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A consideration of brain networks modulating social behavior☆

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ABSTRACT

A primary goal of the field of behavioral neuroendocrinology is to understand how the brain modulates complex behavior. Over the last 20 years we have proposed various brain networks to explain behavioral regulation, however, the parameters by which these networks are identified are often ill-defined and reflect our personal scientific biases based on our area of expertise. In this perspective article, I question our characterization of brain networks underlying behavior and their utility. Using the Social Behavior Network as a primary example, I outline issues with brain networks commonly discussed in the field of behavioral neuroendocrinology, argue that we reconsider how we identify brain networks underlying behavior, and urge the future use of analytical tools developed by the field of Network Neuroscience. With modern statistical/mathematical tools and state of the art technology for brain imaging, we can strive to minimize our bias and generate brain networks that may more accurately reflect how the brain produces behavior.

"Across vertebrates there is a network of interconnected structures in the basal forebrain and midbrain that is fundamental for numerous social behaviors" – *Myself*, in almost every talk I have ever given. It's like a mantra, a canned line that I parrot and don't give much thought to. If you are in the social behavioral neuroendocrinology community, you have likely spoken, read, and/or written similar words in reference to the social behavior network (SBN), originally conceived in 1999 for mammals ((Newman, 1999); 1058 citations, Google Scholar, 01/2022) and expanded to all vertebrate classes in 2005 ((Goodson, 2005); 672 citations, Google Scholar, 01/2022). The idea of the SBN, a network in the brain that underlies social behaviors, is pervasive in our field, and we see new "core networks" and "core circuits" emerge in the literature every few years. Indeed, in addition to the SBN, we now have the Social Decision Making Network (SDMN; (O'Connell and Hofmann, 2011)), the Core Aggression Circuit (Lischinsky and Lin, 2020), the Social Salience Neural Network (Johnson et al., 2017), a neural circuit model of pair bonding (Walum and Young, 2018), and the Socio-Spatial Memory Neural Circuit (Ophir, 2017). Recently, I have been wondering what the criteria are for networks and generally what the proposed functions are of networks and circuits in the brain. The term 'network' is broadly used in our field and others. What do we really mean when we label groups of brain regions as a network? And what value do we gain from having several types of social behavior networks? This perspective piece is not intended to denigrate the work of others, but to call into question what we are referring to when we label groups of brain regions as *X* Network. I will use the SBN as a central example for considering unresolved issues with behavior networks in the brain.

1. Origins of the social behavior network

1.1. Selection criteria for the SBN

In the seminal 1999 paper "The medial extended amygdala in male reproductive behavior: A node in the mammalian social behavior network," Newman first reviews the evidence for functionally distinct circuits within the medial extended amygdala before introducing the novel framework of the SBN. It is worth noting that the SBN was born out of a paper that was primarily about male mating behavior in rodents. Newman presented data from several rodent studies that demonstrated overlap in brain regions in the involvement of a variety of discrete types of reproductive behavior, including mating, parental behavior, and territorial marking. Challenging the traditional notion that specific behaviors were modulated by distinct neuroanatomical units in the brain, Newman proposed the idea that there is a group of brain regions that collectively regulate all social behaviors. This group included: nuclear groups within the medial extended amygdala (i.e., medial amygdala, MeA; bed nucleus of the stria terminalis, BNST), the medial preoptic area (MPOA), the lateral septum (LS), the ventromedial hypothalamus (VMH), the anterior hypothalamus (AH), and the midbrain periaqueductal gray (PAG). These regions were selected based on research

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available at the time that showed they were involved in various types of male and female social behaviors.

To provide more commonality among the chosen SBN brain regions, Newman proposed three criteria for inclusion in the network. "Each is reciprocally interconnected with all of the others, all are populated with neurons that contain gonadal hormone receptors, and each of these areas has been identified as an important site of regulation or activation in more than one social behavior" (Newman, 1999). Regarding reciprocal connectivity among the SBN nodes, 12 papers were cited that were based on 2 studies conducted in Syrian hamsters, 9 studies in rats, and 1 study in cats. These papers had a very heavy focus on identifying anatomical connectivity specifically of steroid-hormone binding neurons, which is not overly surprising given that steroid-mediated reproductive behavior was the focus of Newman's research program. For the gonadal hormone receptor criteria for inclusion in the SBN, 3 papers were cited, each using different methods for labeling steroid receptors, showing the presence of estrogen and/or androgen receptors in all SBN nodes of Mongolian gerbil, Syrian hamster, and Sprague-Dawley rat brains. It is worth noting that there is not exactly a vast array of mammals represented in this sampling. The last criteria, that each brain region in the SBN must be involved in more than one type of social behavior, is supported by citing rodent studies from 27 papers, although there are 40 papers total cited and discussed throughout Newman's paper that support this third criteria. Today, it is no longer surprising that brain regions are functionally multi-faceted and contribute to a variety of cognitive and behavioral processes.

1.2. Overarching hypothesis of the SBN and the expansion to the vertebrate SBN

What is the purpose of the SBN? Generally, the goal was to steer away from thinking of behavior as the result of an "on" or "off" state in particular brain regions. Rather, inspired by colleagues in cognitive neuroscience (see (Mesulam, 1990)), Newman proposed that complex social behavior is an emergent property of distinct patterns of activity across all nodes within the SBN. Thus, distinct patterns of activity should underlie distinct types of social behavior. This conceptualization can be visualized in a hypothetical representation of a topographic map displaying differences in neural activity across the SBN nodes in the contexts of male aggression and male sexual behavior (Fig. 1, reprinted by permission from Elsevier). "Although this model is in some ways very simplified (e.g., each area may have distinct neuronal populations with different response profiles), the idea is nonetheless compelling and supported by a good body of data," – Goodson (2005).

The SBN was expanded and promoted by Goodson in 2005 in his paper "The vertebrate social behavior network: Evolutionary themes and variations." In this Frank Beach Award paper, Goodson discusses data that demonstrate that the nodes in the mammalian SBN have homologies in most vertebrate classes. Homologous regions were identified for birds, bony fish, and reptiles; such regions were identified for amphibians except for a homology to the midbrain PAG (Goodson, 2005). Goodson cited data for midshipman fish (Bass et al., 2000; Goodson and Bass, 2002; Goodson et al., 2003; Forlano et al., 2005) and Japanese quail (Watson and Adkins-Regan, 1989; Balthazart et al., 1994; Aste et al., 1998) showing that the SBN in these 2 species fits *all* 3 criteria for the SBN nodes according to Newman, and that several other avian species (e.g., zebra finch, pigeon, starling, gray partridge, domestic chicken, European starling) as well as the gulf toadfish and oyster toadfish meet 1 or 2 of the 3 criteria. Despite a lack of data demonstrating that estrildid finches meet all 3 criteria for the SBN, Goodson used Newman's framework of considering patterns of neural activity across the SBN to examine how immediate early gene (IEG) responses to exposure to a same-sex conspecific exhibit differential SBN "activation" not in relation to different social contexts, but rather in relation to species differences in group size (territorial vs. gregarious/colonial finches).

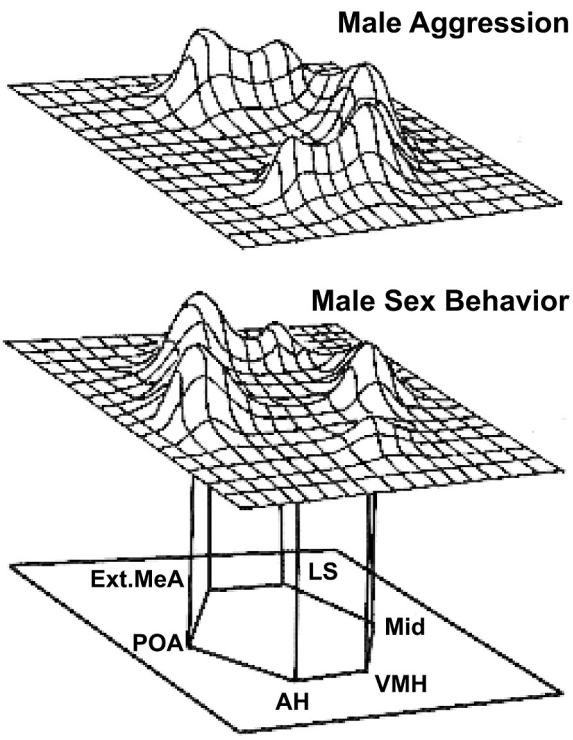

Fig. 1. Patterns of activity across the social behavior network.
Figure and caption reprinted by permission from Elsevier: Hormones and Behavior. The vertebrate social behavior network: Evolutionary themes and variations by James L. Goodson. Copyright 2005.
The social behavior network as originally suggested for mammals (schematics modified from Newman, 1999). The network is comprised of six nodes—the extended medial amygdala (i.e., the medial amygdala and the medial bed nucleus of stria terminalis), the lateral septum (LS), the preoptic area (POA), the anterior hypothalamus (AH), the ventromedial hypothalamus (VMH), and various areas of the midbrain, including the periaqueductal gray. Each of the nodes binds sex steroid hormones and has been implicated in the control of multiple forms of social behavior. Newman (1999) proposes that this network does not contain segregated, linear systems for each kind of behavior. Rather, as shown in these schematic representations of immediate early gene data, each behavioral context is associated with a distinct pattern of activation across the nodes.

