The costs and benefits of sociality in semi-free ranging Barbary macaques (*Macaca sylvanus*)

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Dedication

To my family, who gave me **roots** to grow.

To my friends who, helped me reach out to the **skies**.

To the wind beneath my **wings**.

To this wonderful **earth** for all its wonders, who gave me **dreams,**

and made me start chasing them.

To all the companions, fellow follower of monkeys and kindred spirits,

to wings we grew, learning and understanding and growing **together**.

To all those amazing **moments** and **memories**.

To making the world a little **better** every day, and those who **inspire** me to try!

And most of all: To the **future** and all the wonderful things yet to come!

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Summary

Parasite infections are ubiquitous throughout the animal kingdom, and increased risk of parasite transmission has been suggested as one of the major costs of group living. With bigger group size and higher interaction frequencies, transmission is expected to increase due to higher pathogen exposure. In contrast, social integration and close affiliative relationships are known predictors of increased health, longevity and reproductive success in social animals. Sociality is thus hypothesized to offer fitness benefits by improving health, including reduced susceptibility to infectious diseases. The underlying mechanisms mediating the health benefits of social interactions are still largely unclear, particularly in wildlife. Recent methodological and theoretical advances in the fields of disease ecology and eco-immunology make studying the links between host sociality and parasites more feasible. Consequently, understanding host-parasite dynamics and the role of sociality for health has received increasing attention in behavioural ecology and evolutionary biology.

Gastrointestinal (GI) helminths are a powerful tool to study the links between sociality and health, as they can be assessed noninvasively. However, host-parasite interactions are complex and can function as feedback loops: parasites alter their host's physiology and behaviour, which in turn predict exposure and susceptibility to parasite infection. Often the directionality of the links between host behaviour, sociality and physiology and infection isn't clear due to the correlational nature of conducted studies. Additionally, host behaviour can contribute to both exposure and susceptibility simultaneously and both factors can be intertwined, so understanding the role of sociality for parasite transmission is challenging.

In this thesis I investigate the host-parasite dynamic between GI helminth infections and a social primate, the Barbary macaque (*Macaca sylvanus*), aiming at understanding the causes and consequences of GI helminth infection. Capitalizing on strongyle nematode clearance by routine anthelmintic treatment in a semi-free ranging population, I can take a step beyond correlational studies and draw more causal inferences about the direction of host-parasite interactions, placing a special focus on social behaviour. I combine behavioural observation data (~ 3500 hours) with analyses of molecular markers of immune regulation (urinary neopterin, uNEO), physical condition (urinary C-peptide, uCP) and hypothalamic-pituitary-adrenal (HPA) axis activation and parasite status assessment. This enables me to assess the consequences of parasite clearance and investigate the predictors of reinfection with GI helminths. To account for uncertainty of noninvasively assessed parasite status, I use patch occupancy modelling to estimate infection probabilities and individual reinfection risk. I test whether infection-related behavioural changes are attributable to sickness behaviour or avoidance of infected conspecifics to extrapolate the impact of GI helminth infections on social behaviour and potentially evolution. With regard to parasite transmission, I test whether grooming predicts reinfection risk, indicating transmission due to social contact.

Strongyle nematode infections, mostly caused by *Oesophagostomum* spp., were ubiquitous within the study population, with generally low egg shedding and large inter-individual variation in reinfection risk. Infections did not cause overt symptoms or affect physical condition. They nonetheless elicited sickness behaviour responses, namely increased HPA axis activation in combination with reduced activity. Anthelmintic treatment did not alter uNEO levels, but uNEO increased with age, implying immunosenescence. As coinfections with further GI helminths occurred mostly in old individuals, immunosenescence might influence an individual's ability to cope with GI helminth infections in general. Individual frequency to initiate proximity to others was not predicted by an individual's, but by the potential partner's infection status, indicating avoidance of infected individuals.

Reinfection was predicted by measures of both susceptibility and exposure. The strongest predictor of earlier reinfection was coinfection with further GI helminth taxa. I found no evidence for HPA axis activation and immune function as strong predictors of reinfection. Being in good physical condition tended to increase reinfection risk, indicating the presence of parasite tolerance strategies in Barbary macaques. Time spent in areas likely contaminated with faeces, a measure of exposure to infective parasite stages, emerged as a predictor of increased infection risk, confirming the direct environmental transmission route of strongyle nematodes. High social bond strength with opposite sex partners decreased reinfection probability, probably due to reduced susceptibility resulting from immunomodulatory effects of affiliative interactions. In contrast, grooming a high number of partners and strong bonds with same sex partners emerged as predictors of increased infection probability, implying a social component of transmission. Social interactions can thus have an ambivalent effect, contributing to both protection from and increased risk of GI helminth infections. The discrepancy between same and opposite sex bond effects is likely attributable to differences in interaction patterns, resulting in different relative contributions of same and opposite sex bonds to exposure and susceptibility.

In conclusion, the results suggest that GI parasite infections can influence social behaviour in nonhuman primates. Given the dual role of social interactions for GI helminth transmission, a possible strategy to maximize benefits while limiting costs of sociality could be selective formation of strong bonds with a small number of partners, with the caveat that particular interaction patterns might be more beneficial than others. My results lead to a range of questions which need to be addressed by future research, particularly whether primates mitigate costs of infection by employing tolerance strategies. Causally linking components of social behaviour to exposure and susceptibility will be important for understanding individual variation in infection risk and contribution to transmission through a population. Investigating whether variation in responses to GI helminth infections predict long-term health and fitness outcomes will be vital to assess the impact of host-parasite dynamics on behaviour and potentially host social evolution.

Zusammenfassung

Infektionen mit Parasiten sind im Tierreich allgegenwärtig, und ein erhöhtes Risiko für Parasitenübertragung gilt als einer der größten Nachteile des Gruppenlebens. Mit zunehmender Gruppengröße und Anzahl an Interaktionen sollte es zu häufigeren Kontakten mit Krankheitserregern und damit zu vermehrter Krankheitsübertragung kommen. Im Gegensatz dazu tragen soziale Integration und enge affiliative Beziehungen bei sozial lebenden Tierarten zu besserem Gesundheitszustand, höherer Lebenserwartung und höherem Reproduktionserfolg bei. Es wird daher angenommen, dass durch soziale Interaktionen positive Einflüsse auf die Gesundheit, unter anderem niedrigere Anfälligkeit für Krankheiten, entstehen, die zu Fitnessvorteilen führen. Besonders bei wildlebenden Tieren sind die Mechanismen, über die Sozialverhalten zu Gesundheitsvorteilen führt, noch weitestgehend unbekannt. Jüngste methodologische und theoretische Fortschritte auf den Gebieten der Krankheitsökologie und Öko-Immunologie erleichtern die Erforschung der Verbindungen zwischen Parasiten und dem Sozialverhalten des Wirts. Somit rückt die Erforschung der Dynamik zwischen Wirtstieren und Parasiten und die verbindung zwischen Sozialverhalten und Gesundheit zunehmend auch in den Fokus der Verhaltensökologie und Evolutionsbiologie.

Gastrointestinale Parasiten sind ein vielversprechendes System, um die Zusammenhänge zwischen Sozialverhalten und Gesundheit zu untersuchen, da sie nicht-invasiv analysiert werden können. Allerdings sind Wirt-Parasitenbeziehungen komplex und beinhalten oft Rückkopplungsschleifen: Während Infektionen mit Parasiten das Verhalten des Wirtes beeinflussen, bestimmen Verhalten und Physiologie des Wirtes Kontaktraten mit Krankheitserregern und Anfälligkeit für Infektionen. Da zumeist Korrelationsstudien vorliegen, sind die kausalen Zusammenhänge zwischen den Interaktionen von Wirtsverhalten, Physiologie und Parasiteninfektionen weitestgehend unbekannt. Zusätzlich kann das Verhalten des Wirtes gleichzeitig zum Kontakt mit Krankheitserregern und der Infektionsanfälligkeit beitragen und beide Komponenten können miteinander verwoben sein, so dass es schwierig ist, die Rolle von sozialen Interaktionen für Parasitenübetragung zu entschlüsseln.

Um die Ursachen und Konsequenzen von Infektionen mit gastrointestinalen Helminthen zu verstehen, werden in dieser Dissertation die Zusammenhänge zwischen gastrointestinalen Parasiten, Physiologie, Verhalten und sozialen Interaktionen bei sozialen Primaten, den Berberaffen (*Macaca sylvanus*) untersucht. Dabei mache ich mir die routinemäßige Entwurmung einer halbwilden Population zu Nutze, die zur Freiheit von Infektionen mit Strongiliden führt. Durch die experimentelle Veränderung des Parasitenstatuses können eher Schlüsse über Kausalzusammenhänge der Interaktionen zwischen Wirt und Parasiten, insbesondere im Bezug auf das Sozialverhalten, gezogen werden, als es in Korrelationsstudien möglich ist. Hierzu werden

Verhaltensdaten (ca. 3500 Stunden) mit Analysen von molekularen Marker der Immunregulation (Neopterin im Urin), der körperlichen Verfassung (C-Peptide im Urin) und der Aktivität der Hypothalamus-Hypophysen-Nebennieren-(HPA)-Achse und die Bestimmung des Infektionsstatuses verbunden. Um die methodische Ungenauigkeit der nicht-invasiver Parasitenanalysen zu berücksichtigen, werden Patch-Occupancy-Modelle zur Abschätzung der Infektionswahrscheinlichkeiten und des Risikos der Wiederansteckung genutzt. Zusätzlich wird analysiert, ob infektionsbezogene Verhaltensänderungen eine Folge von Krankheitsverhalten oder der Vermeidung infizierter Artgenossen sind. Dies lässt Rückschlüsse auf den Einfluss von Parasiteninfektionen auf das Sozialverhalten zu, die möglicherweise auf die soziale Evolution der Tiere übertragen werden können. Ich überprüfe auch, ob soziale Fellpflege als möglicher direkter Übertragungsweg das Risiko einer Ansteckung mit Darmparasiten vorhersagt.

Infektionen mit Strongiliden, zumeist *Oesophagostomum* spp., waren in der Studiengruppe allgegenwärtig und zeigten meist geringe Ei-Ausscheidungsraten, aber große interindividuelle Unterschiede in der Wiederansteckungswahrscheinlichkeit. Diese Infektionen verursachten keine offensichtlichen Symptome oder eine Veränderung der körperlichen Verfassung. Sie riefen dennoch Anzeichen für Krankheitsverhalten hervor, messbar als stärkere Aktivität der HPA-Achse und geringere Aktivität infizierter Tiere. Die Entwurmung rief keine Veränderungen der Neopterinlevel hervor. Diese stiegen jedoch im Alter an, was auf Immunoseneszenz hindeutet. Da Infektionen mit weiteren Helminthen vorwiegend in älteren Individuen vorkommen, könnte dies darauf hindeuten, dass Immunoseneszenz die Fähigkeit der Tiere, Parasiteninfektionen einzudämmen, beeinflusst. Die Rate, mit der die Tiere sich Artgenossen annäherten, hing nicht mit dem eigenen Parasitenstatus, sondern dem des Partners zusammen, was auf eine Vermeidung infizierter Artgenossen hindeutet.

Wiederansteckung wurde durch Marker für Parasitenanfälligkeit und -kontakt bestimmt. Der stärkste Prädiktor für eine schnellere Wiederansteckung war eine Ko-Infektion mit weiteren gastrointestinalen Helminthen. Es gab keine Hinweise darauf, dass HPA-Achsenaktivität oder Immunfunktion starke Prädiktoren für eine Wiederansteckung sind. Eine gute körperliche Verfassung führte zu einer tendenziellen Erhöhung des Ansteckungsrisikos, was wahrscheinlich ein Zeichen für Toleranz gegenüber Darmparasiteninfektionen in Berberaffen ist. Der Übertragunsweg von Strongyliden über die Umwelt wurde bestätigt: Tiere, die viel Zeit in Gebieten mit hoher Kotkontamination verbrachten, d.h. wahrscheinlich häufig Kontakt mit infektiösen Parasitenstadien hatten, hatten auch ein erhöhtes Ansteckungsrisiko. Starke soziale Bindungen zu Partnern des anderen Geschlechts verringerten das Infektionsrisiko, wahrscheinlich auf Grund positiver Effekte sozialer Interaktionen auf die Funktion des Immunsystems. Im Gegensatz dazu führten soziale Fellpflege mit einer Vielzahl an Partnern und enge Bindungen mit gleichgeschlechtlichen Partnern zu einer höheren Ansteckungswahrscheinlichkeit, was eine soziale Komponente bei der Parasitenübertragung nahelegt. Dabei deutet die Diskrepanz zwischen den Effekten von Bindungen

zu getrennt- und gleichgeschlechtlichen Partnern wahrscheinlich darauf hin, dass spezifische Verhaltensweisen unterschiedlich stark zum Kontakt mit Parasiten und der Infektionsanfälligkeit beitragen.

Zusammenfassend legen die Ergebnisse nahe, dass Infektionen mit gastrointestinalen Parasiten das Sozialverhalten nichtmenschlicher Primaten beeinflussen können. In Anbetracht der zweischneidigen Rolle sozialer Beziehungen erscheint das Ausprägen weniger, starker Bindungen als mögliche Strategie, die Vorteile von Beziehungen voll auszukosten und gleichzeitig die Nachteile zu minimieren - mit dem Vorbehalt, dass einige Interaktionsmuster mehr Vorteile mit sich bringen können als andere. Durch meine Ergebnisse ergeben sich eine Reihe neuer Fragen, die in zukünftigen Studien beantwortet werden sollten, insbesondere ob Primaten Parasitentoleranzstrategien nutzen können, um die Kosten von Parasiteninfektionen einzudämmen. Zu entschlüsseln, welche Komponenten des Sozialverhaltens mit Kontakt zu Krankheitserregern und der Anfälligkeit für Infektionen zusammenhängen ist wichtig, um die Variation des Infektionsrisikos zwischen einzelnen Tieren und deren Beitrag zur Übertragung von Krankheiten innerhalb einer Population zu verstehen. Zu untersuchen, ob Unterschiede in der Reaktion auf Parasiteninfektionen Langzeitfolgen für Gesundheit und Fitness vorhersagen, ist ein wichtiger nächster Schritt, um den Einfluss der Wirt-Parasitenbeziehung auf das Verhalten möglicherweise die soziale Evolution von Wirtstieren zu verstehen.

Chapter 1

General Introduction

"Friendship is unnecessary, like philosophy, like art.... It has no survival value; rather it is one of those things which give value to survival."

C.S. Lewis – The Four Loves

While C.S. Lewis was undeniably right that friendship makes human life worth living, his observation that it does not contribute to survival could hardly be further from the truth. There is overwhelming support for the idea that social bonds and support are not only vital for personal fulfilment and wellbeing, but also for health and survival. Despite the evidence for the positive impact of sociality on health and longevity in social animals, our understanding of the underlying mechanisms and the evolutionary foundation of this link is still limited. To understand the adaptive value and evolution of human friendship, studying the relationship between social interactions, health and fitness in our phylogenetic brethren, the nonhuman primates, is vital. Investigating the role of health for social evolution has been largely neglected in the fields of behavioural ecology and evolutionary biology, but is attracting increasing attention recently.

While some parts of the picture linking social behaviour with physiology, health and fitness are well understood in wildlife, the complete picture remains elusive. In the following chapter, I will elaborate on the current state of knowledge on the sociality-health-fitness nexus, culminating in the identification of open questions and how this thesis can contribute to answering them.

1.1 Sociality and health

1.1.1 Evolution of group living

One of the major transitions in evolution, changing the level of organization and consequently selection, (Maynard Smith *et al.* 1994) was the switch from solitary to group living (Szathmáry & Smith 1995). As general consensus, conspecifics of one group consistently aggregate and interact more with each other than with other conspecifics, although there are various definitions of what constitutes a group (Krause and Ruxton 2002). More than two thirds of mammal species are classified as solitary (Lukas & Clutton-Brock 2013), indicating that group living is not by default adaptive. Rather, specific benefits of associating with conspecifics, like protection from predation (Rubenstein 1978; Van Schaik 1983) or better access to and defensibility of resources (Wrangham 1980; Packer & Ruttan 1988; Packer *et al.* 1990), can outweigh the costs of long-term associations (Sterck *et al.* 1997; Wrangham 1980; Krause & Ruxton 2002) and lead to the evolution of permanent group living.

Once arisen, group living individuals are subject to a range of trade-off between costs and benefits inherent to gregariousness, sometimes different from original drivers of selection for group living. Explaining the origins and ecology of sociality is a major aim of evolutionary ecology (Clutton-Brock & Janson 2012; Thierry 2013). Consequently, selective forces shaping the evolution of group living are intensely studied (Emlen & Oring 1977; Van Schaik & Van Hooff 1983; Sterck *et al.* 1997) and ecological correlates of its costs and benefits are relatively well understood. Potential fitness costs of group living do not necessarily affect all individuals in the same manner and can depend on individual traits. As an example, mating competition in multi-male groups is considered a major cost for males (Emlen & Oring 1977), whereas female fitness can influenced by limited reproductive success due to feeding competition (Wrangham 1980; Janson & Van Schaik 1988) or the risk of infanticide (Sterck *et al.* 1997; Pusey & Packer 1994). Depending the environmental conditions, feeding competition and the subsequent energetic costs of traveling and foraging can become a limiting factor to group size, leading to markedly different group sizes within the same species (Brown 1982; Snaith & Chapman 2007; VanderWaal *et al.* 2009; Markham & Gesquiere 2017). Integrating various costs and benefits and their impact on shaping fitness in groups of different sizes gave rise to the formulation of optimal group size theory, predicting an optimal, often intermediate, group size to offer the best trade-off and highest fitness benefits (Brown 1982; Sibly 1983). Strategies beyond adapting group sizes to environmental conditions, like cooperation (Packer & Ruttan 1988; van Schaik *et al.* 2004; Henzi *et al.* 2010; Schülke *et al.* 2010) and forming strong affiliative relationships (Silk *et al.* 2003; Cameron *et al.* 2009; Archie *et al.* 2014) can further mitigate costs of group living and increase individual fitness.

