argue that in many cases the neural processes in one brain are coupled to the neural processes in another brain via the transmission of a signal through the environment. Brain-to-brain coupling constrains and shapes the actions of each individual in a social network, leading to complex joint behaviors that could not have emerged in isolation

5 Schippers, M. B. & Keysers, C. (2011). Mapping the flow of information within the putative mirror neuron system during gesture observation. *NeuroImage, 57,* 37-44.
Notes: The putative mirror neuron system may either function as a strict feed-forward system or as a dynamic control system. A strict feed-forward system would predict that action observation leads to a predominantly temporal-->parietal-->premotor flow of information in which a visual representation is transformed into motor-programs which contribute to action understanding. Instead, a dynamic feedback control system would predict that the reverse direction of information flow predominates because of a combination of inhibitory forward and excitatory inverse models. Here we test which of these conflicting predictions best matches the information flow within the putative mirror neuron system (pMNS) and between the pMNS and the rest of the brain during the observation of comparatively long naturalistic stretches of communicative gestures. We used Granger causality to test the dominant direction of influence. Our results fit the predictions of the dynamic feedback control system: we found predominantly an information flow within the pMNS from premotor to parietal and middle temporal cortices. This is more pronounced during an active guessing task than while passively reviewing the same gestures. In particular, the ventral premotor cortex sends significantly more information to other pMNS areas than it receives during active guessing than during passive observation

6 Kokal, I., Engel, A., Kirschner, S., & Keysers, C. (2011). Synchronized drumming enhances activity in the caudate and facilitates prosocial commitment--if the rhythm comes easily. *PLoS.ONE., 6,* e27272.
Notes: Why does chanting, drumming or dancing together make people feel united? Here we investigate the neural mechanisms underlying interpersonal synchrony and its subsequent effects on prosocial behavior among synchronized individuals. We hypothesized that areas of the brain associated with the processing of reward would be active when individuals experience synchrony during drumming, and that these reward signals would increase prosocial behavior toward this synchronous drum partner. 18 female non-musicians were scanned with functional magnetic resonance imaging while they drummed a rhythm, in alternating blocks, with two different experimenters: one drumming in-synchrony and the other out-of-synchrony relative to the participant. In the last scanning part, which served as the experimental manipulation for the following prosocial behavioral test, one of

the experimenters drummed with one half of the participants in-synchrony and with the other out-of-synchrony. After scanning, this experimenter "accidentally" dropped eight pencils, and the number of pencils collected by the participants was used as a measure of prosocial commitment. Results revealed that participants who mastered the novel rhythm easily before scanning showed increased activity in the caudate during synchronous drumming. The same area also responded to monetary reward in a localizer task with the same participants. The activity in the caudate during experiencing synchronous drumming also predicted the number of pencils the participants later collected to help the synchronous experimenter of the manipulation run. In addition, participants collected more pencils to help the experimenter when she had drummed in-synchrony than out-of-synchrony during the manipulation run. By showing an overlap in activated areas during synchronized drumming and monetary reward, our findings suggest that interpersonal synchrony is related to the brain's reward system

7 Atsak, P., Orre, M., Bakker, P., Cerliani, L., Roozendaal, B., Gazzola, V. et al. (2011). Experience modulates vicarious freezing in rats: a model for empathy. *PLoS.ONE., 6,* e21855.
Notes: The study of the neural basis of emotional empathy has received a surge of interest in recent years but mostly employing human neuroimaging. A simpler animal model would pave the way for systematic single cell recordings and invasive manipulations of the brain regions implicated in empathy. Recent evidence has been put forward for the existence of empathy in rodents. In this study, we describe a potential model of empathy in female rats, in which we studied interactions between two rats: a witness observes a demonstrator experiencing a series of footshocks. By comparing the reaction of witnesses with or without previous footshock experience, we examine the role of prior experience as a modulator of empathy. We show that witnesses having previously experienced footshocks, but not naive ones, display vicarious freezing behavior upon witnessing a cage-mate experiencing footshocks. Strikingly, the demonstrator's behavior was in turn modulated by the behavior of the witness: demonstrators froze more following footshocks if their witness froze more. Previous experiments have shown that rats emit ultrasonic vocalizations (USVs) when receiving footshocks. Thus, the role of USV in triggering vicarious freezing in our paradigm is examined. We found that experienced witness-demonstrator pairs emitted more USVs than naive witness-demonstrator pairs, but the number of USVs was correlated with freezing in demonstrators, not in witnesses. Furthermore, playing back the USVs, recorded from witness-demonstrator pairs during the empathy test, did not induce vicarious freezing behavior in experienced witnesses. Thus, our findings confirm that vicarious freezing can be triggered in rats, and moreover it can be modulated by prior experience. Additionally, our result suggests that vicarious freezing is not triggered by USVs per se and it influences back onto the behavior of the demonstrator that had elicited the vicarious freezing in