An additional feature of the SBN that Goodson promoted was the inclusion of peptidergic neurons and neuropeptide receptors. To quote from Goodson (2005): "While the network described above appears to be fundamental to the expression of social behavior in all vertebrate species, it must also express functionally labile features that underlie phenotypic variation in behavior." "Ongoing work suggests that these species-specific network responses are related to divergence in peptidergic neuron activity and species differences in neuropeptide receptor distributions. That is, peptidergic variables may coordinate the species differences in network response." "More so than any other class of neurochemicals, these peptides [vasotocin family of neuropeptides] have been found to be axes of behavioral plasticity and social diversity, and the features of these systems are associated with seasonal variation, sex differences, and species divergence in behavior. Despite these aspects of variation, the locations of AVT/AVP neurons and fibers have been strongly conserved during vertebrate evolution, and the AVT/AVP system is an integral component of the social behavior network in all vertebrate groups."

Whether intentional or not, together, Newman and Goodson provided a guidebook for which brain regions one should examine when inquiring about neural mechanisms underlying social behavior for roughly the past 20 years. Although the concept of a social behavior network may have been intended to serve only as a starting framework,

and to not be taken literally, I would argue that many researchers in our field do indeed view the SBN as more than just a framework, and instead view it as a concrete fixture, so to speak, in the brain.

2. Issues with the social behavior network

In 2005 when the SBN picked up substantial momentum in the behavioral neuroendocrinology community, the SBN, developed from 3 criteria, was widely applied to numerous vertebrates despite *all 3 criteria* only having been shown to be met in Mongolian gerbils, Syrian hamsters, Sprague-Dawley rats, Japanese quail, and midshipman fish. Since 2005, it is likely that one could determine from an extensive literature search whether other species meet all 3 criteria, particularly for commonly used species for steroid-mediated behavioral or tract-tracing studies, such as zebra finches and mice. Indeed, O'Connell and Hofmann conducted an exhaustive literature search examining the criteria in 88 species in 2011 (O'Connell and Hofmann, 2011). Yet, given that in 2005 we as a community accepted only 5 species meeting the SBN criteria as evidence that the SBN is strongly evolutionarily conserved and widespread across all vertebrates, I cannot help but wonder whether we care about the original criteria that formed the SBN. Or perhaps we simply did not pay attention. In full disclosure, I did not pay attention… until now.

I can only presume that although Goodson restated the basic criteria for inclusion in the SBN proposed by Newman, Goodson must not have been overly compelled to strictly adhere to the criteria given that he only provided data for 2 species outside mammals (1 fish, 1 bird) that met all the criteria, but then proposed that the SBN exists in all vertebrates. This raises the question: Do the 3 original criteria matter? If yes, then we have not followed them very closely, which one could argue is not very scientifically rigorous. If no, then does the core network fall apart since other brain regions could, and maybe should, be included?

That the SBN may be limited in scope is not a novel idea. In 2011, O'Connell and Hofmann proposed that all vertebrate animals regulate complex, adaptive behavior via interactions between the SBN and the mesolimbic reward system, and that these circuits together form a larger Social Decision Making Network (SDMN; O'Connell and Hofmann, 2011). Similar to the SBN, the concept of the SDMN has been extremely influential in the field of behavioral neuroendocrinology ((O'Connell, 2011 #1388), 749 citations; (O'Connell and Hofmann, 2012), 478 citations, Google Scholar, 01/2022). The SDMN was built upon the SBN, an expansion of which I think was a great idea, particularly since brain regions critical for social behavior were likely unintentionally excluded in the original conception of the SBN. However, where does one stop when it comes to adding more brain regions to a network? And should a social brain network be built with the SBN as the foundation? What if it is the wrong, or an incomplete, foundation? Below, I discuss structural issues with the foundation in which many of us have built our academic houses upon.

2.1. Original intentions for reproductive behavior, but common usage for all social behaviors

Our biases and academic cultures influence our experimental design, our interpretation of results, as well as the literature we cite. I have always cited papers discussing the SBN in reference to neural mechanisms underlying social behavior because I was raised in that ilk. I would argue that Newman had a sampling bias for steroid hormone papers, understandably given her focus on reproductive behavior. I mention this because a steroid-focused lens may be too narrow for something as grand as a network in the brain that modulates *all* social behaviors. Because of Newman's focus on reproductive social behaviors, it is justifiable to have steroid receptor expression as a criterion for a brain region to be included in the network. Yet, since 2005, we have considered the SBN as a core network for *all* social behavior, reproductive and non-reproductive. Importantly, social behavior can occur in the absence of gonadal hormones. For example, aggressive behavior and social dominance is maintained in male cichlids even after castration (Soma et al., 1996). Steroidogenic factor-1 knockout mice (i.e., born without gonads or adrenal glands, but receive adrenal implants shortly after birth to survive) are not exposed to gonadal sex steroids, yet exhibit more aggression as adults compared to intact controls (Grgurevic et al., 2008). Similarly, male and female mice gonadectomized before or after puberty display parental behaviors toward pups, although less-so than intact controls (Kercmar et al., 2014). Furthermore, while gonadectomy in canines decreases aggressive behavior and mounting, these behaviors are still exhibited, and territorial marking is not impacted (Palestrini et al., 2021). There are numerous such examples showing that the presence of gonadal steroids often facilitates optimal performance of social behavior, but there are many social behaviors that remain present even in the absence of gonadal steroids. An important caveat is that the absence of gonadal steroids does not necessarily indicate that there is an absence of neurosteroids. For example, in rats, while gonadectomy completely eliminates testosterone presence in the blood, it decreases, but does not eliminate, testosterone levels in the brain (Tobiansky et al., 2018). Research using estrogen knockout mouse models also address the dependency of behavior on neurosteroids. For example, estrogen receptor alpha knockout male mice exhibit significantly decreased levels of aggression, but are still capable of being aggressive, whereas estrogen receptor beta knockout male mice exhibit higher degrees of aggression compared to wild-type mice (Hill and Boon, 2009). Therefore, given that there are social behaviors that are not reliant upon steroids, is it justifiable to have a steroid receptor criterion for a behavior network that modulates *all* types of social behavior? Goodson viewed the SBN regions as the "core" network nodes for social behavior. However, if the presence of steroid receptors is too stringent a criterion, are there brain regions that we have overlooked that should be included in this core?

2.2. Potential for unintentional exclusion of qualified brain regions

In addition to questioning whether the presence of steroid receptors should be a requirement for inclusion in the SBN, there is another issue with the brain regions identified as meeting the steroid receptor qualification. In 1999 when Newman published the SBN framework, works cited demonstrating that estrogen and/or androgen receptors are present in the chosen SBN nodes of Mongolian gerbils, Syrian hamsters, and Sprague-Dawley rats were based on technology and knowledge that are simply different from what we now possess and understand. The 3 papers Newman cited were published in 1985, 1990, and 1992. The paper in Sprague-Dawley rats used in situ hybridization to identify locations of estrogen and androgen receptor mRNA, and developed riboprobes complimentary to the mRNA encoding the entire steroid binding domain of the rat estrogen receptor and about 20 base pairs of the coding region for the DNA binding domain for the rat androgen receptor (Simerly et al., 1990). Notably, the presence of mRNA does not guarantee translation into functional protein, and thus in situ hybridization cannot, with full accuracy, provide information on the location of steroid receptors. The paper in Syrian hamsters utilized immunocytochemistry to label estrogen and androgen receptor immunoreactivity in neuronal cell nuclei and used a commercial antibody (H222) for labeling estrogen receptors as well as a custom antibody directed against a synthetic peptide corresponding to the first 21 amino acids of the rat androgen receptor (PG-21 polyclonal rabbit antibody) (Wood and Newman, 1995). Visualization of steroid receptor presence was examined in neuronal cell *nuclei*. This is an important caveat because with advancements in technology, we have since learned that steroid receptors can also be present in cell membranes in addition to the nucleus of cells (Trevino and Gorelick, 2021). Thus, immunocytochemical labeling of steroid receptors also cannot provide a complete picture of distributions of steroid receptors. Furthermore, the Wood and Newman (1995) paper also does not mention steroid receptor presence in the midbrain PAG or the AH (2 of the 6 SBN nodes). The paper cites 3 previous studies