There is, however, another mechanism potentially driving social evolution, which has been largely neglected in behavioural ecology until recently: the link between sociality and health (Kappeler *et al.* 2015). Pathogens have been considered as a potential selective force for social evolution since the 1970s (Alexander 1974; Freeland 1976) and are almost universally present throughout the animal kingdom (Bordes & Morand 2011; Ezenwa 2016). Recognizing the impact of parasitism on individual fitness (Tompkins & Begon 1999; Pedersen & Greives 2008), evolutionary biologists increasingly study the determinants of individual parasite infection risk (Lloyd-Smith *et al.* 2005; Hawley & Altizer 2011; Vanderwaal & Ezenwa 2016) and how infections influence social systems (Chapman *et al.* 2009; Kappeler *et al.* 2015). In the following paragraphs, I will introduce the current state of knowledge of the interplay between social behaviour, health and pathogen infection and how sociality could impact individual fitness.

1.1.2 The adaptive value of social relationships

Individuals form differentiated relationships within their group in most social species throughout the mammalian kingdom, including equids (Cameron *et al.* 2009; Stanley *et al.* 2017), elephants (Moss *et al.* 2011; Goldenberg & Wittemyer 2017), cetaceans (Connor *et al.* 2000; Ellis *et al.*

2017; Louis *et al.* 2017), hyenas (Smith *et al.* 2010) and primates (Silk *et al.* 2003; Mitani 2009; Schülke *et al.* 2010; Wittig *et al.* 2016). If these relationships are characterized by affiliative interactions, biased towards specific partners, and stable over longer periods, they are referred to as social bonds (Silk 2002). Non-random interactions between group members give rise to higher level organisation patterns within the social network (Krause *et al.* 2007; Wey *et al.* 2008; Kasper & Voelkl 2009). Consequently, social network analysis, i.e. investigating social structures through the use of networks constructed from interaction patterns, is increasingly used as a tool to study social behaviour (see for example Godfrey *et al.* 2009; Brent *et al.* 2013; VanderWaal *et al.* 2014). Social network analyses allows researchers to identify the role of network substructure for parasite and information transmission and assess the role of variation in individual network integration, centrality and connectedness on fitness correlates (Franz & Nunn 2009; Griffin & Nunn 2012; Brent 2015; White *et al.* 2017b).

Individuals form social bonds despite temporal and energetic constraints and costs (Dunbar *et al.* 2009) and compete over valuable partners (Palombit *et al.* 2001; Mielke *et al.* 2017), indicating the importance of social bonds. Social bonds convey adaptive benefits beyond mere association within groups and potentially buffer against costs of group living. One of these benefits is support in agonistic encounters in female spotted hyenas (*Crocuta crocuta*) (Smith *et al.* 2010) and male nonhuman primates, where coalitionary support increases reproductive success (Schülke *et al.* 2010; Berghänel *et al.* 2011; Young *et al.* 2013, 2014b). Reproductive success is also increased in strongly bonded females in several species, including bottlenose dolphins (*Tursiops truncates*) (Frère *et al.* 2010), humpbacked whales (*Megaptera novaeangliae*) (Ramp *et al.* 2010), horses (*Equus caballus*) (Cameron *et al.* 2009) and baboons (Silk *et al.* 2003, 2009), and female baboons with strong bonds benefited from higher longevity (Silk *et al.* 2010). Female-female bonds are usually formed with closely related kin (Silk *et al.* 2003, 2009), yet bonding with unrelated males can increase survival (Archie *et al.* 2014), offer protection from infanticide (Palombit *et al.* 1997) and reduce feeding competition (Haunhorst *et al.* 2017) in nonhuman primates.

The relative importance of quality vs. quantity of social bonds is still debated (Silk *et al.* 2018). Alongside the evidence for bond quality predicting fitness correlates (Cameron *et al.* 2009; Silk *et al.* 2010; Archie *et al.* 2014), high interaction partner numbers predicted increased survival during a harsh winter in Barbary macaques (*Macaca sylvanus*) (McFarland & Majolo 2013), better thermoregulation in vervet monkeys (*Chlorocebus pygerythrus*) (McFarland *et al.* 2015), and increased infant survival in a study on chacma baboons (*Papio ursinus*) (McFarland *et al.* 2017). Additionally, the importance of individual integration within the social network beyond dyadic relationships is increasingly recognized (Brent 2015). Measures of individual centrality, integration and importance for information transmission within a group (Wey *et al.* 2008; Kasper & Voelkl 2009; Farine & Whitehead 2015) predict fitness correlates in primates (Brent *et al.* 2013; Brent 2015) and cetaceans (Stanton & Mann 2012; Ellis *et al.* 2017), sometimes with stronger signals than dyadic bonds (Cheney *et al.* 2016).

Similar patterns emerge in humans, where social integration and strong social bonds predict lower mortality (House *et al.* 1988; Holt-Lunstad *et al.* 2010), with effect sizes comparable to known predictors of mortality risk, like smoking or heavy alcohol consumption (Holt-Lunstad *et al.* 2010)

Despite the relatively clear picture of adaptive benefits linked with sociality, strong bonds are not universally beneficial and can even be costly. In marmots (*Marmota flaviventer*), a facultative social species, winter survival was lower in individuals with higher partner numbers and network integration (Blumstein *et al.* 2018), suggesting different selection pressures on obligatory than facultative social species. In blue monkeys (*Cercopithecus mitis stuhlmanni*), consistent strong bonds increased survival, while inconsistent strong bonds had the opposite effect (Thompson & Cords 2018), and in tufted capuchins (*Sapajus apella*), infants of highly social females were at highest risk from infanticide upon alpha male takeovers (Kalbitzer *et al.* 2017). These findings point to context specificity of consequences of bonding and potential fitness trade-offs. The mechanisms linking sociality to fitness outcomes are still poorly understood to date (Uchino 2006; Thoits 2011; Hawkley & Capitanio 2015; Ostner & Schülke 2018). Immediate benefits of social bonding can be increased access to resources, especially food (Tiddi *et al.* 2011; Sabbatini *et al.* 2012; Haunhorst *et al.* 2017), or protection from predation (Micheletta *et al.* 2012). Improved health and consequently survival have been put forward as mediating positive effects of social interactions on fitness, with different mechanisms explaining the link between sociality and health, which will be discussed in detail in the next paragraphs.

1.1.3 Sociality and health – some mechanisms

In humans, the importance of social relationships for individual health and longevity and the detrimental effects of social isolation are well established (Berkman & Syme 1979; Uchino *et al.* 1996; Cacioppo & Hawkley 2003; Holt-Lunstad *et al.* 2010, 2015). Evidence is mostly correlational, yet longitudinal approaches allow the conclusion that sociality is causally connected to longevity (Uchino 2006; Holt-Lunstad *et al.* 2010). Research aiming to explain this causal connection and the mediating mechanisms gave rise to the interdisciplinary field of "social neuroscience" (Cacioppo *et al.* 2000; Eisenberger & Cole 2012). With growing interest in the link between sociality, health and fitness, concepts of social neuroscience increasingly receive attention in behavioural ecology (Engh *et al.* 2006a; Crockford *et al.* 2008; Demas & Carlton 2015; Wittig *et al.* 2016).

Health and fitness are inextricably linked with social environment in gregarious animals, and social dominance status, similar to socio-economic status in humans, can predict health outcomes (Sapolsky 2004; Cavigelli & Chaudhry 2012; Muscatell *et al.* 2016; Marescot *et al.* 2018). Dominance rank predicts aggressive interactions and challenges of the dominance position. These stimuli evoke physiological stress responses, including the activation of the hypothalamic-pituitary-adrenal (HPA) axis which culminates in glucocorticoid (GC) release (Sapolsky 2005). Periods of rank instability or male immigration generally lead to such stress responses (Sapolsky 2005; Engh *et al.* 2006b; Wittig *et*

al. 2008), yet depending on the social system, higher or lower ranking individuals can be subject to more socially stressful conditions (Abbott *et al.* 2003; Sapolsky 2005). Instead of being costly per se, HPA axis activation is an adaptive response to challenges that contributes to survival (Romero 2004; Cavigelli & Chaudhry 2012). GCs have various immunomodulatory functions (Besedovsky *et al.* 1986; Dhabhar 2009), including regulation and termination of inflammatory responses (Besedovsky *et al.* 1986; Eisenberger & Cole 2012). High GC levels can even enhance immune function under certain conditions, as in yellow baboons (*Papio cynocephalus*), where alpha males, but not lower ranking individuals, with high GC levels showed accelerated wound healing (Archie 2013). Social rank position also alters expression patterns of immune-related genes, linking social environment to immune function and disease susceptibility (Tung & Gilad 2013; Snyder-Mackler *et al.* 2016).

While short term activation of the HPA axis is adaptive (Romero 2004), long-term activation is considered to have detrimental effects (Apanius 1998). Although the fitness costs of elevated GC levels in wildlife are currently disputed (Boonstra 2013; Beehner & Bergman 2017), human and laboratory animal studies describe a range of adverse physiological effects of repeated or chronic HPA axis activation (Apanius 1998; Yang & Glaser 2002; Glaser & Kiecolt-Glaser 2005). These include dysregulation of GC excretion, resulting in elevated baseline levels (Yang & Glaser 2002; Cole *et al.* 2009), uncoupling of immune cells from GC regulation (Cole *et al.* 2009), low level inflammation (Dhabhar 2009; Hawkley *et al.* 2013; Hawkley & Capitanio 2015) and a shift towards cell mediated T-helper type 2 (Th2) responses (Elenkov & Chrousos 1999). Experiencing social stressors also leads to sympathetic nervous system (SNS) activation, with negative health effects of repeated stress responses, profound changes in immune gene expression in rhesus macaques (*Macaca mulatta*) (Sloan *et al.* 2008; Capitanio & Cole 2015) and upregulation of inflammatory signalling resulting from increased lymph node innervation by SNS fibres (Sloan *et al.* 2007). These long-term effects of social stress can culminate in increased disease susceptibility (Capitanio *et al.* 1998; Glaser & Kiecolt-Glaser 2005; Dhabhar 2009).

Social isolation, real or perceived, is another very potent stressor linked with adverse health outcomes in gregarious animals (Eisenberger & Cole 2012; Hawkley *et al.* 2013; Hawkley & Capitanio 2015), also predicting worse health and lower life expectancy in humans (Hawkley & Capitanio 2015; Holt-Lunstad *et al.* 2015). Social isolation increases HPA axis activity and inflammatory signalling (Hawkley *et al.* 2013; Hennessy *et al.* 2014), resulting in detrimental health effects that include metabolic and cardiovascular disease and mental illness in humans (Dantzer *et al.* 2008; Kiecolt-Glaser *et al.* 2010; Hawkley & Capitanio 2015). Isolation is thus a second pathway for social environment to shape individual health.

In contrast, social relationships can alter individual physiology beyond the effects of social isolation and stressors: affiliative interactions and social support can profoundly increase health outcomes, also by attenuating responses to perceived threats and thus mitigating costs of social stress

(Cohen & Wills 1985; Kikusui *et al.* 2006; Kiyokawa & Hennessy 2018), referred to as social buffering (Cohen & Wills 1985). The social buffering hypothesis thus offers a mechanism explaining the health benefits of social relationships (Berkman & Syme 1979; House *et al.* 1988; Holt-Lunstad *et al.* 2010). Indeed, socially well integrated individuals have a lower risk of contracting infections and developing symptoms upon experimental exposure with respiratory viruses in humans (Cohen *et al.* 1991, 2003, 2015) and long tailed macaques (*Macaca fascicularis*) (Cohen *et al.* 1997). Social buffering comes in two flavours: structural support, i.e. the integration of individuals within a social network (Cohen & Janicki-Deverts 2009; Holt-Lunstad *et al.* 2010) or being housed with social partners in case of experimental animals (Kikusui *et al.* 2006; Kiyokawa 2018), and direct support, i.e. the presence of or interaction with a conspecific in face of a stressor (Ishii *et al.* 2016; Kiyokawa 2018). Both mechanisms have distinct underlying principles by which they attenuate stress responses (reviewed in Kiyokawa 2018; Kiyokawa & Hennessy 2018): Structural support influences the initial reaction to a stressor, direct support the recovery from a stressor. Beyond lowering the perceived severity of a stressor if support is available, social buffering can alter individual physiology also in absence of an acute stressor (Kikusui *et al.* 2006), leading to beneficial health outcomes.

There are several physiological mechanism by which social buffering can impact susceptibility to infectious and non-infectious diseases. In humans, these include lower SNS activation (Cacioppo & Hawkley 2003; Eisenberger & Cole 2012; Inagaki 2018), lower baseline blood pressure (Uchino *et al.* 1996), lower levels of inflammation (Cacioppo & Hawkley 2003; Kiecolt-Glaser *et al.* 2010), better sleep quality and overall higher maintenance function (Cacioppo *et al.* 2002; Cacioppo & Hawkley 2003). Many of these mechanisms are difficult to assess in natural populations, yet correlates of HPA axis activation and oxytocin release, which both play important roles for stress buffering (Crockford *et al.* 2017; Kiyokawa & Hennessy 2018), can reliably be measured in wildlife to study social buffering effects (Crockford *et al.* 2013, 2017; Young *et al.* 2014a; Beehner & Bergman 2017).

In primates, grooming has been linked with endorphin (Keverne *et al.* 1989) and oxytocin release (Crockford *et al.* 2013) and reduced HPA activation (Shutt *et al.* 2007; Aureli & Yates 2010), illustrating the potential for social interactions to buffer against the adverse effects stressors. Whether social interactions lower overall activation or improve HPA axis regulation is currently under debate, and both processes are not necessarily mutually exclusive. While male Barbary macaques with stronger bonds had lower faecal GC metabolite (fGCM) levels when faced with social and environmental stressors (Young *et al.* 2014a), strongly bonded chimpanzees showed overall lower HPA activity across every day and challenging contexts (Wittig *et al.* 2016). Oxytocin, which can downregulate HPA axis activity (Kikusui *et al.* 2006; Li *et al.* 2017), is increased in socio-positive interactions and intergroup conflicts in chimpanzees (Crockford *et al.* 2013; Samuni *et al.* 2016). Besides anxiolytic effects and HPA axis regulation (Uvnäs-Moberg 1998; Crockford *et al.* 2017), oxytocin can also facilitate social interactions (Witt *et al.* 1992). This indicates that faced with certain

stressors, e.g. the threat of an intergroup encounter (Samuni *et al.* 2016), physiological mechanisms mediate active support seeking, which could functionally alleviate the threat posed by the stressor. Similar patterns were observed in baboons, where individuals reacted to stressors (male rank instability and loss of a bonded partner) not only with increased HPA axis activation, but subsequently focused their grooming network, resulting in fGCM levels or quicker fGCM level return to baseline (Engh *et al.* 2006a; Wittig *et al.* 2008). This interplay between physiology and behaviour could be the evolutionary root of social buffering (Kiyokawa & Hennessy 2018). In summary, social interactions induce various physiological changes that can influence health outcomes and thus predict variance in survival and fitness based on social interaction patterns.

1.1.4 Sociality's role for pathogen exposure

Social contacts may be beneficial for individual health due to improved immune function and lower susceptibility, but also carry risks. Increased exposure to infectious diseases has been suggested as one of the major costs of group living (Freeland 1976), with evidence for higher infection risk in bigger groups (Altizer *et al.* 2003; Patterson & Ruckstuhl 2013). Interactions within a group are usually non-random, and higher level organisation patterns, like subgrouping within a social network, can modulate individual exposure and the transmission of pathogens through the network (Cross *et al.* 2004; Salathé & Jones 2010) and predict transmission more precisely than group size alone (Griffin & Nunn 2012; Nunn *et al.* 2015). Depending on their network position and disease susceptibility, individuals can contribute disproportionally to disease transmission (Woolhouse *et al.* 1997; Lloyd-Smith *et al.* 2005; Hawley & Altizer 2011). Identifying these highly vulnerable individuals is particularly important in the light of conservation and medical interventions, which can require targeting specific individuals to succeed (Smith *et al.* 2009; Rushmore *et al.* 2013).

