Mirror neurons: a bilaterian innovation?

A new look on mechanisms, function and evolution of the mirror neuron system

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Summary

Mirror neurons are considered to play important roles in human social behaviour. Here I theorise, that the social functions of "mirror neurons" are based upon adaptations in the way in which neurons communicate, rather than upon a newly evolved specific type of neural architecture. Vasopressin and oxytocin are specifically implicated in the modulation of neural communication. The role of these hormones in mirror neuron social function involves the generation of sensory neuron calcium waves. These calcium waves are an important element of a perception-action model-like mechanism. In such a model, perception of patterns imposed by external stimuli are matched to patterns of neural representations of an animal's own physical dimensions and motor-capabilities. By way of this mechanism of oscillatory matching, perception of a conspecific can generate stimulating feedback, which can include the matching of affective states. This principle of directing movement towards a proxy of external stimuli as presented by mechanosensory neuron-generated calcium waves is based on simple mechanisms for chemotaxis: movement along a chemical gradient, towards or away from the source. A basic level of mirror neuron guided interaction with conspecifics is ubiquitous in bilateria, with mirror neurons facilitating close body-to-body contact and movement-synchronisation.

Mirror neurons develop through the basic principles of bilaterian central nervous system organisation with its ability to form map-like neural representations. These map-like neural representation of bilaterian animals' own physical qualities and dimensions are very useful for guiding internal fertilisation. In the developmentally plastic bilaterian central nervous system, which forms relatively complex neural representations of the animals own physical parameters, the dimensions and characteristics of these physical parameters -and thus their neural representations-depend strongly on the animal's environment. The mirror neuron related abilities to utilise those representations for species recognition and interaction, contributed strongly to an evolutionary feedback process known as sensory drive, that is, the adaptation of communication systems to environmental circumstances. This suggests that mirror neurons were an important driver of the relatively rapid radiation and diversification of bilaterally symmetric animals that occurred during the Cambrian explosion -between 542 and 525 million years ago.

Summary

Introduction

Mirror neurons were first discovered in the brains of macaque in 1996. Since then, much research into mirror neurons has focussed on studying cortical areas of vertebrate's brains. However, recent developments in neuroscience show that the vertebrate brain is highly plastic. Anatomical and functional distinctions within the brain seem to arise from the intricacies of different sensory pathways contributing to functional brain development. Because of the inherent plasticity of the vertebrate brain, the thesis presented below shall be little concerned with anatomically pinpointing vertebrate mirror neurons or mirror neuron systems. Instead, I explore the hypothesis that mirror neurons are functional units; units coding for- and decoding specific types of information which can develop incrementally and at different levels of central nervous system organisation. In addition, this thesis holds a few more assumptions which defy mainstream ideas in biology, neuroscience and psychology. Assumptions I nevertheless think should be the basis of biopsychological philosophising. Most importantly:

Raw affect precedes the central nervous system, while cognition arises from central nervous system organisation

In this thesis, representations of information in central nervous systems are assumed to reflect abstractions of general cellular states. These different states can represent qualities of negative or positive valence within any cell. When these different cellular states are integrated in a central nervous system, raw affect arises from their dynamic interaction. Positive and negative valence can be abstracted and conveyed to the central nervous system through evolutionary and developmentally specialised receptors and neural pathways. In this view, all cognitive functions arise from dynamic interactions between these pathways of raw affect.

It's interesting to note that in vertebrates, different neurotransmitter producing neurons such as dopamine producing neurons contributing to basal ganglia function, project from the brainstem all the way through diverse subcortical and cortical parts of the brain. These projecting nodes have been associated with emotional functions, and have been suggested to signal valence and salience (e.g. Panksepp, 2003). Although it has been argued this valence is a function of the subcortical structures themselves, it's conceivable this valence is in fact an abstracted quality of a cellular state that is reflected in the peripheric intero- and exteroceptor-types: pain sensation in the periphery is for instance achieved through receptors that are activated through substances that are emitted by damaged cells. Different effects upon cellular state, might also correlate to different second messenger cascades that can be activated through these different receptors. Salience seems mostly

dependent on the relative strength of the dynamics constituted by these ascending signals.

In the early stages of brain development, the cortex consists of rather general neural matrix. The subcortical neural nodes and projections that have been tied to the signalling of valence and salience, are known to contribute to important facets of brain development like point-to-point mapping and Hebbian learning. During these developmental processes, specific patterns, which are probably the most dynamic representations activated within this general neural space at certain stages of development, are thought to be "somatically marked" to designate sub-networks corresponding to specific valences (Damasio et al.,1996). This marking occurs through influence on the neural expression of receptors for chemical signals, such as neurotransmitters and neuropeptides. This mechanism ensures that the most dynamic patterns of information represented in the brain, are tied to the valence of any encountered valence-channel-related salience signals. These sub-networks, or affective circuits, should thus correspond to the valence of the peripheric sensory channel(s) contributing to them.

Invertebrate behaviour and subcortically generated vertebrate behaviour is regularly called 'instinctual'. An 'evolutionary preparedness of instinct' is used to imply such behaviour is affectively rather than cognitively guided (Panksepp, 2003). In my opinion, such views tend to neglect the neurally represented information that contributes to these so called instincts; it seems much more useful to regard evolutionary-developmentally prepared neural patterning as reflecting a form of early-developing cognitions. This thesis speculates on such early developing cognitive capacities in bilaterally symmetric animals, and relates these capacities to mirror neuron functional units.

Neural activation and neural inhibition are intrinsically tied together
Neural activation and inhibition, are assumed to contribute equally to neurally represented information and behavioural effects of neural processes. Parts of the nervous system that are inactive at any time, are as important to perceptual and cognitive coherence as any specific patterns of activation occurring at that same time. In human embryos -for instance-, "up to the gestational age of 18 weeks.....reaching is inaccurate and shows poor control of hand trajectory with characteristic jerky and zigzag movements." (Zoia et al., 2007; p. 223-224). This indicates that learning to control (to inhibit and selectively activate) own muscle activity is an essential part of this early ontogeny.