labeling steroid receptors in Syrian hamsters, however, none of these papers demonstrate the presence of androgen and/or estrogen receptors in the PAG (Li et al., 1993; Wood and Newman, 1993a, 1993b), although one paper did show the presence of estrogen receptors in the AH of female Syrian hamsters (Li et al., 1993; Wood and Newman, 1993a, 1993b). Unfortunately, this makes it questionable whether Syrian hamsters fully met the 3 criteria for the SBN at the time the network was conceived. The third paper cited in Newman, 1999 used dry-mount steroid autoradiography to characterize the distributions of androgen and estrogen receptors in Mongolian gerbils (Commins and Yahr, 1985). Of the three methods for labeling estrogen and androgen receptors mentioned above, autoradiography may provide the most accurate information about where in the brain steroids act, however, autoradiography lacks cellular resolution, and differentiation between nuclear and membrane binding sites would be unclear. Lastly, we now know that there are several steroid receptor subtypes, such as estrogen receptor beta, estrogen receptor alpha, g protein-coupled estrogen receptor 1 (also called GPER1 and GPR30), and androgen receptor. Together, the 3 papers Newman cited for determination of a criterion for SBN brain region inclusion beg the question, "Are there other brain regions that contain steroid receptors that we missed?"

Another criterion for brain region inclusion in the SBN is anatomical connectivity between all nodes. Although tract tracing methods have been available for decades, there have been significant advancements in high-resolution tract tracing methods for neuroanatomical mapping since the 1970s–90s that allow for greater sensitivity of detecting axonal connections (Lanciego and Wouterlood, 2020). 21st century tracing and imaging methods in macaques revealed previously unreported axonal connections, and an estimated 36% of connections identified in the cortex were novel findings (Markov et al., 2014). Similarly, viral tracing methods have been shown to be not only more efficient, but more specific than traditionally used biotinylated dextran amin (BDA) tracers, and viral tracing has revealed novel projection targets in the mouse brain (Wang et al., 2014). Furthermore, modern tracing and software has been combined with high-speed two-photon microscopy coupled with automated vibratome sectioning of the entire mouse brain to generate a whole brain connectome for the mouse (Oh et al., 2014). Simply put, we can literally see more in the brain today than we did at the time the SBN was conceived in 1999. With contemporary tracing and imaging methods, would we now find that several other brain regions could also qualify as being part of a reciprocally interconnected network?

2.3. Nonapeptides and social behavior

Should anatomical connectivity be a criterion for inclusion in the SBN? Goodson highlighted the importance of nonapeptides in modulating social behavior and stated that they are an "integral component of the social behavior network" (Goodson, 2005). The nonapeptides, vasopressin and oxytocin (the mammalian forms), are strongly evolutionarily conserved throughout vertebrate history and are produced in similar brain regions across taxa (Moore and Lowry, 1998; Donaldson and Young, 2008; Goodson, 2008). Several of the SBN nodes contain either nonapeptide-producing neurons or nonapeptide receptors. However, nonapeptides exhibit paracrine modulation and do not necessarily require anatomical connections given that peptide can travel in extracellular space to distal sites in the brain (Landgraf and Neumann, 2004; Ludwig and Leng, 2006). As a community, we value the framework that it is not simply brain regions that produce behaviors, but rather specific cell-types acting within brain regions that produce behavior. Nonapeptides are major influencers of various social behaviors. Should their dynamic nature cause us to consider whether anatomical connectivity is necessary for a brain region to be included in a network? This is discussed further in a section below.

2.4. Appropriateness of the SBN nodes across taxa

An original selection of brain regions based off mammalian behavior and social signaling may not be ideal for a taxa-wide comparison despite the observation of homologous brain regions across taxa. As discussed by Hoke (Hoke et al., 2007; Hoke and Pitts, 2012) and Thompson (2020), mammals receive and produce different social signals than species such as fish, frogs, or birds, and thus brain regions selected for mammalian social behavior may not easily generalize across taxa. For example, the primary mode of communication for mammals is olfaction (Lledo et al., 2005). The BST (an SBN node) receives direct axonal projections from the olfactory bulbs in mammals and is well known for playing a role in social behavior and communication (Scalia and Winans, 1975; Newman, 1999; Been and Petrulis, 2010; Lebow and Chen, 2019; Rigney et al., 2019). In Newman's paper in which the SBN was conceived, there is ample discussion about why the BST is important for rodent reproductive behavior because olfactory and vomeronasal transmission is modulated by steroid-sensitive cells in this region (Newman, 1999). That is, quite understandably, a very valid reason to consider the BST as being critical in mammalian (at least, rodent) social behaviors! However, does the importance of the BST in social communication hold true for other taxa? Although birds do exhibit olfactory communication, the primary modes of communication for most avian species are through auditory and visual signaling (Reiner et al., 2005; Steiger et al., 2008; Driver and Balakrishnan, 2021). There are extremely few tract tracing studies examining olfactory bulb neuronal projections in birds, however, a study in pigeons using radioactive anterograde labeling appears to show no projections to the BST, although there are projections to nucleus taenia (presumed homolog of the mammalian subpallial amygdala) (Reiner and Karten, 1985). Although the BST is important for promoting grouping and courtship behaviors in birds (Balthazart et al., 1998; Kelly et al., 2011; Kelly and Goodson, 2013), it may not necessarily be a crucial node for avian sensory signaling in the way that it is mammals. This begs the question, would connections from visual and auditory systems be more appropriate for an avian social network in the brain? Should up- and downstream sensory and motor system connections factor into social brain networks, and if so, can we still accurately achieve generalization of node anatomy and function across taxa? Lastly, even if sensory and motor systems could be made comparable across taxa, it is important to note that homology relationships can be difficult to resolve, and as suggested by O'Connell and Hofmann as well as Goodson and Kingsbury, should be considered as tentative (O'Connell and Hofmann, 2011; Goodson and Kingsbury, 2013).

2.5. Patterns of activity: a lack of cellular resolution

The overarching hypothesis of the SBN is that distinct patterns of activity across nodes underlie distinct social behaviors exhibited in varying contexts. Goodson conceptualized this using IEGs. I have conducted and continue to conduct my fair share of IEG studies. They can be immensely useful, but IEG studies have substantial limitations. IEG studies allow us to visualize neural responses only at a single timepoint within an animal, so a between-subjects design is required to examine differential patterns of activity underlying varying contexts. This, unfortunately, creates noise in datasets. Methods such as catFISH could allow for examining neural responses at two distinct timepoints within an individual, but there are far more than just two social contexts to test the SBN hypothesis within an individual. Furthermore, IEGs such as Fos provide limited information, such that they indicate only that a neuron has responded to something. What that response is (i.e., up or down regulation) and specifically what that response is in relation to (i.e., ranging from a change in odors or temperature, mere presence of a conspecific, unanticipated attention to an experimenter's hand, to detection of piloerection of a conspecific's fur, etc.) remains unknown.

More concerning is that we lack the cellular resolution necessary to

determine if "activated" neurons are the specific neurons that are anatomically connected to other SBN nodes or are the neurons that contain steroid receptors. Studies examining patterns of activity in the SBN thus far present no evidence that the cells activated in the SBN nodes are actually connected to other nodes in the network. With IEG studies, we may essentially be observing activated power lines running parallel to each other that are not even connected. Perhaps this issue could be at least partially resolved by using technology such as whole brain clearing methods (i.e., CLARITY or iDisco) combined with fluorescent tract tracing and fluorescent labeling of IEGs. However, this would not address the issue of what something like Fos expression represents (up or down regulation). Additionally, we can now achieve better cellular resolution with techniques such as spatially resolved transcriptomics, which can identify not only cell types on the basis of gene expression, but also identify the positional context of those cells in tissue (Lein et al., 2017). This method was crowned Method of the Year by Nature Methods in 2020. "Fruit tart is spatial transcriptomics. You know exactly where each piece of fruit is and what is the relationship of each piece of fruit to the other," Bosiljka Tasic, Allen Institute (Marx, 2021). I, personally, love fruit tart. That we now have fruit tarts in neuroscience is *chef's kiss.*.