One strategy to handle this cost of social aggregation and interaction is social immunity (Cremer *et al.* 2007; Schmid-Hempel 2017), mostly employed by colony living insects. Social insects are particularly vulnerable to pathogen invasion due to the high spatial proximity of closely related individuals (Cremer *et al.* 2007; Schmid-Hempel 2017), and defence against pathogens is usually considered on a colony rather than an individual level. Strategies to prevent pathogen invasion of the colony are the isolation of heavily (Cremer *et al.* 2007) or support of mildly infected individuals (Konrad *et al.* 2012). Grooming individuals with fungal infections can be mutual beneficial in ants, simultaneously alleviating infection and transferring immunity to the respective pathogen (Konrad *et al.* 2012). Similar patterns can be observed in vertebrates if low level exposure to pathogens leads to development of adaptive immunity without developing serious infections (Burnet *et al.* 1972; Hart 2011). Given the close relatedness of individuals within a colony and the subsequent inclusive fitness benefits of giving support, this strategy is generally more common in insects than mammals (Cremer *et al.* 2007; Schmid-Hempel 2017), where intragroup-competition for mates and resources is often harsh (Koenig 2002; van Schaik *et al.* 2004) and individuals do not usually adapt their behaviour to

benefit the group. Thus, insect immunity offers a valuable model system for understanding the evolution of immune responses and social strategies to counter disease risk (Schmid-Hempel 2003), although patterns cannot be directly applied to mammal sociality.

Transmission pathways can be vastly different between pathogens, so social interactions can shape infection risk differently. Sleep site choice, as an example, has been suggested as a defence strategies against contracting vector borne diseases (Nunn & Heymann 2005). Grooming reduces ectoparasite load and subsequent exposure to vector borne diseases, exemplified by lower lice loads in Japanese macaques grooming with many partners (*Macaca fuscata)* (Duboscq *et al.* 2016). In case of diseases transmitted via contact or close proximity, social contacts can have immediate impacts on infection risk. The spread of viral infections in humans closely follows the social network structure (Mossong *et al.* 2008) for influenza, human immunodeficiency virus (HIV) and Hepatitis C (Klovdahl & Australian 1985; Klovdahl *et al.* 1994; Rothenberg *et al.* 1998; Romano *et al.* 2010; Cauchemez *et al.* 2011), and from insects to mammals, highly connected individuals are more likely to be infected with bacteria or viruses (Vicente *et al.* 2007; Godfrey *et al.* 2009; Craft *et al.* 2011; Konrad *et al.* 2012). Close contact is not always a strong predictor of infection risk, as not all interactions contribute equally to pathogen transmission: in meerkats (*Suricata suricatta*), not the most connected, but the individuals giving grooming and receiving aggression are most vulnerable to tuberculosis infection (Drewe 2009), and in Tasmanian devils (*Sarcophilus harrisii*), the transmission of an infectious tumour disease is closely linked to aggressive behaviours (Hamede *et al.* 2013).

Social interactions can also predict acquisition of environmentally transmitted bacteria (VanderWaal *et al.* 2014; Tung *et al.* 2015; Springer *et al.* 2016; Balasubramaniam *et al.* 2018) and gastrointestinal (GI) parasites (Fenner *et al.* 2011; MacIntosh *et al.* 2012; Rimbach *et al.* 2015). High numbers of interaction partners (Wren *et al.* 2016) and central network positions (VanderWaal *et al.* 2013; Rimbach *et al.* 2015; Friant *et al.* 2016a) are the most common predictors of high infection risk. Although predominantly transmitted via the environment, close social contact can contribute to transmission to GI parasites, (Hernandez & Sukhdeo 1995; MacIntosh *et al.* 2012; González-Hernández *et al.* 2014; Friant *et al.* 2016b), leading to heterogeneous results in assigning social behaviours to parasite exposure. The contributions of environmental and social factors to the transmission of GI parasites depend on the parasite in question, yet are difficult to identify, as often environmental exposure is not measured (Pebsworth *et al.* 2012; Grear *et al.* 2013). In this thesis, I aim to disentangle these two components of GI parasite transmission.

1.2 Gastrointestinal parasites

Parasitism is rather the norm than the exception in the animal kingdom (Grencis *et al.* 2014). Pathogens causing severe diseases, e.g. AIDS, tuberculosis, anthrax and malaria receive high levels of attention in humans and wildlife (Rothenberg *et al.* 1998; Nunn & Heymann 2005; Leendertz *et al.*

2006, 2010; Vicente *et al.* 2007; Di Fiore *et al.* 2009; Drewe 2009; Deeks 2011). In comparison, mild diseases, like helminth infections, are often neglected (Hotez *et al.* 2005; Bethony *et al.* 2006; Ghai *et al.* 2014), despite their strong implications for host health and evolution (Freeland 1976; Hawley & Altizer 2011; Ezenwa & Jolles 2015; Ezenwa *et al.* 2016). Helminths is a general term describing a large group of parasitic worms within the phyla *nematoda* and *platyhelmintha* (Díaz & Allen 2007). Here, I will restrict myself to discussing environmentally transmitted GI helminths, including, *Ascaris spp.* and *Trichuris spp.* and strongyle nematodes like hookworms (*Ancylostoma* spp. and *Nercator* spp.), *Trichostrongylus* spp. and *Oesophagostomum* spp..

GI helminth infections are highly prevalent in humans, with an estimated 2 billion people infected (Nutman 2015), yet are surprisingly neglected in human medical research (Bethony *et al.* 2006; Ojha *et al.* 2014). Infections can cause morbidity, developmental retardation and serious complications in severe infections (Degarege *et al.* 2014; Nutman 2015), yet often do not cause overt symptoms (Nutman 2015). Sharing long co-evolutionary histories, host immune systems evolved in GI-helminths presence (Yazdanbakhsh *et al.* 2002; Carvalho *et al.* 2009; Jackson *et al.* 2009). The hygiene hypothesis proposes that absence of infections leads to immune dysregulation (Yazdanbakhsh *et al.* 2002; Carvalho *et al.* 2009), culminating in allergies and asthma (Kitagaki *et al.* 2006; Briggs *et al.* 2016). The immunomodulatory potential of helminths (Nutman 2015) has even resulted in infections being used as therapeutic intervention for inflammatory, autoimmune and allergy-related diseases (Cooper 2002; Lopes *et al.* 2016; Hansen *et al.* 2017). As a consequence, their status as a pathogen is still debated. Similar to infection in humans, GI helminths usually do not cause overt symptoms in wildlife (Stien *et al.* 2002; Krief *et al.* 2008). Nonetheless, GI helminth infections can severely impact hosts on individual and population levels (Tompkins *et al.* 2011), and are a powerful tool to study behavioural and evolutionary host-parasite feedback loops (Tompkins & Begon 1999; Tompkins *et al.* 2011), which led to their increasing importance for the study of wildlife health (Hawley & Altizer 2011; Martin *et al.* 2011; Pedersen & Babayan 2011).

1.2.1 Studying GI helminth infections: Chances and challenges

Soil transmitted helminths have complex, often host specific, life cycles, yet share an essential environmental life cycle stage: eggs are shed in the faeces of infected host and develop into infective stages in the environment, with the time to infectivity depending on species and environmental conditions (Dash 1973; Bethony *et al.* 2006; Viney 2017). Infective stages can be mobile, like strongyle nematode larvae (Dash 1973; Ojha *et al.* 2014), or immobile, like embryonated *Trichuris* eggs (Stephenson *et al.* 2000a). The most common infection route is ingestion of infective stages upon contact with contaminated soil or food. Hookworm and strongyloides larvae can also pierce the skin of the host to initiate infections (Loukas *et al.* 2005; Bethony *et al.* 2006; Viney 2017). Within hosts, helminths develop into adult worms, sometimes passing through multiple organ systems (Hotez *et*

al. 2004; Bethony *et al.* 2006), and begin producing eggs to be shed in faeces, completing the life cycle.

GI helminth infections can be assessed noninvasively via standardized, routinely used coproscopic methods for detection and quantification of egg shedding (Gillespie 2006). As egg morphology can be highly similar between different taxa, identification beyond the genus or taxon level can be challenging. Molecular methods like genotyping (Gasser *et al.* 1999; McLean *et al.* 2012; Roeber *et al.* 2013), identification based on larval morphology (Ota *et al.* 2015), and combined coproscopic and molecular approaches (Budischak *et al.* 2015a; Ota *et al.* 2015) complement microscopic approaches. Egg shedding patterns can be closely correlated to actual worm burden (Roberts & Swan 1981; Seivwright *et al.* 2004), but are not always (Christensen *et al.* 1995; Roepstorff *et al.* 1996). Additionally, infected individuals do not consistently excrete eggs, but characteristics, like age, sex, and reproductive status (Klein 2004) can alter egg shedding patterns. Microscopic analyses are subject to uncertainty due to e.g. detection sensitivity leading to statistical non-detection of low egg numbers in faeces. Consequently, reliable infection assessment requires multiple samples per individual (Gillespie 2006).

1.2.2 Host-parasite interactions

1.2.2a Parasites and host physical condition

Infections with GI helminths correlate with poorer nutritional status from mice to men (Stephenson *et al.* 2000a; Ezenwa 2004b; Irvine *et al.* 2006; Szyszka & Kyriazakis 2013). Mounting immune responses is energetically costly (Ing *et al.* 2000; Bonneaud *et al.* 2003; Derting & Compton 2003; Forbes *et al.* 2016), and failing to meet the energetic demands of immune reactions can increase infection susceptibility. Poorer nutritional status increases GI helminth susceptibility in e.g. rodents (Ing *et al.* 2000; Forbes *et al.* 2016), ruminants (Coop & Kyriazakis 1999) and ungulates (Ezenwa 2004b). Diet also influences susceptibility, with a major role of low protein availability, increasing the risk of GI helminth infections (Chandra 1997; Ing *et al.* 2000; Koski & Scott 2001).

Infections with GI helminths in turn impact host nutritional status due to energy demands of immune responses, reduced food intake (Sykes & Coop 1976; Crompton & Nesheim 2002), impaired nutrient absorption (Coop & Holmes 1996; Koski & Scott 2001; Greer *et al.* 2005) and dietary changes (Kyriazakis *et al.* 1998). Infections can have detrimental effects on hosts, measurable as slower development (Sykes & Coop 1976; Adams *et al.* 1994; Greer *et al.* 2005), lower reproductive success (Coop & Holmes 1996), decreased survival (Gulland 1992; Murray 2002; Pedersen & Greives 2008), and impaired cognitive development in human children (Eppig *et al.* 2010; Degarege *et al.* 2014). Feedback-loops between infection status and host condition can give rise to vicious circles (Koski & Scott 2001) and make determining the directionality of the nutrition-parasite link challenging (Coop & Kyriazakis 1999; Beldomenico & Begon 2010).

1.2.2b Parasite-immune interactions

GI helminth infections profoundly affect the host's immune systems via multiple pathways. HPA axis activation, vital for regulating energy metabolism and inflammatory immune reactions (Hart 1988; Konsman *et al.* 2002), is often linked with GI helminth infections (Pedersen & Greives 2008; Friant *et al.* 2016b). The directionality of the relationship is often unclear, as acute GI helminth infections can induce HPA axis activation, while immunoregulatory effects of HPA dysregulation can increase susceptibility to infections (Apanius 1998; Glaser & Kiecolt-Glaser 2005; Beldomenico & Begon 2016). Similar to nutritional status, the negative effects of stress and infection can exacerbate each other (Beldomenico & Begon 2016).

In addition to acute responses to tissue damage caused by GI helminths, infections elicit specific immune responses, which are generally characterised by strong Th2 activation and anti-inflammatory in nature (Loukas *et al.* 2005; Carvalho *et al.* 2009). Preferential Th1 or Th2 responsiveness is a genetic trait (Else & Grencis 1991; Ezenwa *et al.* 2010), and individuals failing to mount strong Th2 responses generally suffer from chronic rather than transient GI helminth infections (Else & Grencis 1991). More mixed Th1-Th2 responses have been described (Anthony *et al.* 2007) in humans (Pit *et al.* 2001) and experimental studies on pigs (Andreasen *et al.* 2015, 2016), emphasizing the specificity of host immune responses to GI helminths. The two arms of the immune system are mutually inhibitory (Long & Nanthakumar 2004), so a shift towards Th2 type responses decreases Th1 response efficiency. GI helminths are therefore powerful immune modulators (Jackson *et al.* 2009) that can affect hosts' immune efficiency against various parasites (Cox 2001; Lello *et al.* 2004; Graham 2008; Vaumourin *et al.* 2015). GI helminths also actively manipulate host immune signalling in their favour by excreting secretory products (Hsieh *et al.* 2004; Hewitson *et al.* 2009; Grencis *et al.* 2014). Human hookworms and murine *Trichuris,* for example, increase host γ-interferon (IFNγ) signalling, inducing Th1 prone responses (Grencis & Entwistle 1997; Hsieh *et al.* 2004; Hewitson *et al.* 2009). Immunomodulatory effects of GI helminth infections can even persist after parasite clearance (Wright *et al.* 2009) and thus influence hosts beyond acute infections (Jackson *et al.* 2009).

1.2.2c Parasites and host behaviour

Given the profound impact of GI helminth infections on host physiology, their influence on host behaviour is unsurprising. Injuries and infections induce sickness behaviour (Hart 1988), a range of behavioural changes aimed at limiting infection costs and increasing survival chances (Hart 1988; Kyriazakis *et al.* 1998; Konsman *et al.* 2002; Dantzer 2004). Sickness behaviour is mediated by inflammatory cytokine signalling (Dantzer 2001; Konsman *et al.* 2002), induced by e.g. tissue damage in the gut mucosa in the case of GI helminth infections (Dash 1973; Hotez *et al.* 2004; Hsieh *et al.* 2004). Behavioural changes include lethargy and reduced activity, social withdrawal, heat conserving body postures, and anorexia, all contributing to energy conservation and immune response efficiency (Kyriazakis *et al.* 1998; Konsman *et al.* 2002; Hennessy *et al.* 2014). There is ample evidence for

sickness behaviour responses to GI helminths, e.g. reduced activity in cattle (Szyszka & Kyriazakis 2013) and primates (Ghai *et al.* 2015; Chapman *et al.* 2016; Friant *et al.* 2016b), reduced food intake in ruminants (Sykes & Coop 1976; Greer *et al.* 2005) and reduced foraging in infected red-capped mangabeys (*Cercocebus torquatus*) (Friant *et al.* 2016b).

Hosts employ several behavioural strategies to avoid infections (Hart 2011; Curtis 2014), like adapting foraging behaviour (Keymer *et al.* 1983; Hutchings *et al.* 2002; Gunn & Irvine 2003), alternating between territoriality and roaming (Ezenwa & Snider 2016) and avoiding contact with faecal contamination (Curtis 2014; Sarabian & MacIntosh 2015; Amoroso *et al.* 2017; Weinstein *et al.* 2018) to avoid exposure to infective parasite stages. Individuals also avoid direct contact to conspecifics likely to transmit parasites (Curtis 2014): mice express preferences for non-parasitized mating partners (Ehman & Scott 2002), and mandrills (*Mandrillus sphinx*) avoid grooming individuals infected with unicellular GI parasites (Poirotte *et al.* 2017). Infection status is likely assessed via olfactory cues (Ehman & Scott 2002; Olsson *et al.* 2014; Poirotte *et al.* 2017). Contracting GI helminth infections directly from infected conspecifics is unlikely due to their environmental transmission, yet avoiding infected individuals can be adaptive when GI helminth infections correlate with more directly transmissible infections.

1.2.2d Coinfection

GI helminth infections can protect from infection with other helminth taxa as a result of cross-immunity and within host competition (Cox 2001; Lello *et al.* 2004; Vaumourin *et al.* 2015), or increase host susceptibility to infection via immunosuppression (Lello *et al.* 2004). In pigs coinfected with *Trichuris* and *Oesophagostomum*, for example, antibody responses against *Oesophagsotomum* were markedly increased compared to single infections. Within host helminth-helminth interactions can be quite complex, with multiple species impacting each other, including positive feedback loops (Lello *et al.* 2004). GI helminths can also alter host susceptibility to a variety of microparasites and influence duration, severity and transmission of infections (Vaumourin *et al.* 2015), like in the cases of the three of the most important diseases with regard to global human health (Salgame *et al.* 2013), malaria (Hartgers & Yazdanbakhsh 2006), tuberculosis (Rafi *et al.* 2012) and HIV/AIDS (Borkow *et al.* 2007). These interactions are mostly mediated by the immunomodulatory properties of GI helminth infections (Maizels & Yazdanbakhsh 2003; Long & Nanthakumar 2004; Anthony *et al.* 2007), which can impair anti-microparasite immune control (Cox 2001; Graham 2008; Jackson *et al.* 2009). GI helminths can also limit microparasite transmission, underlining the importance of considering GI helminths for disease epidemiology in wildlife: long-term experimental parasite clearance increases Th1 immune function and individual survival in African buffaloes (*Syncerus caffer*). (Ezenwa *et al.* 2010; Ezenwa & Jolles 2015), yet simultaneously accelerates the spread of *Mycobacterium bovis* through the population due to prolonged contribution of treated individuals to *M. bovis* transmission (Ezenwa *et al.* 2010; Ezenwa & Jolles 2015). Similarly, anthelmintic treatment increases

shedding of protozoan *Eimeria* spp. in wild mice (Knowles *et al.* 2013; Pedersen & Antonovics 2013), and malaria burdens (Budischak *et al.* 2018), as blood sucking worms compete with *Plasmodia* for red blood cells as a resource (Graham 2008; Budischak *et al.* 2018). Consequently, coinfections need to be considered to understand the full impact of GI helminth infections on individual and population levels (Ezenwa & Jolles 2011; Martin *et al.* 2011; Tompkins *et al.* 2011; Ezenwa 2016).