Developmental motor inhibition might only be expected to occur when it enhances the ratio of external signal to self-generated noise, and not so much for motor activity that can generate a strong signal which can be used to monitor the environment (see Endler, 1992). An example of the latter could be the discharge of electric fish in species that strongly rely on this discharge for electrolocation.

General thesis outline

Chapter one of this thesis is intended as a general review of the most relevant literature on mirror neurons. This first chapter discusses models and definitions of mirror neurons that are based on functional properties; definitions depending on when these neurons become active and concerning what information they can decode. Scenarios emphasising plasticity in the development of mirror neurons, are discussed in relation to these models and ideas regarding functional properties of mirror neurons and mirror neuron systems.

Exploring the hypothesis that mirror neurons are not strict anatomical-, but functional units that are probably not limited to the vertebrate brain, chapters two and three of this thesis present evidence of these units in the realms of invertebrate biology. Assuming it's easier to discern the workings of rather simple nervous systems as compared to the human brain, chapter two speculates on the mechanisms underlying mirror neurons and their behavioural functions from this invertebrate-perspective. Chapter two specifically tries to link hormonal and neurochemical pathways that affect baseline (neural) cellular states, to mirror-neuron-related cognitive functions.

Chapter three discusses the potential ubiquity of mirror neurons in invertebrate animals. Chapter three also speculates on the early evolution and the evolutionary relevance of mirror neurons, and concludes mirror neurons are probably a regular product of nervous system centralisation. In line with this, this thesis concludes that mirror neurons are very likely to be found in all bilaterally symmetric animals, from worms to mammals.

I. An introduction to mirror neurons

Types and functions of mirror neurons

Originally four types of mirror neurons (MN) were identified in macaque premotor cortex with varying visual- and motor specificities for movements, directions and body areas, specifically concerning face or hand regions (Gallese et al., 1996). 1) Strictly congruent MN, which become activated when performing and viewing the same type of action in the same manner of execution. 2) Broadly congruent MN, which are active when actions performed and observed are comparable but not identical. 3) Non-congruent MN, with little resemblance between observed and performed actions that are correlated to specific activations. And 4) mirror-like neurons, responding to certain actions but without apparent motor correlates. However, regardless the level of congruency, the exact patterns of activity may vary between action and observation (Oztop et al., 2013).

MN are supposed to decode three different types and complexity levels of information: details of motor-parameters, schema level motor-plans, and intentions and goals of actions (reviewed by Oztop et al., 2013). These authors conclude the broad neuroscientific view has been shifting to the latter notion, and although MN have been extensively argued operative in understanding of actions, they concede these neurons do not perform any such function independently from an elaborate "understanding network" (Oztop et al., 2013; p.47). They also suggest the strongest correlations between neural activity and behavioural/observed parameters is probably found in temporal patterns of population level activity- a level of analysis which they find to be under-represented in MN research.

MN have been theorised to be at the basis of social tendencies and abilities such as empathy, language and theory of mind, seen to various degrees in -for instance- birds, apes and humans (e.g. Preston & de Waal, 2002). In the perception-action model (PAM) for example, empathy is argued a phenomenon generated by recognition and reciprocation of an objects emotional state (Preston & de Waal, 2002). In the process of recognising another animal's emotional state, the MN system is a prime operative. Views as expressed in the PAM, suggest visual information concerning a social partner can elicit matching motor programs that modulate an individual's affective state to match (or oppose) that of the social partner. In accordance with this notion, but contrasting the emphasis on MN intention and goal decoding noted by Oztop et al. (2013), the PAM initially utilises simple reflexes such as imitative tongue protrusion and related states. According to the PAM, neural patterns serving more elaborate social cognitions are built upon the neural patterns serving these simple reflexes. The idea that neonatal imitation is a basic level of mirroring has been challenged on

the grounds that these simple reflexes are developmentally very short lived- and non-specific responses (Catmur, 2013). This ,Catmur argues, is evidence that later imitative abilities are probably not performed by the same system. However, the nervous system develops inhibition incrementally (see next paragraph), so it's not quite clear why these simple reflexes would not be used to build new neural representations upon.

Development of mirror neurons

Assuming an ability to map incoming information onto representations of own information according to the degree of overlap in certain aspects of their neural representations underlies the simple-reflex level of mirroring and imitation seen in newborns (e.g. Preston & de Waal, 2002; Casile et al., 2011), part of the representations of this information would consist of neural maps resembling certain spatial characteristics of physical sensory space. Simple forms of these neural maps can be generated through rather basic principles of nervous system organisation; axon guidance along chemical gradients (Chédotal & Richards, 2010). This is a general principle that is already reflected in the development of the flatworm neural system, and that is probably an adaptation that was already present in bilaterians' last common ancestor (Bailly et al., 2013).

Mirror neuron development has been specifically tied to the process of experiential canalisation (Del Guidice et al., 2008). These authors suggest that much of the neural patterns supposedly used by the newborn for the interpretation of stimuli, such as facial cues and expressions, develops prenatally through experiential canalisation; as a result of uninhibited motor-activity and "re-afference", that is, sensory feedback of ones own actions. These authors furthermore suggest that experiential canalisation through re-afference, that is, sensory feedback of ones own actions, and Hebbian learning, are sufficient to give rise to the intricate cortical MN system found in humans (Del Giudice et al., 2008; Keysers & Gazzola, 2014). Although the latter notion is contested by others on the grounds that associative learning is responsible (Cooper et al., 2013), this discussion is on semantics rather than mechanisms. In both views, contiguity (proximity in time) and especially contingency (can one signal usually be assumed to predict the other?) of neural representations of information are essential elements needed for this learning, whether it's called associative or Hebbian. Information generated in experiential canalisation can change the level of detail in more basic sensory spatial maps, while also adding information on temporal motor codes and their correspondence to these spatial maps.

Much focus on mirror neurons has been in the visual domain, but the same neural mechanisms have been suggested to be involved in processing of information from other modalities as well. Mechanosensation such as proprioception (that is, sensing ones own movement), has for instance been argued an often-overlooked contributor to the neural representations underlying MN functional units (Oztop et al., 2013).