Lastly, I would argue that there is a lack of a control for testing that the SBN is indeed "the core" of the social brain as suggested by Goodson (2005). Several studies examine how neural responses vary across the SBN between species or treatment groups (Goodson et al., 2005; Maney et al., 2008; Kabelik et al., 2018; Petersen et al., 2021). Yet, one could pick any number of brain regions at random and expose animals to different contexts and see different "patterns" of activity across the brain regions simply because, individually, the distinct brain regions may differentially respond to varying contexts. Observing different "patterns of activity" does not necessarily mean that the interconnected SBN nodes are functioning in a connected manner. Many studies examining patterns of activity within the SBN or SDMN lack specificity controls and do not account for global noise. Furthermore, what does it mean for a group of brain regions to represent a core? Goodson and Newman acknowledged that these brain regions are connected to several other brain regions that are also important for social behavior. So, what is the functional purpose of a core? Does all information need to go through the core? Is it a central processor? Does core simply mean that the select regions will always be involved in two or more social behaviors? If so, what is the justification for generating the number at which a core becomes a core? Or does core just mean that brain regions are evolutionarily conserved, in which case they are just that – evolutionarily conserved (which is quite neat) – but not necessarily a network.

2.6. Am I asking for too much?

After reviewing the literature cited in Newman, 1999 (Newman, 1999) and Goodson, 2005 (Goodson, 2005), I could not help but question whether Newman and Goodson intended for the SBN criteria to be met *within species* or simply *within taxa*. If they intended for the criteria to be met within taxa, then demonstrating anatomical connectivity between all SBN nodes in a midshipman fish, showing there are steroid receptors present in all SBN nodes of a gulf toadfish, and citing research for several fish species that shows that all nodes are involved in multiple social behaviors would be considered sufficient evidence that the SBN is present in fish. However, in our field, do we not frequently argue that a comparative approach is necessary because we *cannot* assume that species have evolved in similar ways? Perhaps I am being too much of a stickler, but if I am going to say a network is present in a species, I think it would be important for that species to meet all the criteria of said network.

Ultimately, all of the nodes in the SBN are undoubtedly involved in multiple social behaviors across taxa. But does that make them a network? What makes something a network?

3. What are networks?

3.1. Definitions

According to the Merriam-Webster Dictionary, there are 5 definitions for the noun, network. "(1) A fabric or structure of cords or wires that cross at regular intervals and are knotted or secured at the crossings. (2) A system of lines or channels resembling a network. (3a) An interconnected or interrelated chain, group, or system. (3b) A system of computers and peripherals that are able to communicate with each other. (4a) A group of radio or television stations linked by wire or radio relay. (4b) A radio or television company that produces programs for broadcast over such a network. (5) A usually informally interconnected group or association of persons" (Merriam-Webster, 2021). Loosely defined, the crux of a network is that it represents elements that are connected. How that connectivity is represented, though, can vary greatly. In the standard dictionary definitions, networks can be connected via structural means (e.g., cords or wires) and non-structural means (e.g., radio relay, association of persons). In the fields of biology, sociology, psychology, anthropology, and medicine, networks among individuals are examined using social network analysis (SNA) in order to understand the relationships and interactions between individual actors (Martinez-Lopez et al., 2009; Makagon et al., 2012; Farine and Whitehead, 2015); such networks are non-structural in nature. In computer science and information technology, networked devices can be connected via wired (structural) or wireless (non-structural) means. Similarly, in neuroscience connectivity in networks can be achieved through both structural and non-structural mechanisms.

Brain networks and nervous system connectivity began to be widely recognized in the 19th century by neuroscientists such as Santiago Ramón y Cajal, who drew painstakingly detailed connections of neurons throughout the brain (Edited by: Fornito et al., 2016). Arguably the most influential neural system in the field of neuroscience – the reward system – was later identified by Olds and Milner in the mid 20th century (Olds and Milner, 1954; Olds, 1956). The examination of networks in the brain has come a long way since the late 19th century and now even has its own field, called Network Neuroscience, spearheaded by Dr. Danielle S. Bassett and Dr. Olaf Sporns (Bassett and Sporns, 2017). The field of behavioral neuroendocrinology stands to benefit greatly from incorporating perspectives and analytical tools from the field of network neuroscience. Petersen and Sporns noted in 2015 that the definition of 'network' is highly variable, and historically, was often not grounded in biology. They proposed the following formal definition for the term 'network:' A network is a set of pairwise relationships between the elements of a system – formally represented as a set of edges that link a set of nodes (Petersen and Sporns, 2015). This definition stems from the method used to analyze and model brain network data – graph theory. Connectivity in the brain represents a network (a graph) of elements and their pairwise interconnections, made up of nodes and edges (Sporns, 2018). Graph theory can be applied to empirical data in numerous ways, but as an oversimplified example relevant to the discussion here, brain nodes may be whole brain regions or individual neurons, while edges may be their connections (structural or functional), which take on differentially weighted values (Sporns, 2018). Neurobiological networks can be analyzed including whole-brain networks, neuronal networks, synaptic networks, and, at a molecular level, gene and protein networks (Petersen and Sporns, 2015).

Large-scale brain networks are typically represented as being structurally or functionally (i.e., non-structurally) connected. Functional correlation networks are inferred from statistical dependencies between brain function in different brain regions (Petersen and Sporns, 2015; Liegeois et al., 2020). Examination of functional connectivity and identification of functional networks is commonly observed in human research utilizing fMRI (Sung et al., 2018), but also extends to non-human animal research and has recently been extended to prairie voles (Lopez-Gutierrez et al., 2021). Conversely, structural networks are

inferred from anatomical connectivity between brain regions (Petersen and Sporns, 2015; Liegeois et al., 2020). With the beauty of interdisciplinary collaborations, perspectives from mathematics and physics have been incorporated with those of neuroscience to elucidate properties that characterize different structural brain networks. This is shown in Fig. 2 (reprinted with permission from (Lynn, 2019 #2145)), which illustrates the process by which brain networks are identified, beginning with data of physical connections between neurons or brain regions, proceeded by analytical processing to determine degrees of connectivity, and resulting in 5 basic network types, which differentially aid in integration/segregation of information and communication efficiency.

An obvious strength of this approach for network identification is the consideration of data from whole brains using technology such as diffusion tensor imaging and secondary processing that statistically subjects all data to quality control, normalization, and artifact and noise elimination/reduction (Bassett and Sporns, 2017; Lynn and Bassett, 2019). This process can be replicated for non-human animals with 21st century technology that allows for visualization of whole-brain structural connectivity (Oh et al., 2014; Betzel et al., 2018; Cook et al., 2019; Scheffer et al., 2020).

Notably, as can be seen in Fig. 2b, all nodes in a brain network do not necessarily have to *all be interconnected*, as is the criteria for inclusion in the SBN. Is there something unique about a group of brain regions that are all heavily interconnected (setting aside the real possibility that the SBN unintentionally excludes other brain regions that are also interconnected)? The SBN, as originally conceived, shares resemblances with the community structure and hub structure network types. According to Lynn and Bassett, "the large-scale structures of brain networks in several mammalian species have connections organized such that they naturally partition into densely connected communities separated by sparse inter-community connectivity. Moreover, these clusters of high connectivity closely resemble postulated anatomical subdivisions. It has therefore been argued that the so-called community structure of brain networks segregates the brain into subnetworks with specific cognitive functions" (Lynn and Bassett, 2019). This framework resembles Newman and Goodson's idea about the broad purpose of the SBN; it steers away from labeled-line neural modulation of behavior and considers more dynamic and complex mechanisms underlying behavior. Identification of community structure network types could help address the issue mentioned above about having a control to test whether the SBN does indeed serve as a collection of core nodes for all social behaviors. Theoretically, upon identifying several community structure brain networks, one could investigate a network that resembles the current SBN and examine its functionality in comparison to other community structure networks. If a core social behavior network exists, we should observe significantly different functional responses between different networks in social vs. nonsocial contexts. Furthermore, within a social behavior network, activity patterns may vary within the network. Having the ability to look both across and within brain networks would be quite compelling. Additionally, the interconnectivity of the SBN resembles the hub structure network type, which consists of a densely interconnected structural core that minimizes path length and aids in integration of information across a network (Lynn and Bassett, 2019). From this perspective, one could question whether the SBN serves as a core with an ultimate purpose of facilitating efficiency and high processing speeds for the processing of social information. Social behavior is incredibly dynamic and rapidly shifts based on the internal and external context of an animal and its environment. Perhaps the SBN does not necessarily directly modulate all social behaviors, but rather serves as a critical central processing center (i.e., a hub) that then sends instructions to other brain areas and/or networks that eventually lead to the execution of a suite of context-appropriate behaviors. Such a purpose of a network could reconcile