1.2.2e Parasite defence strategies

Considering the effects of GI helminth infections on host physiology and behaviour, developing resistance, i.e. the reduction of parasite burden via efficient immune responses, appears to be an adaptive strategy. There is, however, an alternative strategy to manage infections, namely parasite tolerance, i.e. decreasing the costs of infection without affecting parasite burden (Råberg *et al.* 2009; Medzhitov *et al.* 2012). Mounting immune responses has considerable energetic costs (Colditz 2008, but see above) and can cause immunopathology in case of too strong or inadequate responses. Immunopathology can have more severe results than the damage resulting from infections, like autoimmune reactions, allergies, and severe tissue damage (Graham *et al.* 2005; Maizels *et al.* 2009). Consequently, damage rather than parasite control might be the most important goal of anti GI helminth defences (Read *et al.* 2008; Medzhitov *et al.* 2012; Råberg 2014), with optimal trade-off between costs of infection and costs of immunopathology (Medzhitov *et al.* 2012) depending on parasite pathogenicity (Greer 2008).

Tolerance to infections is measured as the slope of health costs against parasite intensity measures, i.e. weight loss with increasing egg counts, with more tolerant individuals suffering lower costs with higher infection intensity (Hayward *et al.* 2014b; Jackson *et al.* 2014). In wild Soay sheep (*Ovis aries*), tolerance is related to increased reproductive success (Hayward *et al.* 2014b), whereas females with resistance prone immune responses are characterized by increased survival of harsh winters at the expense of lower fecundity (Graham *et al.* 2010), a pattern that extends to GI helminth specific immune responses (Hayward *et al.* 2014a). There are similar trade-off between high tolerance, increasing body condition and survival at the expense of reproductive success in wild mice, with individuals shifting their strategy from resistance to tolerance as they age (Jackson *et al.* 2014). Understanding the causes and physiological correlates of resistance vs. tolerance strategies can thus profoundly contribute to our understanding of wildlife health and the impact of infections on fitness.

1.3 Study aims and approach

1.3.1 Study site and species

To assess the GI helminth related costs and benefits of sociality, I conducted my study on two groups of semi-free ranging Barbary macaques at Affenberg Salem (de Turckheim & Merz 1984) in Southwest Germany. Barbary macaques are the phylogenetically most basal species of the genus

Macaca, most closely resembling ancestral macaque species (Purvis 1995; Morales & Melnick 1998). In their natural habitat, the Atlas Mountains of Morocco and Algeria (Fooden 2007), populations are declining, and Barbary macaques are considered "Endangered" by the IUCN (van Lavieren & Wich 2010). Like macaques in general, Barbary macaques form multi-male multi-female groups with female phylopatry and male dispersal (Mehlman 1986; Aureli *et al.* 1997; Thierry 2007) with a relatively tolerant social style (Thierry *et al.* 1999). They are seasonal breeders with promiscuous mating by both sexes (Small 1990; Kuester & Paul 1992) and a mating season in winter (~October to February), followed by birth season in early summer, peaking around June (Ménard & Vallet 1997; Brauch *et al.* 2007). Like most primates, Barbary macaques differentiated social relationships (Berghänel *et al.* 2011; Young *et al.* 2014a). Males form linear dominance hierarchies, with male relationships predicting support in the frequently occurring coalitions, which are particularly frequent during the mating season (Paul *et al.* 1992; Widdig *et al.* 2000; Berghänel *et al.* 2011; Young *et al.* 2014b). Socio-positive interactions can decrease physiological stress in Barbary macaques (Shutt *et al.* 2007), yet frequent agonistic interactions and prolonged male associations with infants increase HPA axis activity (Henkel *et al.* 2010; Young *et al.* 2014a). Strong social bonds attenuate stress responses to intense aggression and cold stress in males (Young *et al.* 2014a), and social integration as well as a high number of grooming partners increase survival under harsh climate conditions (McFarland & Majolo 2013; Lehmann *et al.* 2016; Campbell *et al.* 2018), making the Barbary macaque an interesting system to study the effects of sociality on health and fitness.

The study site was Affenberg Salem, a 20 ha large outdoor enclosure of beech/spruce mixed forest (see de Turckheim & Merz 1984 for a detailed account of the population and study site). Macaques live outdoors year round under climatic conditions similar to their natural habitat. They are provided once daily with fresh fruits and vegetables and have *ad libitum* access to commercial monkey chow and water, but frequently forage on natural food sources like insects, leaves and beechnuts. Intergroup interactions are frequent and males can migrate between the groups. Two groups have daily contact with park visitors, who are restricted to a path while macaques can move freely within the entire enclosure, and all individuals are fully habituated to human presence. Semi-free ranging housing conditions with minimal human impact (de Turckheim & Merz 1984; Paul & Kuester 1988), and similar group structure and dispersal behaviour as displayed by wild individuals (Paul & Kuester 1985, 1988; Ménard & Vallet 1993; Ménard 1996) allow for studying macaque behaviour closely resembling that wild Barbary macaques.

GI parasite infections are routinely monitored in the population. *Trichuris* spp. and strongyle nematode infections are detected regularly, with *Oesophagostomum* spp. infections confirmed by presence of intestinal nodules in necropsies (Dr. Roland Hilgartner, personal communication; analyses performed by the "Staatliches Tierärztliches Untersuchungsamt Aulendorf"). The study population routinely receives anthelminthic treatment twice per year, offering an ideal opportunity

to study host-parasite dynamics in a nonhuman primate. Host-parasite interactions have mostly been studied using correlational and cross-sectional study designs (Godfrey *et al.* 2009; Fenner *et al.* 2011; MacIntosh *et al.* 2012; Rimbach *et al.* 2015), so the directionality of the links between parasite infections, host physiology and behaviour is largely unclear. Correlational studies are valuable in their own right, yet to draw causal inferences, experimental studies are needed (Pedersen & Greives 2008; Ezenwa *et al.* 2010; Ezenwa & Jolles 2015; Pedersen & Fenton 2015; Chapman *et al.* 2016; Friant *et al.* 2016a, b). Capitalizing on parasite treatment, I can investigate both directions of the relationships between host behaviour, physiology, and GI helminth infection risk to contribute to our current understanding of the links between host sociality, parasites and health.

1.3.2 Assessing health in wildlife

Assessing host physiological status and immune function under natural conditions is a vital step for studying wildlife health (Jackson 2015), yet in contrast laboratory studies, reliable markers of individual condition, stress responsiveness (beyond HPA axis activity) and immune function are not always available. Endocrinological parameters, like steroid hormones, are already routinely measured in field studies (Pedersen & Greives 2008; Muehlenbein & Watts 2010; Young *et al.* 2014a), and a multitude of immune system parameters can be assessed from blood samples, like immune cell reactivity (Ezenwa *et al.* 2010), cytokine levels (Vandeleest *et al.* 2016), antibody levels (Graham *et al.* 2010), blood parasite presence (Springer *et al.* 2015), and immune gene expression (Tung & Gilad 2013). However, handling of wild animals is not always possible for ethical and feasibility reasons, so noninvasive markers of immune function and physical condition are needed.

Recent advances in the fields of medical diagnostics and wildlife endocrinology led to the validation of several promising markers of immune function (Peterson *et al.* 2002; Reimert *et al.* 2008; Higham *et al.* 2015; Behringer & Deschner 2017) and energy balance (Deschner *et al.* 2008; Emery Thompson *et al.* 2009; Girard-Buttoz *et al.* 2011; Schaebs *et al.* 2016) from urine and faeces, two of which are employed here: urinary neopterin (uNEO), a marker of immune function, and urinary C-Peptide (uCP) immune function, a marker of physical condition.

1.3.2a Measuring immune function: urinary neopterin

The pteridin neopterin is released by macrophages, monocytes and dendritic cells in response to IFNγ stimulation and activates Th1-helper cells (Murr *et al.* 2002; Plata-Nazar *et al.* 2010). It is a general marker of Th1 immune activation and responses against intracellular pathogens (Widner *et al.* 1999; Murr *et al.* 2002) widely used in human medical diagnostics. Serum, urinary and faecal levels are linked to various diseases, including gastrointestinal infections and inflammation (Ledochowski *et al.* 2001; Husain *et al.* 2013), viral infections like HIV (Fuchs *et al.* 1988) and viral hepatitis (Reibnegger *et al.* 1988a), bacterial infections like tuberculosis (Fuchs *et al.* 1984), and non-infectious diseases like cancer (Unal *et al.* 2009; Sucher *et al.* 2010), autoimmune and coronary heart disease

(Berdowska & Zwirska-Korczala 2001). High NEO levels indicate higher disease severity and worse prognosis (Unal *et al.* 2009; Sucher *et al.* 2010). NEO is also elevated in response to acute stress (Breinekova *et al.* 2007) and physical strain (Moser *et al.* 2008), potentially due to cellular immune system activation.

NEO is cleared via the kidneys unchanged (Berdowska & Zwirska-Korczala 2001) and can reliably be measured from urine samples. NEO is relatively stable under field conditions, making it a promising marker for immune system monitoring in wildlife (Heistermann & Higham 2015; Higham *et al.* 2015; Behringer *et al.* 2017). Urinary NEO levels have been shown to track simian immunodeficiency virus infections in rhesus macaques (Fendrich *et al.* 1989; Higham *et al.* 2015) and acute respiratory disease in bonobos (*Pan paniscus*) (Behringer *et al.* 2017), providing the biological validity of NEO levels as markers of immune activation. I aimed to assess the feasibility of uNEO as a noninvasive marker of immune regulation in relation to GI helminth infections. Given the cross-inhibition of Th1 and Th2 immune responses (Long & Nanthakumar 2004) and the usually predominant Th2 response against GI helminths (Carvalho *et al.* 2009; Grencis *et al.* 2014), uNEO level variations could indicate infection with or susceptibility to GI helminth infections. These hypotheses were tested in detail in **Chapter 2** and **Chapter 4** of this thesis.

1.4.2b Measuring physical condition: urinary C-peptide

Physical condition, nutritional status and energy availability are important variables to consider for individual health, yet assessing them wild animals is not straightforward. Current methods include assessment of body weight and weight changes (Hayward *et al.* 2014a), relating body mass to body length (Peig & Green 2009), use of a combination of visual markers, such as pelage condition and visually assessed body fat (Borg *et al.* 2014; Friant *et al.* 2016b), or manual palpation, often used in combination with visual assessment (Ezenwa *et al.* 2009). While some of the scores have been validated against invasive measures of body conditions (Ezenwa *et al.* 2009), assessment based on visual cues can be unreliable if handling study animals is not possible. Measuring physiological markers of individual energetic status, like thyroid hormones linked to energy metabolism and growth (Behringer *et al.* 2014; Schaebs *et al.* 2016), and uCP, a measure of nutritional status and energy balance (Deschner *et al.* 2008), can be valid alternatives.

C-peptide, a small polypeptide of pro-insulin, is enzymatically cleaved off pro-insulin during insulin synthesis in pancreatic β-cells (Horwitz *et al.* 1975; Bonser *et al.* 1984) and released into the bloodstream in equimolar numbers with insulin. C-peptide is cleared via the kidneys (Bonser *et al.* 1984) and urinary levels closely resemble plasma insulin levels (Goetz *et al.* 2002; Tsai *et al.* 2006). uCP levels have been experimentally validated as a measure of energetic status in macaques, with levels decreasing under fasting and increasing under re-feeding conditions (Girard-Buttoz *et al.* 2011; Higham *et al.* 2011). They also track food availability, energy intake (Emery Thompson & Knott

2008; Emery Thompson *et al.* 2009), and energy expenditure (Grueter *et al.* 2014) in nonhuman primates. Consequently, uCP levels can be employed to assess individual physical condition. Measuring uCP could readily be applied for this project to address the open questions with regard to the directionality of the relationship between host nutrition and parasite infections.

1.3.2c Aging and immunosenescence

Age is one major predictor of heterogeneity in parasite distribution within a host population (Wilson *et al.* 2002; MacIntosh *et al.* 2010; Poirotte *et al.* 2016). Susceptibility to infections can be influenced by age, with the acquisition of protective immunity being a prominent example (reviewed in Wilson *et al.* 2002). If hosts develop protective immunity against a pathogen infection, infection prevalence or intensity displays a U-shaped distribution: it peaks at a young age, followed by a rapid decrease upon acquisition of protective immunity. If infections are chronic, parasites can accumulate in individuals that fail to elicit efficient immune responses (Else & Grencis 1991; Else *et al.* 1992). Immune function can be flexible and change according to individual condition and life history (Jackson *et al.* 2014). Physiological correlates of aging and senescence have attracted much attention in studies of human health, but are still largely neglected wildlife (Nussey *et al.* 2013; Reichard 2016).

Aging has profound effects on immune system regulation and efficiency, resulting from age related physical decline referred to as immunosenescence. These changes occur consistently in both the innate and adaptive immune system and include altered cytokine profiles, like increases in IFN-y and NEO levels (Frick *et al.* 2004; Murr *et al.* 2004; Leng *et al.* 2011), depletion of naïve T-cell population with simultaneous increase in differentiated T-cell population (Faria *et al.* 2008; Deeks 2011), changes of monocyte phenotypes (Hearps *et al.* 2012; Martin *et al.* 2013) and decline in innate immune response and natural killer cell function (Hawkley & Cacioppo 2004; Goodwin *et al.* 2006; Deeks 2011; Li *et al.* 2011; Solana *et al.* 2012). Another major correlate of immunosenescence is chronic low level inflammation (Fulop *et al.* 2010; Li *et al.* 2011; Solana *et al.* 2012), which can also be induced by social and physiological stress (Hawkley & Cacioppo 2004; Kiecolt-Glaser *et al.* 2010).

The changes corresponding to immunosenescence predict lower vaccination efficiency (Goodwin *et al.* 2006; Čičin-Šain *et al.* 2010) and thus indicate higher disease susceptibility. Immunosenescence is also linked to morbidity, frailty and cognitive decline in humans (Li *et al.* 2011; Parker *et al.* 2013; Wang & Casolaro 2014). Immune physiology and immune aging are comparable between humans and nonhuman primates (Haberthur *et al.* 2010; Messaoudi *et al.* 2011; Meyer *et al.* 2012; Didier *et al.* 2016). The study population at Affenberg Salem provides an excellent system to study age related variation in health and parasite susceptibility, as semi-free ranging conditions, including food provisioning and absence of predation) result in the opportunity to study a high number of senescent individuals. I focus specifically on the feasibility of uNEO levels as a marker of immunosenescence in **Chapter 2** of this thesis.

1.3.3 Behaviour and pathogen transmission

For successful transmission, susceptible host must be exposed to the respective pathogen (Hawley *et al.* 2011). For many host traits and behaviours, their roles and relative contribution to either component of transmission are not clear-cut. Physiological processes can simultaneously determine host susceptibility and behavioural patterns relating to pathogen exposure, creating either positive or negative covariation (Hawley *et al.* 2011). Dominance rank serves as an intuitive example: high ranking individuals usually express specific endocrinological patterns, often characterized by high levels of GCs and testosterone (Sapolsky 2005; Muehlenbein & Watts 2010; Archie 2013), and specific social behaviour patterns, like occupying central positions in a social network and frequently participating in agonistic or affiliative interactions (Sapolsky 2005; Drewe 2009; MacIntosh *et al.* 2012; Tiddi *et al.* 2012). Covariation between susceptibility and exposure can also explain variation of infection risk based on individual characteristics, like sex and rank (Habig & Archie 2015; Habig *et al.* 2018).

Both components of transmission and their respective links with behaviour have been intensely studied (Altizer *et al.* 2003; Cohen *et al.* 2003; Ezenwa 2004a; Sapolsky 2004, 2005; Pedersen & Greives 2008; Muehlenbein & Watts 2010), yet studies assessing both processes simultaneously are relatively rare (MacIntosh *et al.* 2012; Friant *et al.* 2016a), and covariation between exposure and susceptibility has been largely neglected (Hawley *et al.* 2011). Consequently, to which extend certain behaviours contribute to exposure, susceptibility, or both, is still largely unclear. Here, I investigate the role of several exposure and susceptibility measures on GI helminth transmission simultaneously to provide a more complete picture of the interplay between host physiology, behaviour and parasite infections in **Chapter 4**.

1.3.4 Specific aims and contributions to the field

The overall aim of this study is to provide a comprehensive picture of the relationship between GI helminths and their host, the Barbary macaque (illustrated in Figure I), with special focus on the role of social relationships. Taking advantage of experimental strongyle nematode clearance, I test the directionality of the relationships between host physiology, behaviour and strongyle nematodes, assessing costs of infections and predictors of reinfection.

In **study 1 (Chapter 2)**, I focus on assessing the feasibility of uNEO as a marker for immune function in semi-free ranging Barbary macaques at Affenberg Salem. I take two predictors of uNEO levels into account: Anthelmintic treatment, as parasite clearance could shift Th1/Th2 immune balance towards Th1-type responses, and aging, as NEO levels correspond with a range of markers of immunosenescence in humans and nonhuman primate models of aging.