A proto-mirror system

Corresponding to the notion of experiential canalisation of MN, a proto-mirror system has been suggested to underlie MN functionality (Bonaiuto & Arbib, 2010). This proto-mirror system, is supposed to facilitate a more efficient alternative to trial and error learning. According to the proto-mirror model, a performed action and the expectations of its outcome are monitored within an animal's nervous system. When an action does not generate the expected result or generates the expected result but through different means of action than coded in the motor program, depending on success or failure, the sensory feedback on the action is used to reinforce or diminish the neural representations of associated motor patterns. As such, the proto-mirror system basically models the computations for procedural learning utilising its own motor-representations and pattern recognition to interpret and improve its interactions with the environment.

Interpreting information from unfamiliar modalities

According to the view expressed in the perception-action model of empathy, at the brain-level afferent neural patterns serve to judge the (social) relevance of external information that is perceived through modalities the newborns are yet totally unfamiliar with. For instance: the perception-action model suggests that in visually naïve individuals, spatial patterns in the visual modality can be recognised when their neural representations sufficiently overlap with spatial or temporal patterns embedded within the newborns own motor- or mechanosensory representations. For a visually naïve newborn to visually recognise faces and facial actions on the basis of its own muscular activity, it seems necessary for the different modalities of information to be neurally represented in a two-dimensional space within a general neural matrix.

In arthropods, the representation of information from external space has been shown to occur in the central complex, which is similar in function to the basal ganglia in humans (Strausfeld & Hirth, 2013). Part of the arthropod central complex is the fan-shaped body which is reminiscent of a fan-in fan-out network. Fan-in fan-out networks are characterised by high connectivity in a general matrix: every neuron at the fan-in side projects to every neuron at the fan-out side or the intermediate layer

if one is present. In this type of network, patterns can be represented on the fan-in side while allowing neural activity at the fan-out side access to any part of these neural representations (Olshausen et al., 1993). The same type of neural network is also present in molluscs where it can consist of a somewhat more complex fan-in fan-out type with a common transmission layer in between (Shomrat et al., 2011). As such this seems to be a general type of neural wiring in bilateria; one which might possess the qualities needed for such recognition to succeed in newborns: different motor patterns and their spatial coherence can be represented in relative thresholds and corresponding patterns of neural preparation at the fan-in and/or fan-out side. This activity preparation can also be translated to an intermediate transmission layer if one is present. This means motor patterns and their spatial relations can be reflected in the likelihood that certain neurons and neural populations respond to incoming action potentials by producing them themselves. Different modalities of sensory information can be presented at the opposite sides of fan-in fan-out networks. If patterns of neural representations at one side of such a fan-in fan-out network overlap with the patterns of neural preparedness on the opposite side, this may be bound to lead to simultaneous activations of both sides unless inhibition has been learned. As such the fan-in fan-out type of neural network seems perfectly suited for the recognising rough shapes (e.g. facial region-like) and movements of animals (e.g. tongue protrusion-like), even by animals that have never seen other animals before.

Diversity and evolution of mirror neurons
Since their first discovery in macaque, anatomical- and functional evidence for MN has been found in diverse mammals and some birds. There's also behavioural evidence for MN in these same classes of animals, plus for certain reptiles and octopuses (reviewed by Bonini & Ferrari, 2011). On the basis of these findings, these authors suggest that in the course of evolution a "system for tracking own motor behaviour was.. exploited within a social domain to interpret others' actions...for social interaction and communicative purposes." (p.172), with the "system" probably meaning one with a functionality such as the aforementioned proto-mirror system.

However, if MN are truly so important for social interaction, shouldn't close body-to-body interaction between conspecifics of any species be taken as an indication that some level of MN functionality might exist in such an animal's central nervous system? Assuming that any level of social interaction should relate to certain levels of MN functionality, chapters II and III hypothesise on MN functionality within the realms of invertebrate biology. MN social functionality probably involves a procedural learning system, producing MN functional units, combined with

neuromodulatory mechanisms which influence the way in which the formed neural circuits communicate. In line with this reasoning, a scenario of the interplay between MN functional units and specific neuromodulators, is presented in more detail in chapter II. As will be shown in chapter III, the aforementioned "exploitation within the social domain" through MN-like functionality, probably occurred early in the bilaterian lineage. This first social MN function was probably restricted to the facilitation of mating by internal fertilisation.

<center>**II. Integrating mirror neurons and neuromodulation**</center>

Neuromodulation and behaviour

Nervous system centralisation is an adaptation pre-dating the bilaterian lineage, with the same separation of CNS domains seen among many animals within this lineage (Denes et al., 2007). The most modest but also somewhat regressed central nervous system studied in great detail, is that of the nematode worm (*C. elegans*). In adult animals, none of which are strictly female, this system has 302 or 383 neurons, depending on if the animal is a hermaphrodite or has differentiated to a male (Jarrell et al., 2012). This is a highly connected central nervous system, where following only three synapses is usually sufficient to get from any neuron to another. But even simple behavioural functions arising through this modest system have been impossible to explain through modelling of neural connectivity patterns alone (Bargmann, 2012).

According to Bargmann (2012), the failure to neurally pinpoint even simple functions by describing all the connections points to important roles of neuromodulation: products of neuroendocrine systems might be the key determinant of which connections can be active, to which degree and under what circumstances. Neuromodulating substances, including substances performing hormonal functions throughout the body, can determine neural activity patterns by dynamic, differential regulation of neural preparedness. These neuromodulators can influence the likelihood that specific types of neurons produce an action potential (and thus which neighbouring -connected- neurons are likely to reproduce this response), when these neurons are presented with a certain amount of pre-synaptic stimulation. This notion of neuromodulation reflects the idea that the ways in which cells, tissues and organs communicate are more basic to the functions of these cells, tissues and organs, than the exact structures built through this communication (Doyle et al., 2006; p.295). Cells, tissues and organs basically communicate by emitting certain chemicals. Chemical signals passed through the bloodstream serve long range, long duration chemical communication throughout the body. Such endocrine signals are also potent neuromodulators. At the level of the CNS, specialised neural nodes produce hormones that regulate various endocrine pathways. In vertebrates, neural nodes serving diverse endocrine pathways are predominantly found in the hypothalamus and preoptic area. These neural nodes also project into the vertebrate brain.