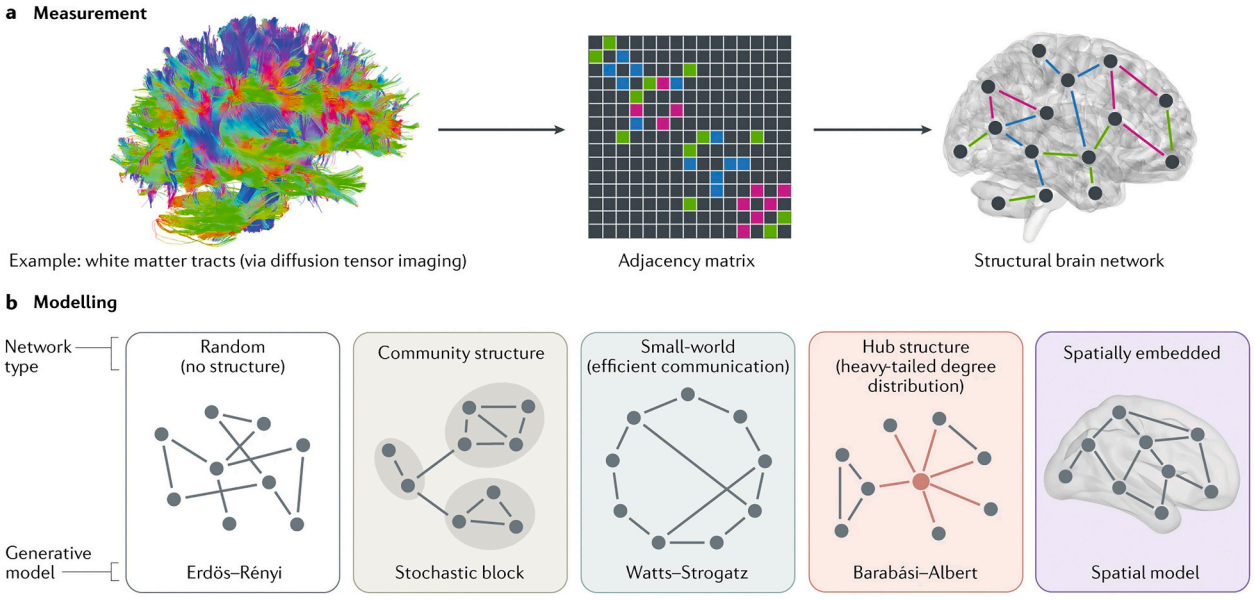

Fig. 2. Measuring and modelling brain network structure.
Figure and caption reprinted by permission from Dr. Danielle S. Bassett and Springer Nature: Springer Nature Switzerland AG, Nature Reviews Physics. The physics of brain network structure, function and control by Christopher W. Lynn & Danielle S. Bassett. Copyright 2019.
a. The measurement of brain network structure begins with data specifying the physical connections between neurons or brain regions, such as white matter tracts measured via diffusion tensor imaging (left panel). The data are discretized into non-overlapping gray matter volumes representing distinct nodes. From this discretization, an adjacency matrix A is constructed, where A_{ij} encodes the connection strength between nodes i and j (center panel; colours represent connection strengths). This adjacency matrix, in turn, defines a structural brain network (right panel) constructed from the original measurements of physical connectivity. b. Architectural features of structural brain networks can be captured using generative network models. The simplest such model is the Erdös–Rényi model, which has entirely random structure. Networks with modular structure, divided into communities with dense connectivity, are constructed using the stochastic block model. Small-world networks, which balance efficient communication and high clustering, are generated using the Watts–Strogatz model. Networks with hub structure, characterized by a heavy-tailed degree distribution, are typically constructed using a preferential attachment model such as the Barabási–Albert model. Spatially embedded networks, with connectivity constrained to exist within a physical volume, are generated through the use of spatial network models.

Newman and Goodson's statements that there are other brain regions not in the SBN that are also important for social behavior. A whole-brain visualization of network connectivity could elucidate whether the SBN nodes represent a central hub involved in basic social processing that receives inputs from sensory systems and sends information to downstream targets, including motor systems.

Yet, simply because we can draw comparisons of statistically generated network types to the SBN does not mean that we should. In fact, I would argue that instead of trying to fit a network idea conceived in 1999 to current, state of the art methods for identifying networks, instead we should reevaluate our existing SBN using said novel methods. Perhaps we should consider starting anew and let whole-brain data identify a brain network that modulates all social behaviors. Then we can proceed to testing the utility of that network to understand dynamic mechanistic shifts that underlie distinct types of social behavior.

3.2. Functional vs. anatomical connectivity

Based on the definitions above, a network does not necessarily need to have physical, structural connections. Connectivity in *structural* brain networks is based on the physical measures of neural wiring between brain regions/nuclei, whereas connectivity in *functional* brain networks is based on the similarity in dynamics between brain regions/nuclei (Bullmore and Sporns, 2009). In neuroscience, functional connectivity is inferred from statistical relationships between activity in distinct brain regions. Similarly, neuromodulators/hormones influence brain function, but do not necessarily require anatomical connectivity in order to be functional, so to speak. In the field of behavioral neuroendocrinology, we care a great deal about hormones and specific cell types, which can be difficult to place within the framework of brain networks. As discussed earlier, the nonapeptides are key modulators of various social behaviors and can act on brain regions in the absence of anatomical connections due to their ability to communicate via paracrine signaling. Given this mode of communication, if we are considering whether or not there is a (or several?) core social behavior network(s) in the brain, should we even apply restrictions such as anatomical connectivity when we know that key neuromodulators of social behavior do not always require synaptic transmission?

3.3. Can we combine network types?

How should we define parameters for a behavior network? From the field of network neuroscience, it seems that it is largely the data that identifies the network. Realistically, there is still human bias in such an approach given that humans collected the data and generated the mathematical models. Regardless, the network neuroscience approach to identifying brain networks is far less biased than how the SBN was conceived. However, an anatomical connectivity requirement alone may not be appropriate for identifying a brain network that modulates social behavior.

Network neuroscientists acknowledge that structural and functional networks may be inseparable given that their overall contributions to neural function are linked and that they share graph-theoretic features (Bullmore and Sporns, 2009; Meunier et al., 2010; Avena-Koenigsberger et al., 2015). Further, as defined by Petersen and Sporns (2015), there are networks at numerous neurobiological scales. Can we combine networks across scales? Is it possible to overlay molecular binding and anatomical mapping? It appears these are often considered as different types of networks and are therefore mathematically/statically processed separately. But could they be combined? Unfortunately, I am simply not the right person to make such mathematical/statistical calls. I can, quite frankly, push water uphill more effectively than I can wrap my head around the math and statistics required to generate and understand brain networks. Regardless of my ineptitude, these are important questions for us to consider as we move forward as a field and hopefully develop collaborations that will allow us to identify brain networks underlying social behavior in a less biased manner.

4. Networks and circuits in the field of behavioral neuroendocrinology

Since Newman's (1999) paper presenting the SBN, our field has proposed various brain networks and complex circuitry that underlie behavior. For example, the SBN (Newman, 1999; Goodson, 2005), the SDMN (O'Connell and Hofmann, 2011), and the Core Aggression Circuit (Lischinsky and Lin, 2020) propose collections of brain regions that are anatomically connected and modulate conserved behavioral and cognitive functions across taxa. Notably, the SDMN and Core Aggression Circuit were arguably "built" from the SBN as a foundation. Additionally, there is the Social Salience Neural Network, which is proposed as a network of interconnected brain nuclei that encode valence and incentive salience of sociosensory cues (Johnson et al., 2017) and the Socio-Spatial Memory Neural Circuit, which proposes to potentially integrate social and spatial information to influence mating decisions (Ophir, 2017). None of these networks or circuits were identified through statistical or mathematical inference. As an aside, it is worth noting that within the field of neuroscience, there is also no agreed upon understanding of what a circuit is compared to a network. All of these networks/circuits mentioned here have overlapping nodes, which, if anything, speaks to the amazing functional conservation of several fore- and mid-brain regions across vertebrates. However, what do we gain from testing multiple individual networks/circuits in the brain, all of which have overlap, that regulate [sometimes] different aspects of social behavior? Does this enhance our understanding of how the brain generates context-appropriate behavior in a dynamic environment?