witnesses, introducing a paradigm to study empathy as a social loop

8 Thioux, M. & Keysers, C. (2010). Empathy: shared circuits and their dysfunctions. *Dialogues.Clin.Neurosci., 12,* 546-552.
Notes: Observing another individual acting upon an object triggers cerebral activity well beyond the visual cortex of the observer in areas directly involved in planning and executing actions. This we will call action simulation. Importantly, the brain does not solely simulate the actions of others but also the sensations they feel, and their emotional responses. These simulation mechanisms are most active in individuals who report being very empathic. Simulation may indeed be instrumental for our understanding of the emotional and mental state of people in our sight, and may contribute heavily to the social interactions with our peers by providing a first-person perspective on their inner feelings. Simulation mechanisms are at work at an early stage of social development and might be defective in young individuals with autism spectrum disorders (ASD). However, the results to date regarding ASD are not clearcut, and an equal number of studies report positive and negative findings

9 Keysers, C., Kaas, J. H., & Gazzola, V. (2010). Somatosensation in social perception. *Nature Reviews Neuroscience, 11,* 417-428.
Notes: The discovery of mirror neurons in motor areas of the brain has led many to assume that our ability to understand other people's behaviour partially relies on vicarious activations of motor cortices. This Review focuses the limelight of social neuroscience on a different set of brain regions: the somatosensory cortices. These have anatomical connections that enable them to have a role in visual and auditory social perception. Studies that measure brain activity while participants witness the sensations, actions and somatic pain of others consistently show vicarious activation in the somatosensory cortices. Neuroscientists are starting to understand how the brain adds a somatosensory dimension to our perception of other people Social Brain Laboratory, Department of Neuroscience, University Medical Center Groningen, A. Deusinglaan 2, 9713AW Groningen, The Netherlands. c.keysers@nin.knaw.nl

10 Kokal, I., Gazzola, V., & Keysers, C. (2009). Acting together in and beyond the mirror neuron system. *NeuroImage, 47,* 2046-2056.
Notes: Moving a set dinner table often takes two people, and doing so without spilling the glasses requires the close coordination of the two agents' actions. It has been argued that the mirror neuron system may be the key neural locus of such coordination. Instead, here we show that such coordination recruits two separable sets of areas: one that could translate between motor and visual codes and one that could integrate these information to achieve common goals. The former includes regions of the putative mirror neuron system, the latter, regions of the prefrontal, posterior parietal and temporal lobe adjacent to the putative mirror neuron system. Both networks were more

active while participants cooperated with a human agent, responding to their actions, compared to a computer that did not, evidencing their social dimension. This finding shows that although the putative mirror neuron system can play a critical role in joint actions by translating both agents' actions into a common code, the flexible remapping of our own actions with those of others required during joint actions seems to be performed outside of the putative mirror neuron system