In **study 2 (Chapter 3)**, I investigate the consequences and potential health costs of strongyle nematode infection linking host physiology and behaviour to parasite infections. To account for

uncertainty in noninvasively assessed infection status, I estimate infection probabilities using patch occupancy modelling. I test if individual infection probability affects HPA axis activation (fGCM levels), body condition (uCP levels) and activity (proportion of time individuals spent active vs. resting) as estimates of sickness behaviour. I also test whether social behaviour is influenced by parasite clearance and which underlying process, sickness behaviour or avoidance of infected conspecifics, explains these changes by including both own and partner infection status as predictors of individual proximity initiations.

In **study 3 (Chapter 4)**, I assess the predictors of reinfection after strongyle parasite clearance. I include measures of exposure and susceptibility and use a combination of patch occupancy modelling and information theoretic model selection to find the models best predicting reinfection patterns. To test whether social bonds protect from infection via reduced susceptibility, I include a measure of social bond strength for same and opposite sex partners. I include fGCM, uCP and uNEO levels and coinfection with further helminths as physiological measures of susceptibility. To disentangle environmental and social components of transmission, I include measures of environmental exposure (individual space use and exposure to faecal contaminations on the soil), and social contact (grooming) simultaneously.

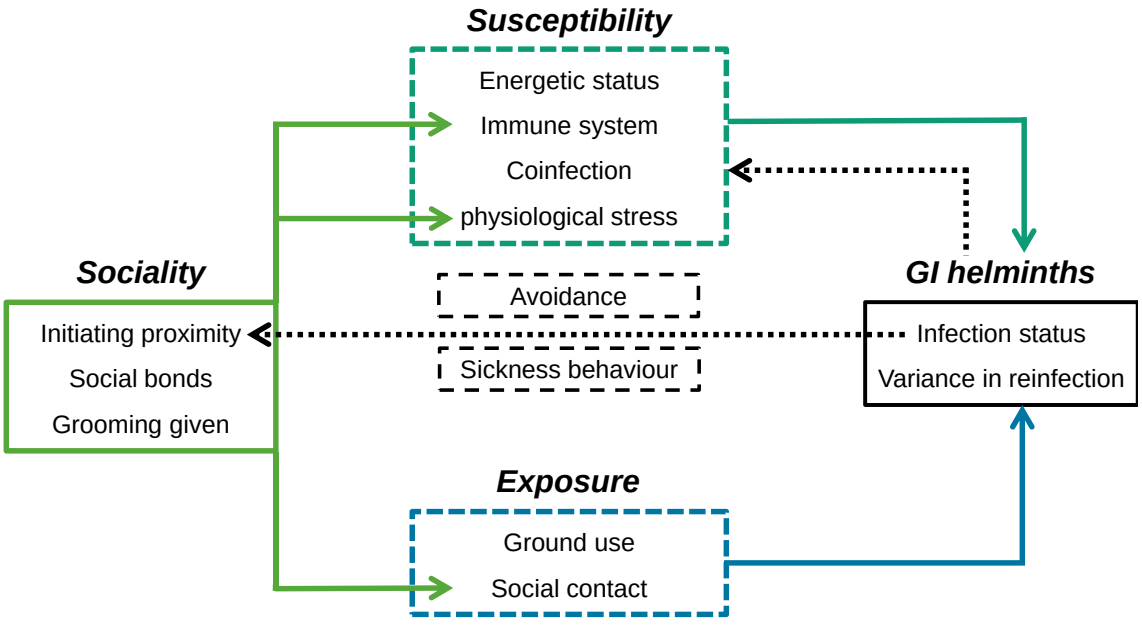

Figure I: Flowchart illustrating the links investigated in this thesis, with solid lines indicating the host to parasite and dashed lines the parasite to host direction. Arrowheads ending at the respective boxes indicate the entire aspect is potentially influenced, while arrowheads crossing into the boxes represent a link to a specific measure. Parasite clearance after anthelmintic treatment allows me to test the connections in both directions.

Chapter 2

Age, but not anthelmintic treatment, is associated with urinary neopterin levels in semi-free ranging Barbary macaques

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Abstract

Studying host parasite interactions and their implications for evolution and ecology recently received increasing attention, particularly with regard to host physiology and immunity. Here we assess variation of urinary neopterin (uNEO), a marker of cellular immune activation and immunosenescence, in response to age and anthelmintic treatment in semi-free ranging Barbary macaques (*Macaca sylvanus*). Urinary NEO levels were measured via enzyme-immunoassay from 179 urine samples of 43 individuals between 5-29 years of age. Efficiency of treatment was assessed by Mc Master flotation on repeated faecal samples, including 18 untreated individuals as control group. We used linear mixed models with age and parasite status as main effects, controlling for sex and physical condition, assessed through urinary C-peptide levels, with social group and ID as random factors. Urinary NEO levels significantly increased with age, suggesting that changes in aging Barbary macaque immune responses are consistent with immunosenescence described in humans and nonhuman primates and can be detected via uNEO measurements. Anthelmintic treatment, however, had no influence on uNEO levels, potentially due to quick reinfections or attenuated immune responses in repeated infections. We conclude that uNEO is a potential non-invasive marker for immune function and particularly immunosenescence in wildlife.

Chapter 3

Physiological and social consequences of gastrointestinal nematode infection in a nonhuman primate

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Abstract

Gastrointestinal nematodes are intensely studied models for host–pathogen interactions in wildlife, yet consequences of infections are not fully understood. Among the potential costs of nematode infection are physiological changes caused by immune system activation, reduction or reallocation of available energy, as well as potential social consequences in terms of decreased social activity or avoidance of infected individuals. We used experimental anthelmintic treatment to investigate effects of strongyle nematode infection in Barbary macaques (*Macaca sylvanus*), comparing 56 treated to 17 untreated individuals. Deworming success was monitored by coproscopy and infection probability estimated from patch occupancy models. Increasing strongyle infection probabilities were associated with increased fecal glucocorticoid metabolite levels and slightly decreased activity and had no significant effect on energy balance quantified as urinary C-Peptide levels. The frequency to approach into close spatial proximity of a partner was predicted by the partner's, but not focal individual's infection status, with a tendency toward infected individuals being approached less frequently. Although effects were weak, they suggest a co-occurrence of sickness behavior and avoidance of infected conspecifics, both possibly shaping social interaction patterns with potential consequences for an individual's social relationships. This study adds to the growing body of research on the complex interactions of sociality, health, and fitness in a group living species.

***Keywords*: avoidance behavior, parasites, physiology, primates, sickness behavior**

Chapter 4

Exposure and susceptibility drive reinfection with gastrointestinal parasites in a social primate

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Abstract

1. Increased risk of infectious disease transmission has been proposed as one major cost of group living. While factors corresponding to transmission via exposure to infectious stages and susceptibility to contracting infections upon contact are relatively well understood, both aspects are rarely investigated simultaneously.
2. Here, we assessed the influence of exposure and susceptibility measures on strongyle nematode reinfection after experimental deworming of Barbary macaques (*Macaca sylvanus*) (n=57). We investigated impacts of behaviour (social bonds, grooming and ground use) and physiology (faecal glucocorticoids, urinary C-Peptides, urinary neopterin, gastrointestinal [GI] helminth coinfection) on the likelihood of reinfection, using patch occupancy modelling and information theoretic model selection to determine the best models predicting reinfection patterns.
3. Coinfection was the most consistent risk factor, spending time on presumably contaminated soil, interacting with many partners and forming strong same sex bonds also tended to increase infection risk. In contrast, strong social bonds with opposite sex partners had a consistently protective effect.
4. Our results indicate that coinfections could serve as an integrative measure of individual disease susceptibility. Furthermore, we show that social contact contributes to both exposure and susceptibility to environmentally transmitted parasites, with the outcome depending on specific interactions patterns.

***Keywords*: anthelmintic treatment, exposure, gastrointestinal parasites, nonhuman primate, reinfection, susceptibility, social relationships**

Chapter 5

General Discussion

In the following chapter, I will summarize and discuss the host-parasite interactions between Barbary macaques and strongyle nematodes with a specific focus on the role of sociality. Having established the effectiveness of treatment against strongyle nematodes in **Chapters 2, 3 and 4**, I will discuss causes and effects of infections, drawing stronger causal inferences than possible in correlational studies. I will set the results in context with the current knowledge of the connections between parasites, behaviour and physiology in wildlife, particularly primates. To this end, I will discuss the impact of GI helminths on health related parameters and the factors predicting reinfections, with regard to both physiology and behaviour. I will briefly discuss the connection between aging and GI helminth infections and the role of aging for individual health parameters. Drawing on results on the relationship between social behaviour and parasite infections, I will discuss how GI helminths can influence sociality and impact social evolution. I will end with an outlook on steps for future research needed to disentangle the roles of social interactions for exposure and susceptibility and to further our understanding of host-behaviour-physiology relationships and their evolutionary implications in wildlife.

5.1 Consequences of GI helminth infections

To ensure their own reproductive success and transmission, GI nematodes usually do not cause overt sickness in their hosts (Greer 2008; Krief *et al.* 2008). In our study population, infection with strongyle nematodes, most prominently *Oesophagostomum* spp., was the norm rather than the exception, with generally low egg counts and comparably low variation in egg shedding (see Figure II). As individuals are likely faced with trickle infections and constant reinfection, persistent egg shedding does not necessarily represent chronic infection, but can also result from a balance between parasite clearance and becoming reinfeced (Wilson *et al.* 2002). Faecal egg counts are not always related to actual worm burden in *Oesophagostomum* infections (Christensen *et al.* 1995; Roepstorff *et al.* 1996), with lowest egg shedding in pigs infected with the highest number of larvae in an experimental study (Christensen *et al.* 1995). Thus, it is difficult to assess parasite resistance in my dataset, but the absence of natural parasite clearance is not necessarily suggestive of a lack of protective immunity (Grencis *et al.* 2014). Despite the overall low egg counts and absence of obvious behavioural signs of infections, infections are not arbitrary to Barbary macaques, as became apparent upon closer investigation of the physiological and behavioural consequences relating to infection.

Treatment did not influence Th1 immunity, measured as uNEO **(Chapter 2)**, but fGCM levels were associated with infection **(Chapter 3)**, with higher levels in infected individuals (Fleming 1997; Pedersen & Greives 2008; Friant *et al.* 2016b), indicating that GI helminths lead to HPA axis activation (Friant *et al.* 2016b). Given the ubiquity of strongyle infections and the low likelihood of natural parasite clearance in the study population (see **Chapter 3** Figure 1), it is likely that infections lead to higher baseline fGCM levels. As chronic HPA axis activation and GI helminth infection generally lead to suppression of immune function and lowered Th1 responses (Maizels & Yazdanbakhsh 2003; Glaser & Kiecolt-Glaser 2005; Grencis *et al.* 2014), this could be considered a health cost with potentially detrimental consequences (Apanius 1998; Glaser & Kiecolt-Glaser 2005).

Individuals infected with strongyle nematodes were less active **(Chapter 3)**, which, like elevated fGCM levels, can be a sign of inflammatory cytokine induced sickness behaviour (Hart 1988; Dantzer 2009). Inflammatory responses due to tissue damage are common in GI helminth infections (Stephenson *et al.* 2000a; Loukas *et al.* 2005; Bethony *et al.* 2006), resulting also from larval encystation in the gut mucosa in case of *Oesophagostomum* infections (Dash 1973; Krief *et al.* 2008; Terio *et al.* 2016). Similar associations of GI helminth infections and reduced activity have been described in correlational (MacIntosh *et al.* 2011; Ghai *et al.* 2014) and experimental studies (Adams *et al.* 1994; Chapman *et al.* 2016; Friant *et al.* 2016b) and interpreted as an attempt to conserve energy (Hart 1988; Dantzer 2001; Konsman *et al.* 2002), or as a result of decreased physical condition due to infection (Coop & Kyriazakis 1999; Ezenwa 2004b). In the present study, physical condition, monitored by uCP levels, was not affected by strongyle nematode infections **(Chapter 3)**. The results closely resemble those of a recent parasite clearance study on semi-free ranging, provisioned mangabeys, reporting increased GC levels and decreased activity prior to treatment, but no relationship between GI nematodes and body condition (Friant *et al.* 2016b), maybe suggestive of a general primate-parasite interaction pattern. The absence of an effect of parasites on physical condition may be the result of provisioning, allowing ample access to high quality food and buffering against nutritional costs of GI nematode infection in both studies, or effectiveness of energy conservation via reduced activity. Considering the suggested effect of high uCP levels leading to increased reinfection risk in the study population at Affenberg **(Chapter 4)**, I suggest the alternative interpretation that good physical condition during persisting infections can result from parasite tolerance as a defence strategy to mitigate the costs of GI parasite infections.

Faced with GI helminth infections and the likelihood of chronic infections (Grencis *et al.* 2014), there are essentially three available strategies: avoidance, which I will discuss in detail below, resistance, and tolerance (Råberg *et al.* 2009; Hart 2011; Medzhitov *et al.* 2012; Curtis 2014). The overall picture in the study population is suggestive of the presence of tolerance mechanisms in response to strongyle infections, which is not mutually exclusive with resistance (Hayward *et al.* 2014a). Considering the low pathogenicity of GI helminths under normal conditions (Greer 2008;

Krief *et al.* 2008), the idea that health costs do not necessarily result from infections, but are consequences of immunopathology and unchecked immune responses (Graham *et al.* 2005; Colditz 2008), has been put forward. Experimental GC level elevations led to higher egg counts, but prevented reduction in weight gain in an experimental study in lambs (Greer *et al.* 2005), indicating a potentially beneficial role of HPA axis activity induced immunomodulation. Similarly, Soay sheep mounting strong resistance responses to GI helminth infections suffered from poorer physical condition than those more tolerant of GI infections (Hayward *et al.* 2014a, b). My results suggest that individuals with high uCP levels prior to treatment become reinfected quicker **(Chapter 4)**. Evidence from both humans and ungulates suggests that parasite burdens after anthelmintic treatment return to levels similar to those before treatment (Grencis *et al.* 2014; Budischak *et al.* 2016), indicating some predisposition to infections. Assuming similar processes in Barbary macaques, high pre-treatment physical condition predicting earlier reinfection can be interpreted as a sign of tolerance rather than higher susceptibility to strongyle infections.

There was no evidence for parasite induced suppression of Th1 immune responses, i.e. lower uNEO levels in infected individuals (Murr *et al.* 2002; Ezenwa *et al.* 2010). This suggests that individuals did not mount strong Th2 responses (Long & Nanthakumar 2004), which could lead to chronic rather than transient GI nematode infections (Else & Grencis 1991; Urban *et al.* 1992; Else & Finkelman 1998). A possible benefit is the mitigation of the energetic costs of mounting an immune response (Bonneaud *et al.* 2003; Derting & Compton 2003) and prevention of increased susceptibility to microparasite infections as a result of parasite induced Th2 immune dominance (Graham 2008; Salgame *et al.* 2013; Ezenwa & Jolles 2015). Testing whether strongyle infections indeed contribute to microparasite transmission or disease progression is beyond the scope of this thesis, but instead of being detrimental, the immunomodulatory effects of GCs could be a sign of parasite tolerance and advantageous, with higher levels in infected individuals leading to increased long-term fitness and health.

The relationship between parasite infection and tolerance is likely not as straightforward as presented here, and distinguishing tolerance from resistance is difficult as mechanisms mediating parasite resistance and tolerance can result in very similar physiological outcomes. Tolerance is typically measured by assessing the costs of infection in relation to infection severity, with tolerant individuals characterized by lower health costs of higher pathogen burdens (Råberg *et al.* 2009; Medzhitov *et al.* 2012; Hayward *et al.* 2014b). Intriguingly, the levels of tolerance vs. resistance displayed by the host could play a role in explaining why GI helminth infections in primates are usually subclinical, but can be detrimental and even cause mortality (Hotez *et al.* 2005; Bethony *et al.* 2006; Krief *et al.* 2008; Degarege *et al.* 2014; Terio *et al.* 2016). Additionally, there is likely not one optimal strategy to handle GI helminth infections: tolerance has been linked to a trade-off between reproduction and physical condition repeatedly (Hayward *et al.* 2014a, b; Jackson *et al.* 2014), with

increased chances of survival after investing in physical condition coming at costs for reproductive success (Graham *et al.* 2010; Hayward *et al.* 2014b). Understanding the health and fitness consequences of employing different defence strategies and under which conditions tolerating infections is more advantageous than mounting immune responses aimed at parasite clearance will be important steps in future research on the impact of GI helminth infections on host evolution.

Parasites can change host behaviour via social withdrawal connected to sickness behaviour, and behavioural strategies of infection avoidance (Dantzer 2004; Medzhitov *et al.* 2012; Hennessy *et al.* 2014; Eisenberger *et al.* 2017). In past studies on nonhuman primates, reduced sociality has been attributed to avoidance of infected individuals (Chapman *et al.* 2016; Friant *et al.* 2016b) rather than sickness behaviour. Both mechanisms are not mutually exclusive and can even reinforce each other, i.e. infected individuals avoiding others likely to be infected in order to avoid exposure to further, especially directly transmitted, pathogens (Curtis 2014; Eisenberger *et al.* 2017). To test whether social behavioural changes result from sickness behaviour or avoidance, I analysed behavioural changes in response to GI helminth infection on a dyadic level, accounting for both individual and potential partner infection status.