As discussed in conversations with Hans Hofmann (co-conceptualizer of the SDMN), perhaps my issues with brain networks within the field of behavioral neuroendocrinology actually stem from a far bigger problem – the problem that neuroscience lacks an overarching theory that clearly lays out principles for how the brain perceives our surroundings and generates appropriate responses (pers. comm.). The consequences of a lack of a comprehensive theory of the brain have been discussed by others. For example, Krakauer et al. argue that while advancements in technology allow us to now probe the brain by examination and/or perturbation of not just a neuron, but now groups of neurons, these technical advancements do not fundamentally change how we understand the link between the brain and behavior (Krakauer et al., 2017). "Without well-characterized behavior and theories that can act as a constraint on circuit-level inferences, brains and behavior will be like two ships passing in the night," Krakauer et al. (2017). I do think that our field, in particular, is well-poised to contribute toward the conceptualization of a comprehensive theory of neural function given that we excel at examining behavior.

I want to be clear that identifying neural circuits underlying behavior is incredibly valuable, and examining complex circuitry is likely our best chance at understanding how the brain produces behavior. However, I fear we may be too quick to apply labels. Is there a danger in attempting to fit brain function to our preconceived notions of how the brain should work and subjecting brain function to biases like the human preference for categories, the desire to package things nicely in a tidy box with a bow?

5. Considerations for the future

Scientists have a tendency to be swept off their feet by novelty and to run away with new, flashy technology and ideas before they have been thoroughly tested and vetted. From one perspective, this is how progress is often made. However, it is crucial that we keep ourselves in check; if we stare down too narrow a road, we may miss important discoveries that are sitting in the periphery. In 2005, the SBN was a novel and shiny new framework that revolutionized the way we think about how the brain modulates social behavior. Unfortunately, we have yet to

effectively test whether the network functions in the manner for which it was hypothesized. Newman proposed the SBN to be used as a framework, but what if we have unintentionally blinded ourselves to considering other viable brain regions, neurochemicals, or networks because we have focused so intently on SBN (and now SDMN) nodes that may not have been selected in the most rigorous fashion? Furthermore, as comparative scientists, are we doing ourselves a disservice and discounting independent evolution and natural variation by continually saying "a network" is conserved, when, in reality, some brain regions and basic, broad social functions are conserved?

Together, Newman and Goodson identified evolutionary conservation in brain regions involved in social behavior. Whether this collection of brain regions represents a core social network in the brain, for me, remains to be seen. Because of that, in my own research, I will continue to examine these brain regions given the wealth of data showing they are important in behaviors of interest to my lab. However, I will refrain from referring to them as a network, and I will strive to examine other brain regions that may be equally or more important to numerous social behaviors than those included in the SBN. We as scientists are supposed to continually question. I think it is time that we thoroughly question how we identify social brain networks and test their utility.

It has been almost a quarter of a century since the conception of the SBN and initial consideration of brain networks that modulate social behavior. With advancements in technology, imaging, and analytical tools, I argue that the SBN and SDMN need, at the very least, considerable updating. Additionally, I think we should exhibit caution when labeling collections of brain regions as networks if we have not thoroughly examined and tested their connectivity (anatomical or functional), specificity, and relationships to other brain regions and networks. We should strive toward a reduction in bias in how we select and define brain networks. Many other fields and areas within neuroscience use advanced mathematical and computational methods for inferring networks. I, like many, am woefully ignorant about such methods, but our field desperately needs a greater influx of advanced analytical tools.

As we move our field forward, we need to reevaluate what we gain from the existing framework of brain networks for social behavior, and perhaps more importantly, how we apply the framework. Although the SBN, and later SDMN, have allowed researchers to pose and test specific hypotheses about behavior within and across species, it seems we currently have a tendency and desire to identify new brain networks that modulate specific behaviors. This raises the question as to whether we think the brain has individual sub-routines for every behavior. Are there really distinct networks for aggression, pairbonding, decision making, and processing social saliency… on top of a network for general social behavior? Or is our current application of the 'networks for social behavior' framework steering away from the idea of a broad, multipurpose network and rather we are simply identifying individual circuits that modulate specific behaviors in a social context-depending manner? We need to better conceptualize the purpose of a brain network and determine sophisticated ways of testing the function(s) and validity of a potential global social behavior network in the brain. Perhaps networks may serve as relay centers that integrate context, weigh information based on internal states, and then send messages to downstream circuits that are responsible for the execution of specific behaviors. With advancements in technology, we can now take an unbiased whole brain approach, use mathematical and computational tools for identifying networks, and then apply techniques such as spatially resolved transcriptomics to determine how specific cell types, and their locations within a network, contribute toward the functioning of a global network in the brain that is involved in all types of social behavior. Perhaps at that point, we can use neuromanipulative tools to perturb the network and examine outcomes. With increasingly advanced tools like neuropixel, in an animal large enough (i.e., a rat, which has a substantial brain surface area capable of holding hardware), we can simultaneously record in real-time from multiple locations in the brain, potentially using multiple probes to record from all nodes in a network while an animal is exposed to varying social contexts. Importantly, if we identify such a global social network in the brain, chances are we will have done so just in one species to begin with. It is crucial that the same approaches to determine said network are used in other species and taxa and that we remain open to the possibility that social brain networks across taxa may look quite different given the broad range of environmental pressures distinct species have evolved under and the multitude of modes of communication (i.e., sensory input) and behavioral expression (i.e., motor output) observed across the animal kingdom. Approaches such as this will require collaborative efforts but have the potential to increase our understanding of how the brain processes information, ultimately leading to an organism that is capable of exhibiting behavior flexible enough to adapt to an ever-changing environment.

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I can't help but wonder what Jim Goodson (my advisor for 8 years as an undergrad and graduate student) would think of me questioning a framework that he steadfastly promoted, and arguably, made famous (okay, low-key famous). One of the greatest things I learned from Jim, though, was to not be afraid to go against what is considered mainstream and that it is okay to hold unpopular opinions – simple lessons that I will forever be grateful for.

References

Aste, N., Balthazart, J., Absil, P., Grossmann, R., Mulhbauer, E., Viglietti-Panzica, C., Panzica, G.C., 1998. Anatomical and neurochemical definition of the nucleus of the stria terminalis in japanese quail (Coturnix japonica). J. Comp. Neurol. 396, 141–157.

Avena-Koenigsberger, A., Goni, J., Sole, R., Sporns, O., 2015. Network morphospace. J. R. Soc. Interface 12.

Balthazart, J., Dupiereux, V., Aste, N., Viglietti-Panzica, C., Barrese, M., Panzica, G.C., 1994. Afferent and efferent connections of the sexually dimorphic medial preoptic nucleus of the male quail revealed by in vitro transport of DiI. Cell Tissue Res. 276, 455–475.

Balthazart, J., Absil, P., Gerard, M., Appeltants, D., Ball, G.F., 1998. Appetitive and consummatory male sexual behavior in Japanese quail are differentially regulated by subregions of the preoptic medial nucleus. J. Neurosci. 18, 6512–6527.

Bass, A.H., Bodnar, D.A., Marchaterre, M.A., 2000. Midbrain acoustic circuitry in a vocalizing fish. J. Comp. Neurol. 419, 505–531.

Bassett, D.S., Sporns, O., 2017. Network neuroscience. Nat. Neurosci. 20, 353–364.

Been, L.E., Petrulis, A., 2010. Lesions of the posterior bed nucleus of the stria terminalis eliminate opposite-sex odor preference and delay copulation in male Syrian hamsters: role of odor volatility and sexual experience. Eur. J. Neurosci. 32, 483–493.

Betzel, R.F., Medaglia, J.D., Bassett, D.S., 2018. Diversity of meso-scale architecture in human and non-human connectomes. Nat. Commun. 9, 346.

Bullmore, E., Sporns, O., 2009. Complex brain networks: graph theoretical analysis of structural and functional systems. Nat. Rev. Neurosci. 10, 186–198.

Commins, D., Yahr, P., 1985. Autoradiographic localization of estrogen and androgen receptors in the sexually dimorphic area and other regions of the gerbil brain. J. Comp. Neurol. 231, 473–489.

Cook, S.J., Jarrell, T.A., Brittin, C.A., Wang, Y., Bloniarz, A.E., Yakovlev, M.A., Nguyen, K.C.Q., Tang, L.T., Bayer, E.A., Duerr, J.S., Bulow, H.E., Hobert, O., Hall, D. H., Emmons, S.W., 2019. Whole-animal connectomes of both Caenorhabditis elegans sexes. Nature 571, 63–71.