11 Keysers, C. & Gazzola, V. (2009). Expanding the mirror: vicarious activity for actions, emotions, and sensations. *Current Opinion in Neurobiology, 19,* 666-671.
Notes: We often empathically share the states of others. The discovery of 'mirror neurons' suggested a neural mechanism for monkeys to share the actions of others. Here we expand this view by showing that mirror neurons for actions not only exist in the premotor cortex or in monkeys and that vicarious activity can also be measured for the emotions and sensations of others. Although we still need to empirically explore the function and development of these vicarious activations, we should stop thinking of vicarious brain activity as a peculiar property of the premotor cortex: instead it seems to be a very common phenomenon which leads social stimuli to recruit a wide range of seemingly private neural systems
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12 Keysers, C. & Fadiga, L. (2008). The mirror neuron system: new frontiers. *Social neuroscience, 3,* 193-198.
Notes: Since the discovery of mirror neurons, much effort has been invested into studying their location and properties in the human brain. Here we review these original findings and introduce the main topics of this special issue of Social Neuroscience. What does the mirror system code? How is the mirror system embedded into the mosaic of circuits that compose our brain? How does the mirror system contribute to communication, language and social interaction? Can the principle of mirror neurons be extended to emotions, sensations and thoughts? Papers using a wide range of methods, including single cell recordings, fMRI, TMS, EEG and psychophysics, collected in this special issue, start to give us some impressive answers
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13 Jabbi, M., Bastiaansen, J., & Keysers, C. (2008). A common anterior insula representation of disgust observation, experience and imagination shows divergent functional connectivity pathways. *PLoS.ONE., 3,* e2939.
Notes: Similar brain regions are involved when we imagine, observe and execute an action. Is the same true for emotions? Here, the same subjects were scanned while they (a) experience, (b) view someone else experiencing

and (c) imagine experiencing gustatory emotions (through script-driven imagery). Capitalizing on the fact that disgust is repeatedly inducible within the scanner environment, we scanned the same participants while they (a) view actors taste the content of a cup and look disgusted (b) tasted unpleasant bitter liquids to induce disgust, and (c) read and imagine scenarios involving disgust and their neutral counterparts. To reduce habituation, we inter-mixed trials of positive emotions in all three scanning experiments. We found voxels in the anterior Insula and adjacent frontal operculum to be involved in all three modalities of disgust, suggesting that simulation in the context of social perception and mental imagery of disgust share a common neural substrates. Using effective connectivity, this shared region however was found to be embedded in distinct functional circuits during the three modalities, suggesting why observing, imagining and experiencing an emotion feels so different

14 Keysers, C. & Gazzola, V. (2006). Towards a unifying neural theory of social cognition. *Progress in Brain Research, 156,* 379-401.
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Humans can effortlessly understand a lot of what is going on in other peoples' minds. Understanding the neural basis of this capacity has proven quite difficult. Since the discovery of mirror neurons, a number of successful experiments have approached the question of how we understand the actions of others from the perspective of sharing their actions. Recently we have demonstrated that a similar logic may apply to understanding the emotions and sensations of others. Here, we therefore review evidence that a single mechanism (shared circuits) applies to actions, sensations and emotions: witnessing the actions, sensations and emotions of other individuals activates brain areas normally involved in performing the same actions and feeling the same sensations and emotions. We propose that these circuits, shared between the first (I do, I feel) and third person perspective (seeing her do, seeing her feel) translate the vision and sound of what other people do and feel into the language of the observers own actions and feelings. This translation could help understand the actions and feelings of others by providing intuitive insights into their inner life. We propose a mechanism for the development of shared circuits on the basis of Hebbian learning, and underline that shared circuits could integrate with more cognitive functions during social cognitions

15 Keysers, C. & Perrett, D. I. (2004). Demystifying social cognition: A Hebbian perspective. *Trends in Cognitive Sciences, 8,* 501-507.
Notes: For humans and monkeys, understanding the actions of others is central to survival. Here we review the physiological properties of three cortical areas involved in this capacity: the STS, PF and F5. Based on the anatomical connections of these areas, and the Hebbian learning rule, we

propose a simple but powerful account of how the monkey brain can learn to understand the actions of others by associating them with self-produced actions, at the same time discriminating its own actions from those of others. As this system appears also to exist in man, this network model can provide a framework for understanding human social perception