Despite the reduced activity in response to infection, individuals did not initiate proximity less often or depart more often from others if they were infected with GI helminths **(Chapter 3)**. This illustrates the importance of maintaining social bonds for social animals like nonhuman primates (Silk *et al.* 2009; Micheletta *et al.* 2012; Ostner & Schülke 2014), even in situations where energy needs to be allocated away from overall activity. Instead, individuals seemed to avoid infected conspecifics, as they were less likely to approach infected partners. Avoiding infected individuals is frequently reported for directly transmitted unicellular parasites (Kavaliers & Choleris 2011; Curtis 2014; Poirotte *et al.* 2017) and GI helminths (Kavaliers & Colwell 1995). Avoidance is likely mediated by olfactory cues (Kavaliers & Colwell 1995; Hennessy *et al.* 2014; Poirotte *et al.* 2017) corresponding to innate immune system activation (Olsson *et al.* 2014). Therefore, it is probably not directed towards GI helminth infected conspecifics, but rather to individuals displaying general signs of sickness and infection (Hart 2011; Curtis 2014). Although Th1 responses were not obviously influenced in my study population **(Chapter 2)**, strongyle infections could be predictive of infections with microparasites (Cox 2001; Fenton *et al.* 2008; Graham 2008) transmitted via physical contact (Balasubramaniam *et al.* 2016; Poirotte *et al.* 2017; Springer *et al.* 2017), with avoidance as a viable strategy to minimize the risk of disease transmission.

At first sight, given the overall tendency of reduced social contact linked to inflammatory cytokine mediated sickness behaviour (Hennessy *et al.* 2014; Eisenberger *et al.* 2017) and infection with GI parasites (Chapman *et al.* 2016; Friant *et al.* 2016b), the absence of social withdrawal as part of sickness behaviour in the study population seems counterintuitive. However, the expression of sickness behaviour in response to inflammatory cytokines is context dependent in laboratory studies

and can be suppressed in e.g. mating or pup rearing context (Hennessy *et al.* 2014). Furthermore, in both rodents and rhesus macaques, inflammatory signalling can lead to increased social contact (Willette *et al.* 2007; Hennessy *et al.* 2014; Eisenberger *et al.* 2017), especially with familiar partners. Faced with infection, seeking out social support may be beneficial for survival and even contribute to enhanced immune efficiency (Hennessy *et al.* 2014), e.g. if social interactions convey thermoregulatory benefits (McFarland *et al.* 2015). Consequently, individuals could adapt their social behaviour to their own infection status and their social environment, i.e. infection status of available partners, simultaneously, creating complex interactions between sociality and GI nematode infection. If individuals with similar social environments are also experience similar exposure and susceptibility to infections (Hawley *et al.* 2011; Ezenwa *et al.* 2016), parasite infections could contribute to sub-structuring within a social group. High clustering within networks can reduce transmission of pathogens and overall parasite prevalence within a group (Griffin & Nunn 2012; Nunn *et al.* 2015), adding a further level of complexity.

Strongyle infections did not appear to alter immune function in Barbary macaques, but immune-parasite interactions could be influenced by individual aging. In the study population, uNEO levels increased with age **(Chapter 2)**, resembling patterns in humans (Hawkley & Cacioppo 2004; Murr *et al.* 2004; Deeks 2011; Didier *et al.* 2016) and indicative of decreasing immune function in older individuals (Murr *et al.* 2004). Older Barbary macaques did not only suffer from decreased immune function, but also experienced increased fGCM levels, reduced activity and poorer physical condition, observations often made in aging primates and humans (Fulop *et al.* 2010; Didier *et al.* 2016). These findings are also in line with increased low level inflammation in older individuals (Hawkley & Cacioppo 2004; Deeks 2011).

Lacking longitudinal data, I can only speculate on the directionality between GI parasite infection and age related physiological changes, yet want to argue that parasite infections were likely the result, not the cause of age-related decline of immune function. Egg shedding patterns in individuals aging a few months to almost 30 years were age dependent (see Figure II). For strongyle nematodes, egg counts remained largely constant after increasing for the first few years of life, with higher variation and counts in aged individuals. For the concomitant GI helminth taxa at Affenberg, *Capillaria* spp. and *Trichuris* spp., egg shedding patterns roughly followed a U-shaped distribution. Egg shedding peaked early in life, ceased by the time individuals reach adulthood and resumed in old individuals, with increasing egg counts as aging progressed.

Increased GI parasite richness with older age is common in primates and reported for e.g. Japanese macaques (MacIntosh *et al.* 2010) and Capuchin monkeys (*Cebus capucinus*) (Parr *et al.* 2013). The absence of parasite eggs throughout most of adult life suggests that the Barbary macaques of my study population developed protective immunity or strong immune responses capable of clearing

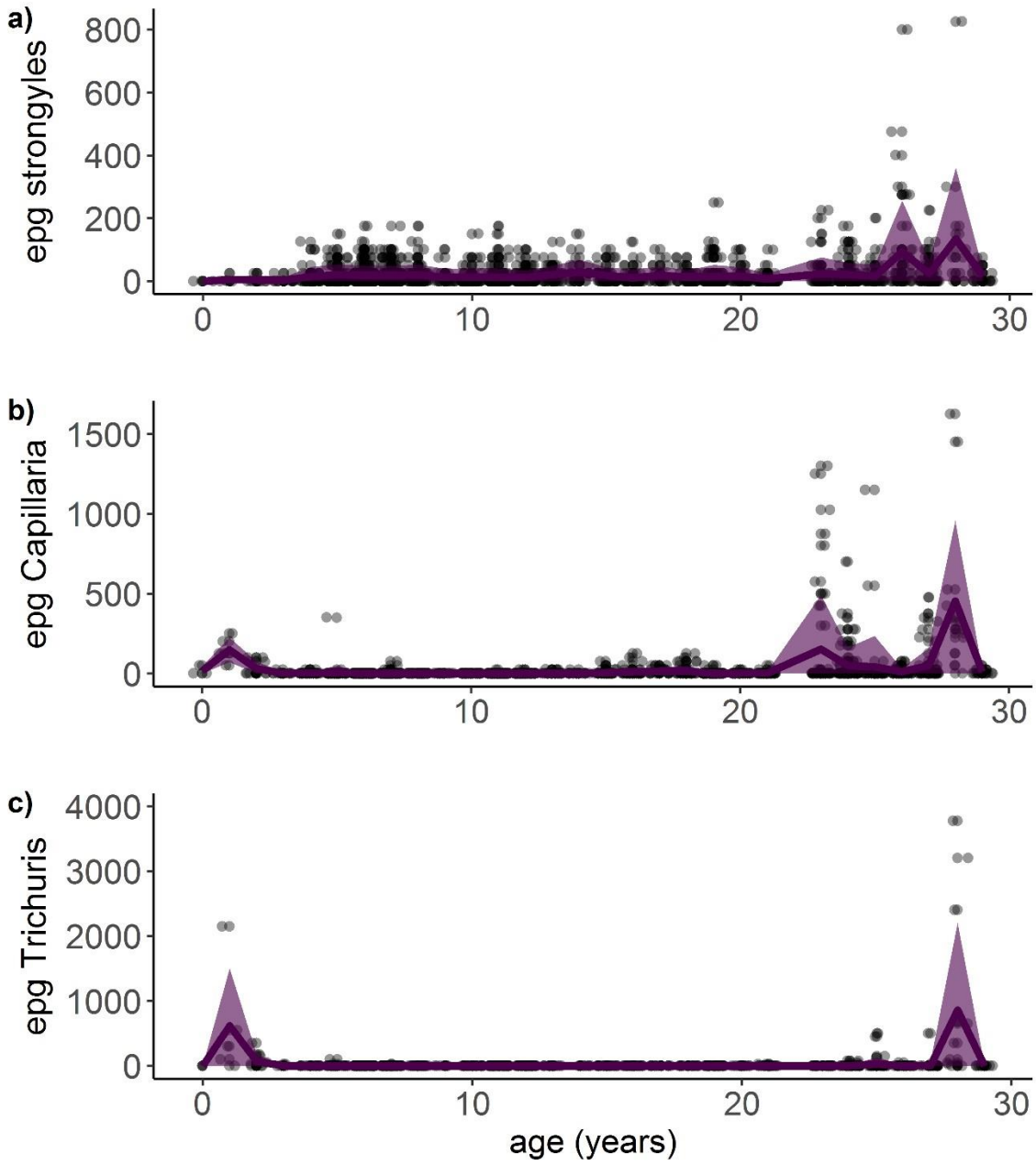

Figure II: Overview over eggs per gramm faces (epg), including 1436 samples analysed for focal individuals and additional 46 samples of infant to subadult individuals not included in the study. Data represent the age range of the Barbary macaques at Affenberg Salem, ranging from infants (individuals younger than one year coded as 0) to 29 years of age. Datapoints represent individual samples, lines mean eggs per gram faeces (epg) shaded areas the corresponding standard deviations of epg.

Capillaria and *Trichuris* infections (Else *et al.* 1992; Wilson *et al.* 2002; Grencis *et al.* 2014; Andreasen *et al.* 2015). Immunosenescence leads to increased Th1 signalling and a decline in adaptive immune system function (Murr *et al.* 2004; Faria *et al.* 2008; Bauer *et al.* 2009), potentially leading to the failure of protective immunity against GI helminths. Given the similar effects of aging and GI helminth infections on physiology, like increased HPA axis activity and inflammation, helminths could exacerbate the negative effects of aging, potentially leading to vicious circles and accelerating age related health deterioration (Hawkley & Cacioppo 2004; Beldomenico & Begon 2016). The study of

physiological correlates of aging and age related mortality under natural condition has only recently attracted the attention of evolutionary ecologists (Hayward *et al.* 2009; Nussey *et al.* 2013; Reichard 2016), yet considering senescence and its drivers and effects has great potential to further our understanding of the interaction between ecology, life-history, physiology, parasites and health, especially in long-lived species like nonhuman primates.

5.2 GI helminth transmission: Determinants of exposure

Understanding parasite transmission pathways and how they relate to individual behaviour is vital for explaining inter-individual variance in infection risk as well as disease epidemiology. Despite the wealth of studies linking social network positions and behaviour to parasite transmission (Vicente *et al.* 2007; Drewe 2009; Godfrey *et al.* 2009; Fenner *et al.* 2011; VanderWaal *et al.* 2013, 2014; Weber *et al.* 2013), the exact mechanisms for GI helminth transmission in nonhuman primates remain elusive. Depending on the species, higher transmission risk has been described for individuals central in grooming (MacIntosh *et al.* 2012) or contact networks (Rimbach *et al.* 2015). Other studies report grooming partner diversity (Wren *et al.* 2016), high integration in proximity networks (Friant *et al.* 2016a), or combinations of partner numbers and spatial association (González-Hernández *et al.* 2014) to predict infection, but no impact of contact network integration (Friant *et al.* 2016a). Based on findings presented in **Chapter 4**, I will discuss how these discrepant findings could be explained and reconciled.

Strongyle nematodes have direct life cycles with mobile infective L3 larvae and their transmission usually occurs upon contact with contaminated soil or food (Dash 1973; Bethony *et al.* 2006; Viney 2017), yet a social component of transmission via direct contact to conspecifics has been suggested (MacIntosh *et al.* 2012; González-Hernández *et al.* 2014; Wren *et al.* 2016). Transmission could be linked to specific behaviours, like aggressive encounters in infectious tumour transmission in Tasmanian devils (Hamede *et al.* 2013) and receiving aggression and giving grooming in tuberculosis transmission in meerkats (Drewe 2009). To test for both environmental and social transmission pathways, I utilized measures of ground use and time in areas of high contamination as estimators of environmental exposure and active grooming as the most likely behaviour to contribute to transmission via social contact, based on the frequent hand to mouth contact **(see Chapter 4)**. While ground use per se did not predict reinfection after treatment, spending time on contaminated soil did. Frequent social contact can contribute to GI helminth transmission (MacIntosh *et al.* 2012; Rimbach *et al.* 2015; Friant *et al.* 2016a), and infection risk increased with high grooming partner numbers and strong same sex bonds **(Chapter 4)**, suggestive of a social component of strongyle nematode transmission.

Faecal contamination of the soil or water-source is widely recognized as a major source of exposure to GI helminths (Pebsworth *et al.* 2012; González-Hernández *et al.* 2014), yet rarely tested

specifically. I suggest that proximity effects like detected for mangabeys (Friant *et al.* 2016a) are not mediated by the shared use of space per se, but result from a correlation between sharing space with conspecifics and spending time on contaminated soil. This argument can also explain the lack of proximity predicting infection risk in other studies (Rimbach *et al.* 2015), if contact with infective stages does not coincide with spatial proximity to others in the study groups. In Eastern chipmunks (*Tamias striatus*), not current, but past association networks, considering the time-gap between egg shedding and larvae becoming infective, predicted infection risk (Grear *et al.* 2013), illustrating the importance to consider parasite life cycles for studying transmission. In my study, ground use was not correlated with time spent in contaminated areas and did not predict infection risk, illustrating that rough approximations of exposure may not adequately capture the actual process underlying parasite transmission.

Various strongyle nematodes actively attempt to increase their transmission by positioning themselves in locations with higher likelihood of ingestion by their target host (Stromberg 1997), leading to host counterstrategies, like avoiding to forage in highly contaminated areas (Hutchings *et al.* 2002). Mobile hookworm larvae actively follow host cues and cling to dog hair (Granzer & Haas 1991), and grooming can facilitate transmission of *H. polygyrus* larvae from mouse fur (Hernandez & Sukhdeo 1995). Thus, transmission via contaminated fur can be an additional strongyle nematode transmission route. Grooming with a high number of partners increased infection risk in Barbary macaques (**Chapter 4**) and vervet monkeys (Wren *et al.* 2016), indicating higher risk to encounter infective larvae when grooming more different individuals. Grooming duration did not predict infection, but to which extent fur contamination is random or connected to certain partner attributes cannot be tested in the current dataset.

5.3 GI helminth transmission: Determinants of susceptibility

I found two major susceptibility measures predicting reinfection patterns, which will be discussed in the following: Infection with further GI helminths prior to treatment, and strong social bonds with opposite sex partners (**Chapter 4**).

Infections with multiple parasites are considered to be the norm rather than the exception (Graham 2008; Bordes & Morand 2011; Ezenwa 2016). Double infections can aggravate infection intensity and duration: Mice coinfected with *Nippostrongylus brasiliensis* and *H. polygyrus bakeri*, show significantly higher egg counts and egg shedding duration of *N. brasiliensis* than single infected individuals (Budischak *et al.* 2015b). Coinfections can decrease susceptibility to GI helminths based on competition for resources (Lello *et al.* 2004; Budischak *et al.* 2015b; Vaumourin *et al.* 2015) or changes in the host immune system, including the production of cross-reactive antibodies (Cox 2001; Lello *et al.* 2004) and parasite excretion of cytokine-like substances (Grencis & Entwistle 1997; Grencis *et al.* 2014). An example is the significantly increased anti-*Oesophagostomum* antibody response

in *Oesophagostomum-Trichuris* infected vs. single infected pigs (Andreasen *et al.* 2015). With inhibitory and enhancing effects operating simultaneously, interactions between multiple parasites can be complex, as demonstrated by a study of wild rabbits: *Mosgovoyia pectinate* or *Trichostrogylus retortaeformis* infections were linked with lower *Graphidium strigosum* burden, whereas *Cittotaenia denticulata* and *G. strigosum* infections both increased likelihood of *T. retortaeformis* infections (Lello *et al.* 2004).

In my study population, I detected three morphotypes of two parasite orders: Strongyle nematodes of the order *Strongylida*, and the enoplid parasites *Capillaria* spp. and *Trichuris* spp. of the order *Trichurida*. Given the distant relatedness, cross-immunity reactions are unlikely, yet *Trichuris* infections have been shown to enhance anti-*Oesophagostomum* infections in pigs (Andreasen *et al.* 2015). However, coinfection with *Capillaria*, *Trichuris*, or both, led to higher reinfection risk with strongyle nematodes. Coinfections were largely limited to aged individuals likely to be subject to immunosenescence, so the presence of *Capillaria* and *Trichuris* could be an integrative signal of overall poorer host condition and immunocompetence. Prevalence of intestinal inflammatory and infectious diseases increases with age due to immunosenescence-related changes in the gut mucosal immune system (Mabbott *et al.* 2015). Young mice infected with *Trichuris muris* develop efficient immune responses with worm expulsion, whereas older individuals become susceptible to chronic infection (Humphreys & Grencis 2002), with the underlying changes possibly extending to overall GI helminth susceptibility.

Immunosenescence probably contributes to coinfection and strongyle infection risk, but is likely not the only process involved, demonstrated by the lack of evidence for an impact of urinary NEO levels on reinfection. In Soay sheep, experiencing adverse environmental conditions earlier in life explained variation in egg counts beyond chronological age (Hayward *et al.* 2009), indicating that life history contributes to individual capacity to manage infections and age related changes in parasite responses. In the study population, increasing age was implied to reduce reinfection risk (**Chapter 4**), suggesting protective immunity against strongyle nematodes (Wilson *et al.* 2002). I suggest that in the case of Barbary macaques, infection with enoplid parasites could be a signal of increased susceptibility beyond uNEO, uCP and fGCM levels or chronological age, capturing individual life history, senescence and health deterioration. Coinfections are intensely studied to understand parasite communities and transmission dynamics (Salgame *et al.* 2013; Ezenwa & Jolles 2015; Rynkiewicz *et al.* 2015; Ezenwa 2016), but are rarely considered as potential signals of overall host susceptibility (Pedersen & Fenton 2015; Friant *et al.* 2016a).