Donaldson, Z.R., Young, L.J., 2008. Oxytocin, vasopressin, and the neurogenetics of sociality. Science 322, 900–904.

Driver, R.J., Balakrishnan, C.N., 2021. Highly contiguous genomes improve the understanding of avian olfactory receptor repertoires. Integr. Comp. Biol. 61 (4), 1281–1290.

Farine, D.R., Whitehead, H., 2015. Constructing, conducting and interpreting animal social network analysis. J. Anim. Ecol. 84, 1144–1163.

Forlano, P.M., Deitcher, D.L., Bass, A.H., 2005. Distribution of estrogen receptor alpha mRNA in the brain and inner ear of a vocal fish with comparisons to sites of aromatase expression. J. Comp. Neurol. 483, 91–113.

Fornito, A., Zalesky, A., Bullmore, E.T. (Eds.), 2016. Fundamentals of Brain Network Analysis. Academic Press. https://doi.org/10.1016/B978-0-12-407908-3.00001-7.

Goodson, J.L., 2005. The vertebrate social behavior network: evolutionary themes and variations. Horm. Behav. 48, 11–22.

Goodson, J.L., 2008. Nonapeptides and the evolutionary patterning of sociality. Prog. Brain Res. 170, 3–15.

Goodson, J.L., Bass, A.H., 2002. Vocal-acoustic circuitry and descending vocal pathways in teleost fish: convergence with terrestrial vertebrates reveals conserved traits. J. Comp. Neurol. 448, 298–322.