Vasopressin and oxytocin neuromodulatory function

Like MN, two products of these neurosecretory pathways: vasopressin and oxytocin (AVP/OT), have been extensively linked to various types of social behaviour. These neuropeptides have been suggested to be involved in anything from aggression to courtship, mating, egg-laying, empathy,

<center>12</center>

parental care and even autism in diverse species (Bartz & Hollander, 2006). Like MN, AVP/OT have been hypothesised part of a specialised social neural network (Stoesz et al, 2013; Kelly & Goodson, 2014). Developmental processes leading to the expression of AVP/OT neuroendocrine nodes have been around in a modest form at least since the bilaterian split (Tessmar-Raible, 2007; Tessmar-Raible et al., 2007). Regarding the evolutionary origins of the AVP/OT system, it has been hypothesised this was already present to some degree in the brains of bilaterians' last common ancestors. These nodes consisting of only a few neurons were probably involved in light- and chemical perception, and physiological and behavioural adjustment to environmental circumstances corresponding to the light-cycle and chemical gradients (Tessmar-Raible et al., 2007). These mechanisms of adjustment likely included neuromodulatory changes in patterns of preparedness and transmission in the neural system. Light sensitivity, for instance, is still reflected in the circadian rhythm of vasopressin release in the mammalian suprachiasmatic nucleus (e.g. Ingram et al., 1999).

Precise patterning of neurochemical projections into the cortex is largely activity dependent (Chédotal & Richards, 2010; Stoesz et al., 2013). Neuromodulators such as AVP/OT are known to affect both axon guidance and direction (Imai, 2009), neural processing through effects on G-protein coupled receptors and their effects on cAMP mediated cellular and extracellular $Ca2+$ balance. They can also regulate interneuron ion-channels and thus the level of synchronisation of different neurons (e.g. Bargmann, 2012). Although several have been suggested, there are no known mechanisms for AVP/OT to cross the blood brain barrier while there are some indications that peripherally administered AVP/OT can influence neural processing and social behaviour (Bartz & Hollander, 2006). This might suggest that peripherally administered AVP/OT does not influence the CNS directly, but influences the sensory input at the bodily level. So starting in the periphery, sensory effects of AVP/OT could constitute an important mode of developmental influence on the socially specialised neural network in which they operate.

Nematode mirror neurons
The sinusoid movements of male and hermaphrodite nematode worms differ slightly in their shape of body waves and their body-bend frequency, the latter of which is higher for males (Fagan & Portman, 2014). Because this is probably a form of biological movement highly alike ones own, experiential canalisation of nematode mechanosensory information can create neural representations that are well suited for judging the social relevance of external movement, even when perceived by animals relatively naïve to the environment. If the neural patterns used for this

recognition are indeed the product of sensing ones own movement, this is a mirror-like system at least. If we were to monitor nematode neural activity in order to compare the action-generated-versus the action-observed situation, some of the neurons involved could probably be argued to qualify as broadly congruent MN in the mechanosensory domain.

The nematode worms' proprioceptive feedback on its own movement would make a potential best guess for aspects of socially relevant stimuli. Unrelated to mating, it would also make a very effective optimising mechanism of movement-ability, quite like the proto-mirror system for procedural learning discussed in chapter one. Based on the simple notion that the musculature system of any animal has certain limitations, and that these limitations are the key determinants for the patterns of motor-control activity that are best suited to generate optimal movement. Such feedback can allow the motor-control system to develop these optimal patterns simply because optimal movements are the most likely to produce the most consistent results; these patterns would automatically come to have the maximum level of contiguity and contingency. As discussed in chapter I, the development of MN functional units seems to be an inherent result of this learning (central nervous) system.

Nematode neuromodulation

Effects of elevated serotonin during axon growth and neural map formation, show G-protein coupled cAMP regulation of cellular Ca2+ balance can disturb point to point mapping, de- or increasing the density of neural projections running from one layer of the brain to another (Chédotal & Richards, 2010). This suggests that the level of resolution of the information generated upstream from adjacent receptors can be reduced or heightened under the influence of G-coupled-receptor neuromodulatory pathways. A principle of resolution-adjustment which is also reflected in retinal coupling: the electrical synchronisation of cones and rods, locally combining their output, through melatonin-induced dopamine-suppression (Ribelayga et al., 2008). This latter principle of electrical coupling under the influence of neuromodulators is also an important function of nematode worms "hub and spoke" neural node (RMG), which is an essential part of the nematode neural network for regulating social behaviours such as pheromone-attraction and aggregation. Here, neuromodulatory electrical coupling serves as a gating mechanism for sensory information, or one altering neural thresholds at the RMG which could be relayed to sensory neural space through gap-junctions (Macosko et al., 2009).

Although the nematode worm does not have the mammalian neuromodulatory peptides AVP/OT, genetic and molecular analyses show these animals posses G-protein coupled receptors that are related to vertebrate receptors for these peptides: ntr-1 and ntr-2 (Garrison et al., 2012). Nematode worms have a gene, ntc-1, which is quite similar to the mammalian AVP/OT encoding regions. A synthetic peptide resembling nematocine, the product of this sequence, binds to both receptors and in doing so activates a signalling pathway which decreases cAMP levels within the cells. When these cellular signalling pathways are activated through nematocine receptor-1, this generates short-lived Ca2+ oscillations. Such oscillations in second messenger concentrations are absent when nematocine binds to receptor-2. Expression of nematocin occurs in both sexes. The sites of this expression are thermosensory neurons and a proprioceptive region (DVA) directly receiving input from diverse sensory neurons. Nematocin is also expressed in a male motor-control region, which serves the turning around the head of a hermaphrodite during mating. During the mating sequence the male moves backward along the hermaphrodite that's moving forward in a sinusoid motion, while remaining in close ventral contact to it with the posterior part of its body. The DVA receives input from male sensory-ray neurons: part of a rather complex sensory structure of 9 bilateral pairs of elongated receptors. This structure develops in the males' tail and is involved in what appears to be the noticing of movement related to physical contact with a potential mate. Some of these ray neurons (of rays 5, 7 and 9) can express dopamine (Liu & Sternberg, 1995; Garrison et al., 2012).