The second strong predictor of reinfection was social bonds with opposite sex partners (**Chapter 4**), which reduced reinfection risk. There was no evidence of sex specific effects (**Chapter 4**), suggesting similar effects for both sexes. The protective effect probably resulted from lower susceptibility rather than lower exposure, as strong social bonds are inextricably linked with high

levels of affiliative interactions. Lower susceptibility is likely mediated by better immune function and defence against pathogens in strongly bonded or socially well integrated individuals, i.e. social buffering (Cohen & Wills 1985; Cohen *et al.* 1991, 1997; Kikusui *et al.* 2006; Cohen & Janicki-Deverts 2009; Kiyokawa & Hennessy 2018), with the well described protective effect against infectious diseases extending to GI helminths. The physiological processes mediating the buffering effect can be rooted in several pathways, which I will briefly discuss here.

The social buffering mechanism receiving most attention from behavioural ecologists is attenuation of HPA axis activity in face of a stressor. Socio-positive interactions and support from conspecifics reduce HPA axis activation from mouse to men (Shutt *et al.* 2007; Hennessy *et al.* 2009; Eisenberger & Cole 2012; Kiyokawa & Hennessy 2018), whereas social isolation, social instability and repeated exposure to severe stressors lead to increased HPA activity, dysregulation of HPA signalling and ultimately detrimental health effects (Capitanio *et al.* 1998; Cole *et al.* 2009; Hennessy *et al.* 2009; Hawkley *et al.* 2013). HPA axis activity is frequently linked to GI helminth infections (Chapman *et al.* 2006; Muehlenbein 2006; Pedersen & Greives 2008; Muehlenbein & Watts 2010; Setchell *et al.* 2010), and strong bonds have been demonstrated to attenuate physiological stress responses in wild male Barbary macaques (Young *et al.* 2014a) and chimpanzees (Wittig *et al.* 2016). In a range of studies (Barnard *et al.* 2003; MacIntosh *et al.* 2012; Friant *et al.* 2016a), including this one, HPA axis activation was not correlated with GI parasite infection risk, indicating that HPA axis regulation might not be the main mechanism linking sociality to decreased parasite infection risk. An influence of HPA axis activation cannot be excluded, yet my results suggest the presence of other mechanisms underlying the protective effect of social bonds.

A second signalling pathway for stress responses is the SNS, which has been largely neglected in studies of social buffering in natural populations due to the limits of noninvasive assessment. SNS activation often occurs in parallel to HPA axis activation and is similarly important for immune signalling, e.g. via nervous signalling to lymphatic tissue (Elenkov *et al.* 2000; Sloan *et al.* 2008; Eisenberger & Cole 2012; Capitanio & Cole 2015). Socio-positive interactions reduce SNS activation (Eisenberger & Cole 2012; Inagaki & Eisenberger 2016), facilitating the stress reducing effects of social buffering (Kiyokawa & Hennessy 2018) and offering an alternative route of social interactions to affect health. Additionally, release of oxytocin and endorphins in responses to both stressors and socio-positive interactions could play a role for social buffering (Keverne *et al.* 1989; Curley & Keverne 2005; Kikusui *et al.* 2006; Uchino 2006; Eisenberger & Cole 2012; Li *et al.* 2017; Plein & Rittner 2017). Oxytocin can improve health outcomes by HPA axis downregulation (Kikusui *et al.* 2006; Li *et al.* 2017), and enhanced wound healing (Archie 2013; Li *et al.* 2017), and is suggested to play a role in mediating the anti-inflammatory effects of endorphins (Eisenberger & Cole 2012; Hennessy *et al.* 2014). Both signalling pathways can contribute to immunomodulation, facilitating later reinfection in individuals with strong opposite sex bonds, which could be a mechanism linking

strong bonds and social integration to increased longevity and reproductive success (Silk *et al.* 2003, 2010; Uchino 2006; Cameron *et al.* 2009; Holt-Lunstad *et al.* 2010). However, social interactions can contribute to exposure, and social bonding is not universally beneficial with regard to GI helminth infections. Quite contrary, strong bonds with same sex partners increased reinfection risk. In the following section, I will explain this discrepancy and assess the costs and benefits of sociality with regard to parasite infections in the study population, extending to the implications for social evolution in a wormy world.

5.4 Costs and benefits of sociality – or: how to not get cut by sociality's double-edged sword

Social relationships, albeit crucial for both sexes, are connected to a whole range of challenges and benefits traded off against each other. Both same and opposite sex bonds can increase reproductive success and survival (Silk *et al.* 2003, 2009; Schülke *et al.* 2010; Archie *et al.* 2014), implying similar beneficial effects of bonding for both sexes. In my study, contrary to the protective effect of strong opposite sex bonds, same sex bonds increased reinfection risk, irrespective of individual sex **(Chapter 4)**. I want to offer several, non-mutually exclusive explanations for this finding.

Faced with intense stressors, the presence of unfamiliar conspecifics can attenuate fear and stress responses in laboratory rodents (Ishii *et al.* 2016; Kiyokawa *et al.* 2018). However, buffering effects can be partner dependent, like oxytocin release in chimpanzees, which occurs when grooming with bonded, but not non-bonded partners (Crockford *et al.* 2013). Attenuated stress responses could result from a lower perceived threat of the stressor in presence of conspecifics, as the danger of confronting the stressor might be reduced with increasing numbers (Kikusui *et al.* 2006; Kiyokawa & Hennessy 2018; Kiyokawa *et al.* 2018). Depending on the situation, buffering effects should be specific to partners able to mitigate the threat of the stressors (Kikusui *et al.* 2006; Kiyokawa & Hennessy 2018), like access to strongly bonded partners who reliably provide support in agonistic interactions (Schülke *et al.* 2010; Berghänel *et al.* 2011), which reduces HPA axis activation in male macaques (Young *et al.* 2014a). Depending on the situation, different partner characteristics might be capable of facilitating buffering effects, explaining the different effects of same and opposite sex bonds.

A second explanation is that despite using the same measure, sum of the top three dyadic CSI (Silk *et al.* 2006), to social bonds, same and opposite sex bonds could be linked to different mediators of exposure and susceptibility. Social behaviour is inextricably linked with both exposure to pathogens and changes in physiology that can mediate susceptibility (Hawley *et al.* 2011; Ezenwa *et al.* 2016; White *et al.* 2017a), and disentangling the precise exposure and susceptibility correlates of

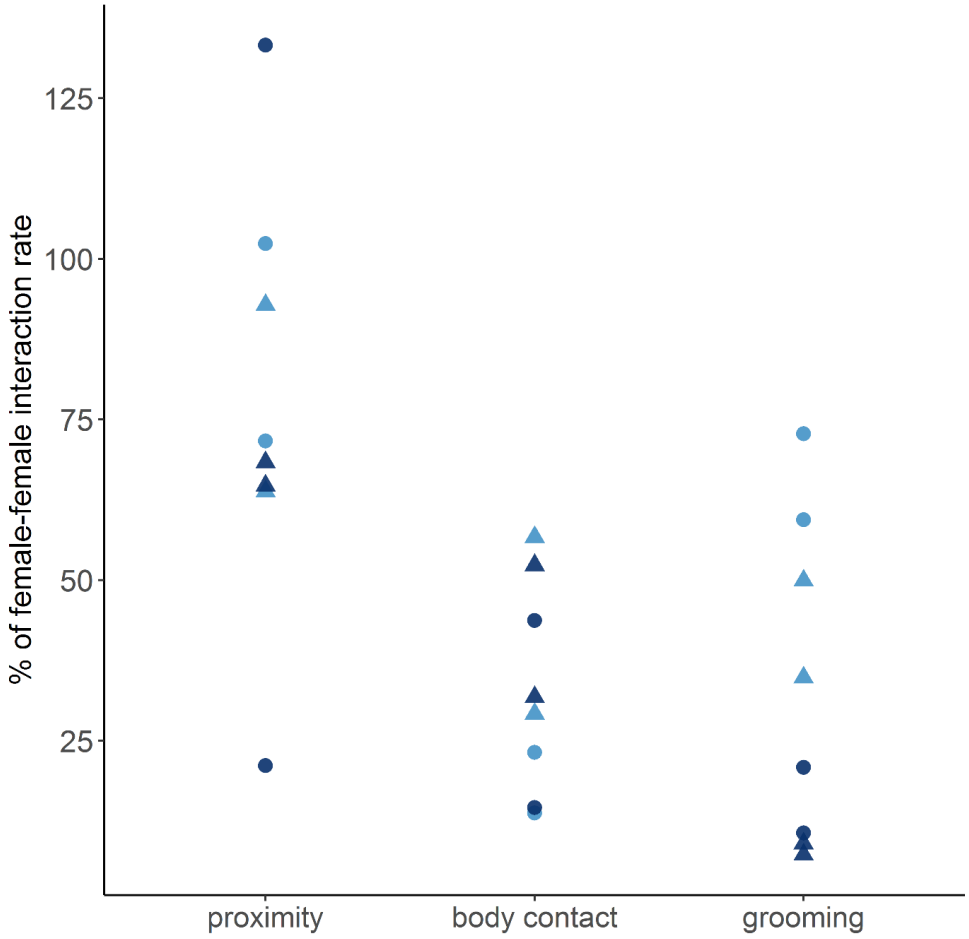

Figure III: Comparison of social interactions used for dyadic CSI construction in relation to average female-female interaction rates. Values for male-female dyads are coloured light blue, values for male-male dyads in dark blue. Displayed are average interaction rates (dots = duration, triangles = frequency) divided by average female-female value of the respective interaction in the same study group (i.e. values above 1 signify higher interactions rates than found on average for female-female dyads). In both male-male and male-female dyads, both body contact and grooming are much less frequent than in female-female dyads, and grooming is markedly lower in male-male dyads than dyads with female partners.

behaviour is challenging. Same sex bonds could be linked with the costs of higher exposure rather than the benefits of reduced susceptibility, as bond strength with same, but not opposite sex partners, was weakly correlated with number of grooming partners **(Chapter 4)**, implying that forming strong same sex bonds is linked with higher overall sociability (Brent *et al.* 2013; Seyfarth *et al.* 2014). Additionally, as interaction patterns between the sexes are very different, the mechanisms mediating increased reinfection risk in individuals with strong same sex bonds could be different for males and females, although the effect on infection could be similar.

Female cercopithecine primates are more socially active than males (Haunhorst *et al.* 2016), and showed higher rates of affiliation, particularly body contact and grooming, in the study population (see Figure III), with male-male dyads usually grooming ten time less frequently than female-female

dyads, and male-female dyads grooming roughly half as much as female-female dyads. Physical contact, particularly grooming, triggers the physiological responses leading to enhanced immune function and attenuated stress responses (Shutt *et al.* 2007; Aureli & Yates 2010; Eisenberger & Cole 2012), yet carries the risk of contracting GI helminth infections from grooming partners (Granzer & Haas 1991; Hernandez & Sukhdeo 1995). High rates of grooming, seen in female-female bonds, could thus increase exposure beyond a level that can be compensated by the lowered susceptibility, while males groom other males too rarely to induce immunomodulatory changes that decrease susceptibility. Additionally, bond formation and maintenance could be a stressor for males, as triadic male-infant interactions elementary for bond formation in male Barbary macaques (Berghänel *et al.* 2011) require stressful infant interactions (Henkel *et al.* 2010). In contrast to same sex bonds, opposite sex bonds could offer the best balance between exposure and susceptibility.

There are further points to consider for assessing the full picture. *Cercopithecine* females preferentially bond with closely related female (Silk *et al.* 2003, 2009, 2010), leading to a connection between bonding and genetics. Traits of parasite tolerance and resistance have heritable components (Graham *et al.* 2010; Hayward *et al.* 2014a, b). As individuals using a parasite tolerance strategy generally have higher egg counts (Hayward *et al.* 2014b), those individuals contribute more to transmission (Medzhitov *et al.* 2012) and potentially increase infection risk for closely bonded partners. Infections should also be detected earliest in these individuals due to higher egg shedding, even if they have similar exposure and susceptibility to individuals using a parasite resistance strategy. Additionally, closely bonded females could face similar exposure to infective stages if socially inheriting network positions linked with exposure risk (Ilany & Akçay 2016). Consequently, social bonds, especially between females, could be linked to reinfection via shared genetic traits, possibly confounded with shared social environment. Assessing the role of relatedness for exposure, susceptibility and tolerance strategies is beyond the scope of this thesis in the absence of relatedness information.

Reinfection risk could also be linked to social interactions beyond the dyadic level. Opposite effects of social interactions on parasite transmission are not limited to this study in macaques: Balasubramaniam *et al.* (2016) found low infection risk with *Shigella*, a bacterial pathogen, in central individuals of two groups of rhesus macaques, but high infection risk in central individuals in a third group, potentially resulting from different group sub-structure. Group structure and clustering can limit parasite transmission (Salathé & Jones 2010; Nunn *et al.* 2015), so transmission patterns can differ between groups of similar sizes. In my study population, the effect of same sex social bonds is most prominent in the study group with higher interaction rates, group cohesion and lower clustering (unpublished data). Lower levels of sub-structuring could increase overall exposure to infective parasite stages, intensifying the effect of social transmission (Salathé & Jones 2010; Griffin & Nunn 2012; Nunn *et al.* 2015). Considering the proposed mechanisms explaining the discrepancy

between same and opposite sex bond strength und GI helminth infection risk, concluding that same sex bonds are risk and opposite sex bonds are protective factors for GI helminth transmission is premature. Rather, we need to disentangle the underlying mechanisms and the relative contributions of social behaviours on exposure and susceptibility. Also, GI helminth infection risk does not negate the benefits of strong social bonds with same sex partners unrelated to infection (Cameron *et al.* 2009; Schülke *et al.* 2010; Silk *et al.* 2010; Smith *et al.* 2010; Haunhorst *et al.* 2017), so forming strong same sex bonds could be favourable even if connected to the costs of GI helminth infections.

In accordance with the longstanding hypothesis that pathogens are one of the main driving forces of social evolution in primates (Freeland 1976) and recent work, both empirical and theory building, emphasising the potential for behaviour-parasite-feedback loops (Poulin 2010; Ezenwa & Snider 2016; Ezenwa *et al.* 2016), GI helminths impacted host social behaviour, and host sociality simultaneously predicted infection risk. Sickness behaviour responses implied costs of infections, although determining possible long-term costs of infections and differences in individual parasite defence strategies (Hayward *et al.* 2009; Medzhitov *et al.* 2012; Jackson *et al.* 2014) is beyond the scope of the study. Given the dual effect of social behaviour, individuals could be expected to alter their behaviour to minimize infection risk while optimizing the buffering effects of social bonding. I will discuss how Barbary macaques could achieve this in the following paragraphs.

Considering the potential role for partner diversity increasing GI helminth transmission risk (Rimbach *et al.* 2015; Friant *et al.* 2016a; Wren *et al.* 2016), forming strong bonds with few partners and avoiding the space commonly used by infected conspecifics (Grear *et al.* 2013) seems to be the ideal strategy. Forming strong bonds can increase transmission risk, so likely there is a trade-off between interaction quality and quantity, with facilitation of enhanced immune function by affiliative interactions, especially grooming (Keverne *et al.* 1989; Shutt *et al.* 2007; Crockford *et al.* 2017). Assuming an optimal balance between exposure costs and susceptibility benefits of sociality, the question how these behavioural strategies of bond formation and avoidance of infected conspecifics could be mediated arises. Inflammatory cytokines are strong candidates for neuro-endocrine signals linking social environment with immune function and mediating behavioural responses to both, stressors and infection (Eisenberger & Cole 2012; Hennessy *et al.* 2014; Eisenberger *et al.* 2017). Inflammatory cytokines are not only released in the context of acute infections (Hart 1988; Dantzer 2001; Konsman *et al.* 2002), but also in social isolation (Cacioppo & Hawkley 2003; Hawkley & Capitanio 2015), most likely as an adaptive response: Inflammatory cytokines prime the immune system for inflammatory responses in anticipation of higher likelihood of injury in individuals separated from the protection of the group (Eisenberger & Cole 2012; Eisenberger *et al.* 2017). Inflammatory signalling generally leads to avoidance of conspecifics, but increases social interactions with familiar partners (Willette *et al.* 2007; Hennessy *et al.* 2014). Contact with bonded partners in turn initiates anti-inflammatory signalling (Hennessy *et al.* 2014; Crockford *et al.* 2017; Kiyokawa

2018). Consequently, inflammatory cytokines could play a part in facilitating the maintenance of social bonds and interactions in individuals infected with GI helminths.

Oxytocin signalling could play a role in detection and avoidance of infections. From mice to men, olfactory signals are used to identify infections in conspecifics (Kavaliers & Colwell 1995; Olsson *et al.* 2014) and sources of contamination (Poirotte *et al.* 2017). Oxytocin contributes to social recognition, potentially playing a role for processing the olfactory signals needed for recognition and avoidance of infected individuals (Kavaliers & Choleris 2011). With oxytocin and inflammatory signalling contributing to immunoregulation (Uvnäs-Moberg 1998; Hennessy *et al.* 2014; Kiyokawa & Hennessy 2018), they are likely part of a feedback loop mediating both social behaviour and immune function to facilitate adaptive responses to individual social environment. These mechanisms could include seeking out support in case of severe stressors, infections and social isolation (Hennessy *et al.* 2014) and avoiding exposure to pathogens. If these processes translate into fitness effects, parasite infections could well contribute to the evolution of differentiated relationships and be a driver of social evolution, even if they are not immediately linked to health or reproductive costs.