Goodson, J.L., Kingsbury, M.A., 2013. What's in a name? Considerations of homologies and nomenclature for vertebrate social behavior networks. Horm. Behav. 64, 103–112.
Goodson, J.L., Evans, A.K., Bass, A.H., 2003. Putative isotocin distributions in sonic fish: relation to vasotocin and vocal-acoustic circuitry. J. Comp. Neurol. 462, 1–14.
Goodson, J.L., Evans, A.K., Lindberg, L., Allen, C.D., 2005. Neuro-evolutionary patterning of sociality. Proc. Biol. Sci. 272, 227–235.
Grgurevic, N., Budefeld, T., Rissman, E.F., Tobet, S.A., Majdic, G., 2008. Aggressive behaviors in adult SF-1 knockout mice that are not exposed to gonadal steroids during development. Behav. Neurosci. 122, 876–884.
Hill, R.A., Boon, W.C., 2009. Estrogens, brain, and behavior: lessons from knockout mouse models. Semin. Reprod. Med. 27, 218–228.
Hoke, K.L., Pitts, N.L., 2012. Modulation of sensory-motor integration as a general mechanism for context dependence of behavior. Gen. Comp. Endocrinol. 176, 465–471.
Hoke, K.L., Ryan, M.J., Wilczynski, W., 2007. Integration of sensory and motor processing underlying social behaviour in tungara frogs. Proc. Biol. Sci. 274, 641–649.
Johnson, Z.V., Walum, H., Xiao, Y., Riefkohl, P.C., Young, L.J., 2017. Oxytocin receptors modulate a social salience neural network in male prairie voles. Horm. Behav. 87, 16–24.
Kabelik, D., Weitekamp, C.A., Choudhury, S.C., Hartline, J.T., Smith, A.N., Hofmann, H. A., 2018. Neural activity in the social decision-making network of the brown anole during reproductive and agonistic encounters. Horm. Behav. 106, 178–188.
Kelly, A.M., Goodson, J.L., 2013. Functional significance of a phylogenetically widespread sexual dimorphism in vasotocin/vasopressin production. Horm. Behav. 64, 840–846.
Kelly, A.M., Kingsbury, M.A., Hoffbuhr, K., Schrock, S.E., Waxman, B., Kabelik, D., Thompson, R.R., Goodson, J.L., 2011. Vasotocin neurons and septal V1a-like receptors potently modulate songbird flocking and responses to novelty. Horm. Behav. 60, 12–21.
Kercmar, J., Snoj, T., Tobet, S.A., Majdic, G., 2014. Gonadectomy prior to puberty decreases normal parental behavior in adult mice. Horm. Behav. 66, 667–673.
Krakauer, J.W., Ghazanfar, A.A., Gomez-Marin, A., MacIver, M.A., Poeppel, D., 2017. Neuroscience needs behavior: correcting a reductionist bias. Neuron 93, 480–490.
Lanciego, J.L., Wouterlood, F.G., 2020. Neuroanatomical tract-tracing techniques that did go viral. Brain Struct. Funct. 225, 1193–1224.
Landgraf, R., Neumann, I.D., 2004. Vasopressin and oxytocin release within the brain: a dynamic concept of multiple and variable modes of neuropeptide communication. Front. Neuroendocrinol. 25, 150–176.
Lebow, M.A., Chen, A., 2019. Correction: overshadowed by the amygdala: the bed nucleus of the stria terminalis emerges as key to psychiatric disorders. Mol. Psychiatry 26 (8), 4561.
Lein, E., Borm, L.E., Linnarsson, S., 2017. The promise of spatial transcriptomics for neuroscience in the era of molecular cell typing. Science 358, 64–69.
Li, H.Y., Blaustein, J.D., De Vries, G.J., Wade, G.N., 1993. Estrogen-receptor immunoreactivity in hamster brain: preoptic area, hypothalamus and amygdala. Brain Res. 631, 304–312.
Liegeois, R., Santos, A., Matta, V., Van De Ville, D., Sayed, A.H., 2020. Revisiting correlation-based functional connectivity and its relationship with structural connectivity. Netw. Neurosci. 4, 1235–1251.
Lischinsky, J.E., Lin, D., 2020. Neural mechanisms of aggression across species. Nat. Neurosci. 23, 1317–1328.
Lledo, P.M., Gheusi, G., Vincent, J.D., 2005. Information processing in the mammalian olfactory system. Physiol. Rev. 85, 281–317.
Lopez-Gutierrez, M.F., Gracia-Tabuenca, Z., Ortiz, J.J., Camacho, F.J., Young, L.J., Paredes, R.G., Diaz, N.F., Portillo, W., Alcauter, S., 2021. Brain functional networks associated with social bonding in monogamous voles. elife 10.
Ludwig, M., Leng, G., 2006. Dendritic peptide release and peptide-dependent behaviours. Nat. Rev. Neurosci. 7, 126–136.
Lynn, C.W., Bassett, D.S., 2019. The physics of brain network structure, function and control. Nat. Rev. Phys. 1, 318–322.
Makagon, M.M., McCowan, B., Mench, J.A., 2012. How can social network analysis contribute to social behavior research in applied ethology? Appl. Anim. Behav. Sci. 138.
Maney, D.L., Goode, C.T., Lange, H.S., Sanford, S.E., Solomon, B.L., 2008. Estradiol modulates neural responses to song in a seasonal songbird. J. Comp. Neurol. 511, 173–186.
Markov, N.T., Ercsey-Ravasz, M.M., Ribeiro Gomes, A.R., Lamy, C., Magrou, L., Vezoli, J., Misery, P., Falchier, A., Quilodran, R., Gariel, M.A., Sallet, J., Gamanut, R., Huissoud, C., Clavagnier, S., Giroud, P., Sappey-Marinier, D., Barone, P., Dehay, C., Toroczkai, Z., Knoblauch, K., Van Essen, D.C., Kennedy, H., 2014. A weighted and directed interareal connectivity matrix for macaque cerebral cortex. Cereb. Cortex 24, 17–36.
Martinez-Lopez, B., Perez, A.M., Sanchez-Vizcaino, J.M., 2009. Social network analysis. Review of general concepts and use in preventive veterinary medicine. Transbound. Emerg. Dis. 56, 109–120.
Marx, V., 2021. Method of the year: spatially resolved transcriptomics. Nat. Methods 18, 9–14.
Merriam-Webster, 2021. Network. Merriam-Webster.com Dictionary. https://www.merriam-webster.com/dictionary/network.
Mesulam, M.M., 1990. Large-scale neurocognitive networks and distributed processing for attention, language, and memory. Ann. Neurol. 28, 597–613.
Meunier, D., Lambiotte, R., Bullmore, E.T., 2010. Modular and hierarchically modular organization of brain networks. Front. Neurosci. 4, 200.
Moore, F.L., Lowry, C.A., 1998. Comparative neuroanatomy of vasotocin and vasopressin in amphibians and other vertebrates. Comp. Biochem. Physiol. C Pharmacol. Toxicol. Endocrinol. 119, 251–260.
Newman, S.W., 1999. The medial extended amygdala in male reproductive behavior. A node in the mammalian social behavior network. Ann. N. Y. Acad. Sci. 877, 242–257.
O'Connell, L.A., Hofmann, H.A., 2011. The vertebrate mesolimbic reward system and social behavior network: a comparative synthesis. J. Comp. Neurol. 519, 3599–3639.
O'Connell, L.A., Hofmann, H.A., 2012. Evolution of a vertebrate social decision-making network. Science 336, 1154–1157.
Oh, S.W., Harris, J.A., Ng, L., Winslow, B., Cain, N., Mihalas, S., Wang, Q., Lau, C., Kuan, L., Henry, A.M., Mortrud, M.T., Ouellette, B., Nguyen, T.N., Sorensen, S.A., Slaughterbeck, C.R., Wakeman, W., Li, Y., Feng, D., Ho, A., Nicholas, E., Hirokawa, K.E., Bohn, P., Joines, K.M., Peng, H., Hawrylycz, M.J., Phillips, J.W., Hohmann, J.G., Wohnoutka, P., Gerfen, C.R., Koch, C., Bernard, A., Dang, C., Jones, A.R., Zeng, H., 2014. A mesoscale connectome of the mouse brain. Nature 508, 207–214.
Olds, J., 1956. Pleasure centers in the brain. Sci. Am. 195, 105–116.
Olds, J., Milner, P., 1954. Positive reinforcement produced by electrical stimulation of septal area and other regions of rat brain. J. Comp. Physiol. Psychol. 47, 419–427.
Ophir, A.G., 2017. Navigating monogamy: nonapeptide sensitivity in a memory neural circuit may shape social behavior and mating decisions. Front. Neurosci. 11, 397.
Palestrini, C., Mazzola, S.M., Caione, B., Groppetti, D., Pecile, A.M., Minero, M., Cannas, S., 2021. Influence of gonadectomy on canine behavior. Animals (Basel) 11.
Petersen, S.E., Sporns, O., 2015. Brain networks and cognitive architectures. Neuron 88, 207–219.
Petersen, C.L., Davis, S.E.D., Patel, B., Hurley, L.M., 2021. Social experience interacts with serotonin to affect functional connectivity in the social behavior network following playback of social vocalizations in mice. eNeuro 8.
Reiner, A., Karten, H.J., 1985. Comparison of olfactory bulb projections in pigeons and turtles. Brain Behav. Evol. 27, 11–27.
Reiner, A., Yamamoto, K., Karten, H.J., 2005. Organization and evolution of the avian forebrain. Anat. Rec. A Discov. Mol. Cell. Evol. Biol. 287, 1080–1102.
Rigney, N., Whylings, J., Mieda, M., de Vries, G., Petrulis, A., 2019. Sexually dimorphic vasopressin cells modulate social investigation and communication in sex-specific ways. eNeuro 6.
Scalia, F., Winans, S.S., 1975. The differential projections of the olfactory bulb and accessory olfactory bulb in mammals. J. Comp. Neurol. 161, 31–55.
Scheffer, L.K., Xu, C.S., Januszewski, M., Lu, Z., Takemura, S.Y., Hayworth, K.J., Huang, G.B., Shinomiya, K., Maitlin-Shepard, J., Berg, S., Clements, J., Hubbard, P. M., Katz, W.T., Umayam, L., Zhao, T., Ackerman, D., Blakely, T., Bogovic, J., Dolafi, T., Kainmueller, D., Kawase, T., Khairy, K.A., Leavitt, L., Li, P.H., Lindsey, L., Neubarth, N., Olbris, D.J., Otsuna, H., Trautman, E.T., Ito, M., Bates, A.S., Goldammer, J., Wolff, T., Svirskas, R., Schlegel, P., Neace, E., Knecht, C.J., Alvarado, C.X., Bailey, D.A., Ballinger, S., Borycz, J.A., Canino, B.S., Cheatham, N., Cook, M., Dreher, M., Duclos, O., Eubanks, B., Fairbanks, K., Finley, S., Forknall, N., Francis, A., Hopkins, G.P., Joyce, E.M., Kim, S., Kirk, N.A., Kovalyak, J., Lauchie, S. A., Lohff, A., Maldonado, C., Manley, E.A., McLin, S., Mooney, C., Ndama, M., Ogundeyi, O., Okeoma, N., Ordish, C., Padilla, N., Patrick, C.M., Paterson, T., Phillips, E.E., Phillips, E.M., Rampally, N., Ribeiro, C., Robertson, M.K., Rymer, J.T., Ryan, S.M., Sammons, M., Scott, A.K., Scott, A.L., Shinomiya, A., Smith, C., Smith, K., Smith, N.L., Sobeski, M.A., Suleiman, A., Swift, J., Takemura, S., Talebi, I., Tarnogorska, D., Tenshaw, E., Tokhi, T., Walsh, J.J., Yang, T., Horne, J.A., Li, F., Parekh, R., Rivlin, P.K., Jayaraman, V., Costa, M., Jefferis, G.S., 2020. A connectome and analysis of the adult drosophila central brain. elife 9.
Simerly, R.B., Chang, C., Muramatsu, M., Swanson, L.W., 1990. Distribution of androgen and estrogen receptor mRNA-containing cells in the rat brain: an in situ hybridization study. J. Comp. Neurol. 294, 76–95.
Soma, K.K., Francis, R.C., Wingfield, J.C., Fernald, R.D., 1996. Androgen regulation of hypothalamic neurons containing gonadotropin-releasing hormone in a cichlid fish: integration with social cues. Horm. Behav. 30, 216–226.
Sporns, O., 2018. Graph theory methods: applications in brain networks. Dialogues Clin. Neurosci. 20, 111–121.
Steiger, S.S., Fidler, A.E., Valcu, M., Kempenaers, B., 2008. Avian olfactory receptor gene repertoires: evidence for a well-developed sense of smell in birds? Proc. Biol. Sci. 275, 2309–2317.
Sung, Y.W., Kawachi, Y., Choi, U.S., Kang, D., Abe, C., Otomo, Y., Ogawa, S., 2018. A set of functional brain networks for the comprehensive evaluation of human characteristics. Front. Neurosci. 12, 149.
Thompson, R.R., 2020. An updated field guide for snark hunting: comparative contributions to behavioral neuroendocrinology in the era of model organisms. Horm. Behav. 122, 104742.
Tobiansky, D.J., Korol, A.M., Ma, C., Hamden, J.E., Jalabert, C., Tomm, R.J., Soma, K.K., 2018. Testosterone and corticosterone in the mesocorticolimbic system of male rats: effects of gonadectomy and caloric restriction. Endocrinology 159, 450–464.
Trevino, L.S., Gorelick, D.A., 2021. The interface of nuclear and membrane steroid signaling. Endocrinology 162.
Walum, H., Young, L.J., 2018. The neural mechanisms and circuitry of the pair bond. Nat. Rev. Neurosci. 19, 643–654.
Wang, Q., Henry, A.M., Harris, J.A., Oh, S.W., Joines, K.M., Nyhus, J., Hirokawa, K.E., Dee, N., Mortrud, M., Parry, S., Ouellette, B., Caldejon, S., Bernard, A., Jones, A.R., Zeng, H., Hohmann, J.G., 2014. Systematic comparison of adeno-associated virus and biotinylated dextran amine reveals equivalent sensitivity between tracers and novel projection targets in the mouse brain. J. Comp. Neurol. 522, 1989–2012.
Watson, J.T., Adkins-Regan, E., 1989. Neuroanatomical localization of sex steroid-concentrating cells in the japanese quail (Coturnix japonica): autoradiography with

[3H]-testosterone, [3H]-estradiol, and [3H]-dihydrotestosterone. Neuroendocrinology 49, 51–64.
Wood, R.I., Newman, S.W., 1993a. Intracellular partitioning of androgen receptor immunoreactivity in the brain of the male Syrian hamster: effects of castration and steroid replacement. J. Neurobiol. 24, 925–938.
Wood, R.I., Newman, S.W., 1993b. Mating activates androgen receptor-containing neurons in chemosensory pathways of the male Syrian hamster brain. Brain Res. 614, 65–77.
Wood, R.I., Newman, S.W., 1995. Androgen and estrogen receptors coexist within individual neurons in the brain of the Syrian hamster. Neuroendocrinology 62, 487–497.