Nematocin receptors are expressed to some degree, in head and tail neurons of both hermaphrodites and males. These receptors are most ubiquitous in male sensory structures implicated in mating function, some of which are chemosensory while many are mechanosensory and proprioceptive. Nematocin receptor-1 is expressed in sensory structures that are involved in vulva detection and in the sensory rays (most notably rays 1,5,7 and 9). Nematocin receptor-2 is also expressed in the male tail region, but in a set of sensory-motor neurons mostly involved in sperm transfer. Both receptors are necessary for mating-related turning behaviours, while nematocin receptor-1 seems essential for adequately responding to initial physical contact with hermaphrodites. Nematocin null mutants, animals that do not express nematocin, show a reduced responsiveness to physical contact with hermaphrodites. When they do eventually respond, nematocin null-mutants tend to slip more often during the mating sequence. It also takes them more turns around the hermaphrodite to complete the sequence and they often fail to complete it altogether. The greater level of failure when performing the mating sequence indicates the animals have trouble in successfully translating the hermaphrodites shape, dimensions and movements into adjustments to their own.
Disturbance of nematocin expression is detrimental to all male mating behaviours. Disturbance of

nematocin expression in the DVA proprioceptive neural node only, has a negative influence on the response to initial contact and on the efficiency of vulva detection. Garrison et al. hypothesise that activation of ray neuron nematocin receptor-1 by the nematocin produced in the proprioceptive (DVA) neural node at the start of the mating sequence, might convey feedback influencing neural thresholds of diverse circuits to constitute an appetite (appetitive function) for the required interaction (Garrison et al., 2012). This appetitive function seems to include mechanisms that facilitate recognising species-specific movements as relevant. Given the proprioceptive function of DVA, like MN this ability seems based on certain aspects of information that the animal learned about its own movement.

In sum, AVP/OT -like peptides regulate physical manoeuvring and synchronising of movements during the close body-to-body contact involved in nematode mating. Nematocine, the nematode version of these peptides, can generate $Ca2+$ oscillations in sensory neurons. These oscillations seem to facilitate recognising a potential mate by its movements, they 're also part of a mechanism that generates an appetite for interacting with this potential mate.

Mirror neurons and neuromodulation
Although the neural and behavioural effects of nematocin are in no way fully explanatory of the functions of AVP/OT, they do suggest that there might be a link between these peptides and MN functionality. In nematode worms, the DVA proprioceptive neural node produces nematocin when the touch of a conspecific is first detected through the rays, providing an appetitive feedback signal (Garrison et al., 2012). An important part of this feedback signal could be in facilitating a free-flow-resonance of this sensory information to upstream sensory-motor areas, for instance by $Ca2+$ regulated lowering of activation thresholds for certain sensory channels over others. This could make for a perception-action model-like deep processing through free flow of certain sensory neural patterns into motor-neural space. Like a proto-mirror system, this motor-neural space is entrained to the mechanosensory apparatus of the animal. The fact that these motor patterns seem to be utilised to coordinate close body-to-body movement with other nematodes, suggests these patterns are experientially canalised MN functional units that are part of a nematode MN system. The depth of processing through this MN system is likely to be influenced by the resolution and detail of temporal patterns and their spatial differentials that can be conserved through neural signal transduction, for instance through AVP/OT affecting gap-junctions and the electrical coupling of neurons. Nematocin increases coherent behaviour of nematodes through affecting the interplay of diverse neural circuits (Garrison et al., 2012). Much of this coherence seems to be achieved by

nematocin allowing certain aspects of mechanosensory information to flow freely through sensory space while relatively inhibiting contradictory response-properties associated to other aspects or parts of these ascending streams of information such as inhibiting the nematode tendency to recoil when touched. As neuromodulators such as AVP/OT can alter cellular second-messenger dynamics that influence neural excitability, e.g. oscillations in Ca2+, a main part of its function might lie in setting different activation thresholds for different ascending types of sensory channels and their connected or receptor-marked brain-level sub-networks. AVP/OT probably functions in concert with some, and antagonism with other neurochemicals in this regard (e.g. Van Honk et al., 2010; Van Rijswijk, 2012 unpublished). This principle of instigating concert and antagonism of different valence-related sensory channels through neuromodulation, means that slight shifts in relative neuromodulatory output can cause much more complex shifts in the excitability of certain parts of the network over others.

In sum, nematodes arguably possess a MN system. AVP/OT seem to influence the level of processing that can go on within this system. These neuromodulators can influence the level of processing through regulating the likelihood of signal transduction through diverse sensory channels or by affecting the level of detail that can be transferred though the system.

In vertebrates, dopamine is crucially involved in inhibition and gating of movement for instance in the basal ganglia. This system therefore presents an obvious candidate for functions of entrainment between the mechanosensory- and motor domains comparable to the function of the proto-mirror system. It's also regularly associated with reinforcement and reward, which are probably tied to pattern recognition and procedural learning, and are as such involved in various social functions (Stoesz et al., 2013). However, the exact neurotransmitters used and the sites where they can influence learning-related plasticity can vary across species (Shomrat et al., 2011). Dopamine and other neurotransmitters are substances that are involved in any learning that's going on: they directly correspond to the forming or diminishing of neural connections in general or developmentally specified neural matrices. Neuromodulators seem to regulate learning at a higher level: they determine when what can be learned in which part of the brain, they also regulate neural thresholds of developmentally specified neural populations thereby determining the likelihood that different neural patterns are activated or inhibited.

Focussing on arthropods, behavioural evidence to suggest an MN functional units are indeed common neural features throughout the bilaterian lineage is presented in the next chapter. In addition, the capacity to develop MN functional units composing the earliest forms of social cognition, is suggested to have constituted a positive evolutionary feedback loop. In this feedback loop, the ability to form MN functional units facilitated more coherent behaviours including conspecific recognition and internal fertilisation. These behavioural effects all contributed to the reproductive success of animals in possession of such a learning system.

III. Much more mirror neurons

Spider love and bee-dances

More evidence for MN being a ubiquitous kind of neural functional unit comes from research into arthropod perception. For instance, vibratory signals are an important part of wandering spiders' pre-copulatory behaviours. In this pre-copulatory phase, sensory guidance is heavily involved in spatial orientation, sexual arousal and appetite, and in suppressing behaviour that is unwarranted by the context (Barth, 1993). Behaviour unwarranted in the context of mating usually includes a predatory response. Wandering spider vibratory signals are perceived through diverse mechanosensory structures, which are also activated when these animals move. Some of these mechanosensory structures are explicitly proprioceptive, while others have more general functions. Besides a function in pre-copulatory guidance, some of these sensory functions are for instance involved in prey and predator detection, and pathways eliciting predatory response or flight respectively. In the pre-copulatory function, the information of signals used should probably show considerable overlap with self-generated patterns. While for the predatory/flight function, the only quality that matters might be the relative amount of activation as compared to the regular self-generated signal. Both forms of biological-movement perception, probably involve some degree of MN functionality. For the former, some of the involved neurons should at least be broadly congruent, while for the latter involvement of non-congruent MN would suffice.

Perhaps, the most obvious piece of arthropod behaviour indicative of MN functionality comes from the honeybee waggle-dance. During their adult life and under the influence of experience, honeybees are known to grow neural space in areas related to representations in the visual modality (Durst et al., 1994). In many insects, this representation can include a map-like representation of the sky, which is often based on certain properties of polarised light coming from the sun (Heinze & Homberg, 2007). The honeybee waggle-dance is used to symbolise the route and distance, plus the quality of a food source. Worker bees can distil these parameters and compare them to those of other dances they recently witnessed. On the basis of this comparison, they select a best option and use the parameters displayed by its dancer to navigate their way to the food source. It seems that a trade off between distance and food quality, can be assessed through the relative neural dynamics produced by certain parameters of the dance. More importantly, flying a route, dancing a route and witnessing a dance probably involve activations of the same neural representations. These representations should be comparable in different bees. So, if not a conclusion, an involvement of strictly congruent MN in the visual domain of honeybee communication seems a clear-cut hypothesis at least. These honeybee MN functional units apparently even decode information at the

level of intentions and goals. Among the bees a direct transfer of motivation to move in relation to an external target by proxy of its neural representation in relation to the animals' own seems to occur.

The Cambrian explosion, bilateral symmetry and mirror neuron complexity

Almost all existing animal phyla came into existence somewhere between 542 and 525 million years ago, in a period known as the Cambrian explosion. This great radiation and diversification of species, was partly due to changing atmospheric conditions. However, greater behavioural flexibility due to greater developmental plasticity has been argued a most important force behind the Cambrian explosion (Campbell & Reece, 2005; p.629). In this regard the patterning genes such as the HOX, are supposed to have been of particular influence. These genes have been associated to bilateral symmetry through establishment of the anterior-posterior (head-tail) body axis, and have probably been crucially involved in CNS formation since bilaterians' last common ancestor (Bailly et al., 2013). The bilaterian body-plan seems to allow more distinctive signalling and recognition, simply because the distinguishing qualities of own movements are generated as, and can thus be perceived as, the relative activity of distinct opposite ventral and dorsal surfaces. These can furthermore be divided in two laterally mirrored surfaces which seems likely to create coherent patterns in an animal's movements and the neural representations thereof. These representations potentially have far greater detail and complexity than those of radially symmetric animals, and are likely to contribute to diverse MN functional units. The highly organised peripheric to CNS neural patterning and the accompanying ability to form map-like representations during this early stage of development, surely benefits the incremental formation of these MN functional units.

Mirror neuron-like aspects of chemotaxis

In their earliest forms, neurally centralised map-like representations of the external environment probably encompass relatively much chemosensory space. A basic MN-like functionality seems inherent to such representations: the neural representations of movement along a gradient in chemosensory space should be quite similar for situations where an animal moves towards a source and situations where a source moves towards the animal. In many species, chemical signals play important roles in species recognition and localisation of potential mates. In bilaterians' last common ancestor, the neural architecture for chemosensory representation seems to have been very limited, consisting mostly of a few neurochemical nodes (Tessmar-Raible et al., 2007). Simple neurochemical nodes, could reflect the relative distance to an external chemical source through the pace or strength of their oscillatory neural output. The parameters of this output seem to generate an

appetitive signal, or the opposite in case of noxious stimuli. A signal that is reflected in motor-effects: a direction of movement towards or away from a source of a chemical gradient. This would probably make for something of a perception-action model-like mechanism, which could be organised even without a real CNS. It's conceivable that the earliest social MN functionality was only made possible by this pre-social ability to locate- and an appetitive tendency to move towards chemical substances specifically emitted by (receptive) conspecifics. Even in the case of externally fertilising organisms, this would seem a highly adaptive feature; potentially increasing fertilisation rate substantially. If so, MN functionality might have its origin in this tendency to direct motor activity towards such oscillatory proxies for environmental stimuli. AVP/OT function, in nematode mating for instance, includes $Ca2+$ oscillations in proprioceptive structures. Patterns of cellular oscillations in second-messengers, imposed through differential mechanosensory stimulation, might translate into differential motor activity for synchronising of movement to the source of the externally imposed mechanosensory input. It's conceivable, success or failure to adjust to this source is translated to cellular signals of reward and punishment. That is, the success or failure of matching patterns of motor-response to mechanosensory patterns, inherently involves state-related reward/reinforcement or punitive signals respectively. Such new function of oscillatory matching in the mechanosensory domain, could be a consequence of the evolution of mechanosensory neuron AVP/OT receptors and accompanying oscillatory effects of their stimulation. It could also be due to adaptations influencing under which cellular environments the expression of specific receptors is promoted, leading to developmental marking with such receptors to include mechanosensory neurons.

Mirror neurons and internal fertilisation
On the basis of commonalities in sperm morphology, internal fertilisation has also been hypothesised an adaptation of early bilateria (Buckland-Nicks & Scheltema, 1995). Although the phylogenetic data does not match current understandings (e.g. Bailly et al., 2013), the basic idea is still quite reasonable because internal fertilisation is a feature common in both major clades deriving from a split early in the bilaterian lineage. But even if this assumption of internal fertilisation as an early bilaterian innovation is not correct, internal fertilisation has been highly adaptive and is found only in bilaterally symmetric animals. Internal fertilisation requires species recognition, the exact localisation of a mate and subsequent body-to-body coordination. All of these seem to benefit from the manner in which a bilateral body can generate more distinct movements. Together with MN-related oscillatory matching of sensory/motor neural activity in a learning CNS, the bilaterian body-plan and CNS organisation should have been very useful for the guiding of

internal fertilisation. The MN functional units that seem bound to develop in such a system, may have created a positive evolutionary feedback loop influencing the enormous evolutionary diversification of bilateral body-plans and the spread of internal fertilisation itself. The first internal fertilisation event, which may have occurred multiple times in the early bilaterian lineage, might have been prompted by MN-related reinforcement and an urge or appetite to seek out social stimuli, and especially the MN-related ability for coordinated manoeuvring in close body-to-body contact.

Mirror neurons and sensory drive

Evolutionary feedback through a "sensory drive" influencing mating and sexual selection, has been hypothesised a major vector for specialisation and speciation, most notably by Endler (1992). Key to this feedback are the correlations between sensory capacity, communicative abilities, and the environment an animal tends to grow up in and choose. Endler's emphasis in this work was on colouration patterns of guppies, and their effects on predation risk and courtship- efficiency under different lighting conditions (i.e. in different habitats), but was also hypothesised to apply to other modalities of perception. Sensory drive would for instance be expected to occur in the evolution of chemosensory capabilities. Evolution of the nematode proprioceptive tail-sensory structures, where the numbers and spatial layout of peripheral receptors apparently contracted -through variation and natural selection-, upon the ability to perceive useful signal qualities, seems a prime example of a present-day mechanosensory result of such sensory drive. However, as argued in chapter I, neural architecture such as fan-in fan-out networks can serve in recognising visual patterns according to representations developed through other modalities. This implies that even in the absence of visual memory of a movement, colouration patterns might serve to emphasise certain aspects of movement patterns that can aid in species recognition and courtship. During development of these movement patterns, specific abilities and sensory feedback thereof are determined by environmental parameters. Therefore, MN development might be best considered a process of experiential canalisation (Gottlieb, 1991) of the neural functional units that are essential to sensory drive (Endler, 1992).

Beyond mating

In many animals, the social domain stretches far beyond mating and can include brood care, parental care, pair bonding and various types of year-round sociality. However, many species with extended forms of sociality show significant seasonality in these tendencies. Seasonality of social behaviours has been shown to coincide with size differences in AVP/OT neural nodes. These nodes can be substantially enlarged in songbirds during mating season, for instance (e.g. Goodson &

Thompson, 2010). The seasonality of these differences is probably related to gonadotropin-releasing hormone (GnRH) which regulates sex-steroid production while sex-steroids influence AVP/OT expression rates. GnRH production itself, is regulated by stress related signals which can exert inhibitory effects on different steps in the route leading from GnRH to sex-steroid production (Viau, 2002). To release AVP/OT function from its seasonal limitations and allow more extensive social interaction to occur likely takes a combination of environmental factors including the social milieu, and neuromodulatory adaptations (e.g. Lema, 2006). The former are probably strongly related to food availability and social factors influencing sex-steroid production and stress-related corticosteroid production. The latter likely include duplication events of neuroendocrine nodes, and of neuropeptides and co-evolving peripheric- and CNS receptors (Ocampo Daza et al., 2012).

Conclusion

Since their original discovery, mirror neurons were hypothesised to be vital to human social cognition. However, there is strong evidence to suggest that mirror neuron functional units, are a consequence of adaptations that occurred early in the bilaterian lineage. These adaptations involve genetic changes linked to establishment of the anterior-posterior body-axis, as well as to mechanisms guiding highly patterned neural development within the bilaterally symmetric body. Besides generating the rough lay-out of an early CNS that's quite similar in basic architecture throughout the bilaterian lineage, this patterning mechanism opened up neural possibilities to gain more elaborate cognitions of own motor-capacities and correlated physical dimensions. This bilaterian central nervous system constituted a proto-mirror system: a developmentally plastic system, which greatly extended the ability of procedural learning of more complex movement patterns. The social function of the mirror system likely arose as a consequence of adaptations to neuromodulators, especially vasopressin/oxytocin -like peptides and their receptors. For instance: adaptations influencing the way in which hormonally directed intra- and extracellular $Ca2+$ oscillations, can variably alter neural excitability of different sensory organs and neural pathways. Adaptations to neuromodulatory functions which may have been prerequisite for the close body-to-body manoeuvring required by internal fertilisation, a mode of reproduction which also seems to be an early bilaterian adaptation. Evidence suggests this adaptation exploited mechanisms for chemotaxis, already used for directing movement towards or away from chemical gradients. These mechanisms for chemotaxis probably served a pre-social function, that is, detecting chemical signals of conspecifics to heighten success rates of external fertilisation. Key to the mechanisms of chemotaxis, seems to be the apparently appetitive directing of motion, towards or away from a neurochemical oscillator representing an environmental chemical source. Vasopressin and oxytocin are known to influence oscillatory activity of mechanosensory neurons. It's therefore conceivable, that the social function of mirror neurons arose as a consequence of this principle of motor-direction towards an oscillatory neural node, being implemented in mechanosensory space. This new involvement of vasopressin in mechanosensory neuromodulation, might have generated the ability to match motor-patterns to oscillatory differentials of second messengers, such as $Ca2+$. Differentials reflecting mechanosensory patterns that are imposed by external (conspecific) movement stimulating mechanosensory receptors. This pattern-matching, facilitating close body-to-body interaction with conspecifics, seems to require deep or detailed sensory-to-motor, perception-to-action processing of relatively elaborate patterns of neural stimulation.

Considering internal fertilisation, and considering the apparent appetitive function of the nematode neural circuitries hypothesised to have MN qualities in chapter II, MN can facilitate some degree of affective synchronisation in many -if not most- bilaterian animals. This implies that there can be an affective proxy of intentions and goals (i.e. the highest complexity level of MN decoding), which is intrinsically tied to the lower levels of MN decoding: the details of motor-parameters, and schema level motor-plans. The extend to which MN functionality developmentally yields phenomena such as empathy, seems most heavily dependent upon brain-size and the duration of easy acquisition; how many specific populations of neurons show relatively high levels of developmental plasticity and for how long. The duration of easy acquisition is often bound by sensitive periods (e.g. parental imprinting). When neural capacity and plasticity are not a limiting factor, the ensuing social-cognitive functions clearly depend on the extend to which specific types of social behaviour -and at what intensities- have proven adaptive in the genetic- and cultural history of an animal, or useful/gratifying in its personal history. In evolutionary time as well as during the lifetime of an animal, adaptations in all these domains are likely to correspond to alterations in neuromodulation. Sex-steroid production is intricately linked to the social environment while sex-steroids influence AVP/OT expression directly, this provides a strong feedback on AVP/OT neuromodulation of MN.

A main function of neuromodulation is in designating which parts of neural space can be active and to what degree. AVP/OT neuromodulation seems to allow a deeper or more detailed processing of biologically relevant information. Deeper- or more detailed processing through MN functional units includes a free-flow-resonance mechanism, linking perception to corresponding actions. Such perception-to-action mechanism could involve Ca2+ regulated lowering of activation thresholds for certain sensory channels over others, and electrical coupling of neighbouring neurons, for instance through AVP/OT affecting gap-junction densities and neural thresholds/activity levels. This deeper processing seems to include the inhibition of more basic responses to what is in essence the perception of biological movement. Inhibition of more basic responses seems to affect the predatory response during spider courtship and mating, and escape behaviour like the nematode tendency to recoil at touch. The same MN functionality used for judging social relevance is likely used to discern more basic biological relevance of movements. As such, the depth or detail of processing seems to correlate to the level of MN congruency that can be achieved before a response is mounted. The depth or detail of processing that's possible seems to determine if the response is non-social or social. The depth or detail of processing might also depend on how much neural architecture such as fan-in fan-out networks can be active at any given moment. As discussed in chapter I, in this type of neural architecture patterns can be represented on one side while allowing

neural activity at the other side access to any part of these representations. This can allow for comparison or matching of patterns of neural activity representing information from different modalities. The more representations at the opposite sides of such architecture overlap in time and spatial dimensions, the stronger their simultaneous activation will be. The amount of such coherence between different streams of neural information can correspond to rewarding or punishing properties of stimuli. This seems to be implied for instance, by the well-known dopamine-associated rewarding properties of what essentially seems to be pattern recognition. Neuromodulators can influence the resolution of neural transmission. Thus the level of detail of representations and of neural preparedness, reflected for instance in $Ca2+$ regulated thresholds of different layers of these networks, may differ accordingly. Such differences in detail could have strong effects upon the ability for pattern recognition. When judging patterns from an external modality through a perception-action model-like mechanism, according to commonalities with own-movement-generated patterns, too little detail within the representations of the external modality would yield more false positives, while too much would be detrimental to detecting actual patterns (more false negatives). In many species, the deep or detailed processing of social information seems to be seasonally limited, mostly facilitating reproductive behaviour. When it is in effect, reinforcement or reward seems an inherent consequence to the successful matching of these sensory- and motor patterns. MN functional units also seem likely to be used to judge non-social biological relevance, such as for predator- and prey detection. Deep or relatively detailed pattern-level of processing might not be necessarily required in non-social interaction. Depth and detail of processing seem to correlate to the level of mirror neuron congruency that can be achieved. Accordingly, non-social interaction can be readily achieved through non-congruent mirror neurons, while the more complex an interaction the more congruence the involved mirror neuron functional units should show. Behavioural evidence indicates that mirror neuron functionality is widespread in bilateria, exists in both main clades and is a feature already present in the last common ancestor of this lineage. This suggests the great diversification of bilaterian animals during the Cambrian explosion was sparked by the ability of the bilaterian central nervous system to generate mirror neuron functional units. Thereby yielding the neural architecture containing details of motor-parameters and schema level motor-plans which can function in conspecific recognition, and which can serve to coordinate the simplest forms of social interaction. The way that mirror neuron functional units can guide internal fertilisation may have created substantial positive evolutionary feedback propelling the spread and diversity of bilaterally symmetric animals.

Endler hypothesised that evolutionary feedback through sensory drive would optimise signal to noise ratios (Endler, 1992). As these are in fact ratios of true positives and true negatives to false positives and false negatives, the resolution of neural transmission- and activity patterns could matter a lot in this equation. The cost of false positives and false negatives can differ substantially between different types of information and different settings or contexts. On an evolutionary time scale adaptation to these relative costs would be reflected in the relative fitness of particular resolution trade-offs in and between the different sensory modalities. At the scale of an animal's personal life such adaptations are reflected in the resolutions of different modalities of information an animal experiences and in the propensity of certain types of information to influence different motivational states. Evolution of neuromodulation should probably favour an ability to adjust to these relative costs, through developmental optimisation of the resolution of neural transmission- and activity patterns. Evolution of primate vision for example, seems to have favoured adaptations facilitating high signal to noise ratios through high resolution of this modality. This maximises perception of true positives and true negatives, and minimises false positives and negatives. If signals from such high-resolution external modality are matched to proprioceptive representations in a perception-action model-like mechanisms that influences motivational/affective states, any genetically and environmentally driven differences in development of the resolutions of neural representations could be psychologically and behaviourally relevant. Developmental skew, leading to perception in relatively low resolution of a high-resolution modality for example, would be expected to yield more false positives upon comparison to representations of proprioceptive- or other mechanosensory information within a perception-action model-like motivational mechanism. As such, it would be interesting to see if there exists a correlation between uncorrected short-sightedness and social disorders such as reactive aggression and social anxiety. Especially when found in children, such correlation could imply this visual-to-proprioceptive pattern-matching indeed occurs in visually naïve animals. As with AVP/OT, the relation between MN-functionality and the different valences of social behaviour is not clear-cut: an MN capacity in itself is not more likely to facilitate empathy, than it is to facilitate antipathy.

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