This general rule to optimize the costs and benefits of interactions might not apply equally to all individuals and pathogen, especially when considering life-history trade-offs between maintenance and reproduction (Archie 2013; Hayward *et al.* 2014a; Jackson *et al.* 2014). An obvious example is the case of sexually transmitted diseases, where exposure and potential reproductive success are intimately linked (Klovdahl & Australian 1985; Hawley *et al.* 2011), but similar covariation can be expected between behaviours correlating with exposure and individual susceptibility. High ranking males, particularly alpha males, are often characterized by high testosterone and GC levels linked to high susceptibility to infection (Muehlenbein & Bribiescas 2005; Muehlenbein & Watts 2010; Gesquiere *et al.* 2011; Archie *et al.* 2012), yet are apparently better able to tolerate the challenges of their endocrine status without overt negative health effects (Archie *et al.* 2012; Muscatell *et al.* 2016). Some individuals might thus be capable of occupying high exposure or susceptibility behavioural niches, with different social strategies being more advantageous for these individuals.

Forming strong and selective bonds may be advantageous in relation to pathogen transmission in general and GI helminth transmission in particular, but different social strategies might be more beneficial under certain environmental circumstances. The question whether quality or quantity of social bonds matters most is still debated (Cohen & Wills 1985; Cohen & Janicki-Deverts 2009; Holt-Lunstad *et al.* 2010; Ostner & Schülke 2018; Silk *et al.* 2018), yet having high numbers of interaction partners can be literally life-saving: Faced with harsh environmental conditions, survival in Barbary macaques was best predicted by high numbers of grooming relationships, possibly as a result of better opportunity for social thermoregulation in face of extreme temperatures (McFarland & Majolo

2013; Lehmann *et al.* 2016; Campbell *et al.* 2018). In rhesus macaques on Cayo Santiago, the number of living kin predicted survival in adult females (Brent *et al.* 2017), and having more weak bonds increased infant survival in chacma baboons (McFarland *et al.* 2017). Similarly, high network centrality or a vital position for information transmission is simultaneously linked with parasite risk (Fenner *et al.* 2011; Godfrey 2013; VanderWaal *et al.* 2013; Rimbach *et al.* 2015; Friant *et al.* 2016a; White *et al.* 2017b), and increased fitness (Brent 2015; Cheney *et al.* 2016; Firth *et al.* 2017), although the underlying mechanisms are not well understood to date.

Expanding beyond the health effects of GI helminths, being overly selective with regard to interaction partners could also have negative consequences. Being socially selective can help to defend against adverse effects of directly transmitted helminths, but might not offer much protection from transmission of pathogens using different transmission routes, exemplified by the network independent infection patterns with unicellular intestinal parasite infections in spider monkeys (*Ateles hybridus*) and mangabeys (Rimbach *et al.* 2015; Friant *et al.* 2016a). Additionally, social immunity usually described in social insects (Cremer *et al.* 2007), has been suggested to occur in social mammals: if exposure to low levels of a pathogen can induce the development of acquired immunity (Hart 2011), frequent close contact and "sampling" of group pathogens becomes an adaptive strategy (Burnet *et al.* 1972; Hart 1990) with benefits potentially outweighing those of protection from GI helminth infections. In short, assuming one general optimal strategy might be a gross oversimplification, as depending on environmental condition, individual life history and physiology, alternative strategies could yield the biggest health and fitness benefits, especially in light of non-parasite selective pressures operating on the interface between social behaviour.

Chapter 6

Conclusion and future directions

"There is nothing like looking, if you want to find something. You certainly usually find something, if you look, but it is not always quite the something you were after."

J.R.R. Tolkien – The Hobbit

Setting out to investigate the host-parasite dynamics between Barbary macaques and GI helminths and contribute to the current understanding of the interplay between social behaviour, physiology, infection and health, I indeed found several unexpected results, alongside answers to my research questions. Here, I want to briefly summarize my findings, assess how they contribute to the fields of eco-immunology, disease ecology and wildlife health, and point out possible future research directions.

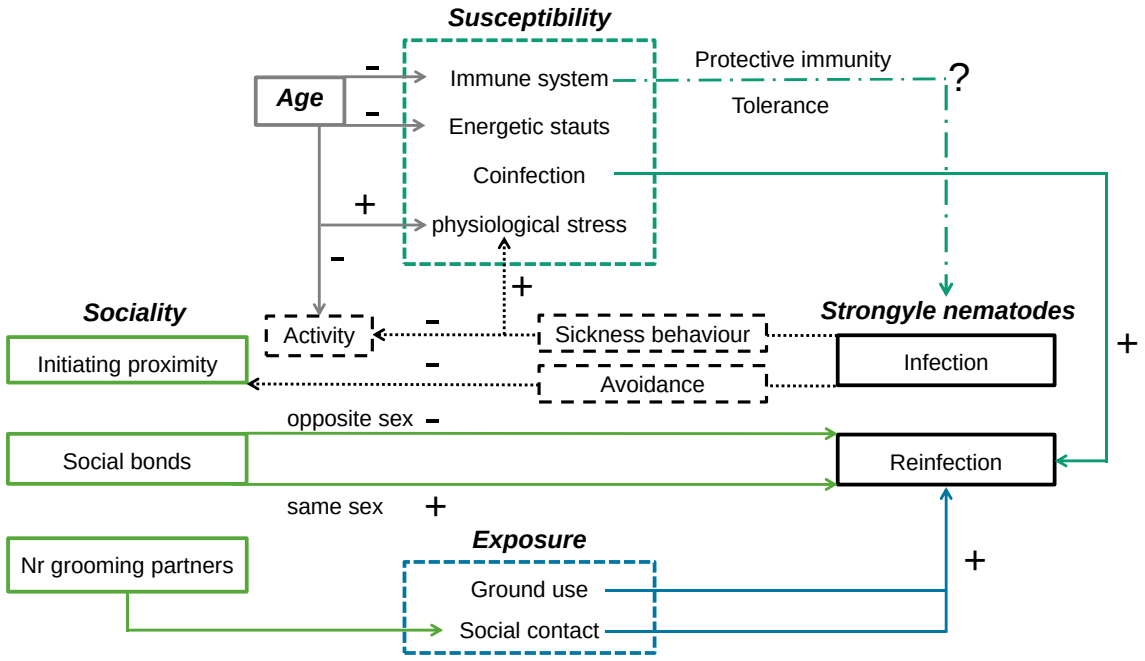

Figure IV: Flow chart illustrating the host-parasite relationship between Barbary macaques and strongyle nematodes as by the results of the thesis. Solid lines indicate the predictors influencing reinfection after parasite clearance, dashed lines the effects of parasite infections. Increases in behavioural and physiological measures and reinfection probability are indicated by a plus sign, decreases by a minus sign next to the respective line. The semi-dashed line indicates plausible links between host immune system and strongyle infection, which were not tested explicitly in the study. Age emerged as a strong predictor of host physiology and behaviour and was thus added to the chart to complete the picture.

Assessing the effects of GI helminth infection on Barbary macaques, I found effects of sickness behaviour in response to infections, suggesting that infections lead to health costs. Despite the body of knowledge we have on primate-helminth interactions, the immediate costs of infection and how they translate into long-term effects on survival and reproduction is still unclear for many primate-helminth pairs, especially with regard to causes and consequences of inter-individual variance. Body condition was not influenced by treatment and individuals with high body condition were implied to have higher reinfection risk, which could be suggestive of parasite tolerance in the study population. Assessing parasite tolerance and the consequences of employing resistance vs. tolerance strategies opens an intriguing research avenue, calling for long-term studies incorporating specific measures of parasite tolerance under natural conditions. This might also help to assess whether sickness responses to GI helminth infections are the expression of health costs or can mitigate costs and thus even be beneficial. If this was the case, individuals with higher amplitudes of sickness behaviour responses are expected to benefit from increased fitness in the long run.

Helminth coinfections were the strongest risk factors for strongyle nematode reinfection. This finding is likely not generalizable, as within-host parasite dynamics are complex and species specific. Based on the finding that coinfections were largely limited to aged individuals, I suggest that this result is best explained by failing protective immunity against enoplid parasites in older individuals, resulting in health deterioration and increased susceptibility to GI helminths in general. I found no evidence for interactions between Barbary macaque immune balance and helminth infections, but demonstrate the usefulness of uNEO as a marker of immunosenescence. Immunosenescence, decreasing the capability to handle GI helminth infections, and similar effects of age related physiological changes and GI helminth infections, suggest the possibility of vicious circles between immune system deterioration, parasite infection and physical decline. Which factors contribute to "healthy" aging and how these are influenced by parasite infections are interesting question to address in future, longitudinal studies, particularly in light of life-history trade-offs.

Concerning the interplay between social behaviour and parasite transmission, I found evidence of both avoidance of infected individuals and social interactions predicting parasite transmission. While social interactions contribute to susceptibility and exposure simultaneously, the level at which sociality translates into exposure and susceptibility depends on the nature and frequency of interactions. Interaction frequencies and partner numbers most likely feed into exposure, whereas bond quality and socio-positive interactions most likely contribute to buffering effects on susceptibility. In case of the Barbary macaques, HPA axis activation does not appear to be the main mechanism linking sociality to susceptibility. The role of alternative routes, which could not be assessed in this thesis, offers potential explanations for the discrepancy between the protective effect of opposite sex bonds and risky same sex bonds. Additionally, there might be physiological traits underlying both social bond formation and susceptibility. The offered explanations are not mutually

exclusive, and disentangling which aspects of sociality correlate with exposure and susceptibility as well as the extent of covariation between both transmission components remain open questions. Another interesting question is whether social interactions can play a role in mitigating costs of infections via endocrine signalling impacting the extent to which tolerance or resistance strategies are employed.

Considering the dual role of social relationships for parasite transmission, it is not surprising that I found indications of avoidance of infected individuals. How individuals identify infected conspecifics and if these avoidance strategies are effective in reducing infection risk remains to be determined. Intriguingly, the physiological mechanisms facilitating sickness behaviour and the beneficial effects of social interactions could also contribute to avoiding infected or non-bonded individuals. This suggests that mechanisms operate on the reinforcement of social selectivity and relationship differentiation while simultaneously regulating immune function and adapting it to social environment in social animals. Assessing the roles of oxytocin and inflammatory cytokines for regulating social behaviours, susceptibility and immune responses to parasites are thus important tasks for future studies aiming at understanding the costs and benefits of sociality in an infection and health context.

In summary, I found costs of sociality via increased exposure, and benefits via reduced susceptibility, to GI helminth infections and the potential of GI helminth infections to contribute to social evolution, particularly the formation of differentiated bonds. It seems that "quality over quantity" is a good rule of thumb when it comes to social bonds and reducing costs of parasite infections, while preserving health related benefits of sociality. However, GI helminths and their transmission are just one piece of the jigsaw puzzle, with many more factors like personality, social isolation, life-history, early life adversity, microbiome composition and of course further pathogens, like bacteria and viruses, contributing to the sociality-health-fitness nexus. In light of rapid advances in molecular and statistical methods for the analyses of these complex interactions, future studies hold great potential for major contributions to our understanding of wildlife health, eco-immunology, disease ecology and host-parasite dynamics. Investigating how sociality translates into health, healthy aging and fitness will not only be important in understanding the evolution of sociality, but also offer insights for human medical studies, social medicine, the evolutionary roots of human social relationships, ultimately allowing us to understand why friendship does not only give value to survival, but might be a key for it as well.

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ich bin der, der endlos schweigt und der, der laute Lieder singt;
ich kann maximal verletzen und bin maximal verletzt,
meine Ängste sind gewaltig, doch meine Hoffnung stirbt zuletzt.

...

Meine Geduld, die ist unendlich, doch ich halte es nicht aus,
wenn man in 1000 Worten sagt, Wofür es gerade mal 3 braucht...
Ich bin ein riesengroßer Eisberg, schmelz' genau so schnell dahin;
Ich brauch' grenzenlose Freiheit, solange ich nicht einsam bin!

...

Ich stehe felsenfest im Leben, treibe ziellos auf dem Meer,
mach's mir gerne kompliziert, wo es doch oftmals einfach wär';
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An deiner Seite, **© Schandmaul** (aka the best band in the world – thanks to the band for allowing me to use their lyrics here!)

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Curriculum Vitae

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Education

06/14 – 08/18 **Ph.D. program "Behaviour and Cognition"**; University of Göttingen, Germany
Thesis title: The costs and benefits of sociality in semi-free ranging Barbary macaques (*Macaca sylvanus*)
Supervisors: Dr. Julia Ostner, Dr. Oliver Schülke
Dept. of Behavioural Ecology, University of Göttingen, Germany

10/10 - 01/13 **M. Sc. program "Master of Developmental, Neural and Behavioural Biology"**
University of Göttingen, Germany
Focus: Neuro- and behavioural biology, graduation with honours, grade 1.0
Master thesis: Analysis of wild Assamese macaque *MHC-DRB*

10/07 - 06/10 **B. Sc. program "Biomedical Science (Humanbiologie)"**
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Focus: Neurobiology, graduation grade 1.7
Bachelor thesis: Regulation of hTRPV4 by intracellular calcium concentration

Employment and research experience

02/13 - 05/14 **Dept. of Behavioural Ecology, University of Göttingen, Germany**:
Teaching assistant: Course "social behaviour and communication"
Research assistant: Literature research and grant writing for DFG Research Unit SoHaPi (FOR 2136)

Peer reviewed articles

2019 **N. Müller,** M. Heistermann, C. Strube, M. Franz, O. Schülke, J. Ostner. Exposure and susceptibility drive reinfection with gastrointestinal parasites in a social primate. *Function Ecology,* doi: 10.1111/1365-2435.13313

2018 N. Paschek, **N. Müller**, M. Heistermann, J. Ostner, O. Schülke. Subtypes of aggression and their relation to anxiety in Barbary macaques. *Aggressive Behavior,* 45(2), 120–128

2018 **N. Müller**, M. Heistermann, C. Strube, Z. Morbach, N. Lilie, M. Franz, O. Schülke, J. Ostner. Physiological and social consequences of gastrointestinal nematode infection in a nonhuman primate. *Behavioral Ecology,* doi:10.1093/beheco/ary168

2017 **N. Müller**, M. Heistermann, C. Strube, O. Schülke, J. Ostner. Age, but not anthelmintic treatment, is associated with urinary neopterin levels in semi-free ranging Barbary macaques. *Scientific Reports*, doi:10.1038/srep41973

2014 **N. Müller**, J. Ostner, O. Schülke, L. Walter. Towards the non-invasive assessment of MHC genotype in wild primates: Analysis of wild Assamese macaque *MHC-DRB* from fecal samples. *American Journal of Primatology*, DOI: 10.1002/ajp.22225

Conference contributions

2017 Symposium organization: **"Host-pathogen interactions: from sociality to susceptibility";** *35th International Ethological Conference & Summer Meeting of the Association for the Study of Animal Behaviour*, Estoril, Portugal
N. Müller et al. Macaques, sociality and parasites – (How) do social interactions predict parasite infection? (oral presentation)

7th European Federation for Primatology Meeting, Strasbourg, France
N. Müller et al. Macaques, sociality and parasites – (How) do social interactions predict parasite infection? (invited talk)

Meeting of the German Veterinary Medicine Society, Hannover, Germany
N. Müller et al. The connection between health, age, and parasite infection in semi-free ranging Barbary macaques at Affenberg Salem. (oral presentation)

15th Conference of the Primatological Society (Gesellschaft für Primatologie), Zürich, Switzerland
N. Müller et al. Physiological and social consequences of gastrointestinal parasite infection in semi-free ranging Barbary macaques. (oral presentation)

2016 *26th Meeting of the International Primatological Society*, Chicago, USA
N. Müller et al. Effect of experimental anthelmintic treatment on urinary C-peptides in semi-free ranging Barbary macaques (*Macaca sylvanus*) at Affenberg Salem. (oral presentation)

2015 *14th Conference of the Primatological Society* (Gesellschaft für Primatologie), Leipzig, Germany
N. Müller et al. Comparing social networks before and after experimental deworming in Barbary macaques at Affenberg Salem. (poster)

2013 *IX. Göttinger Freilandtage: The Sociality-Health-Fitness Link*, Göttingen, Germany
N. Müller et al. Towards the non-invasive assessment of MHC genotype in wild primates - Analysis of wild Assamese macaque *MHC-DRB* from fecal samples. (poster)

9th International Conference on Behaviour, Physiology and Genetics of Wildlife, Berlin, Germany
N. Müller et al. Towards the non-invasive assessment of MHC genotype in wild primates - Analysis of wild Assamese macaque *MHC-DRB* from fecal samples. (poster)

Grants

2018 Robert-Glaser-Conference Grant (awarded by the *Gesellschaft für Primatologie*)

2014 - 2016 Ph.D. Scholarship of the German Academic Scholarship Foundation for excellent students

2014 Actively contributed to grant writing for DFG-Research Unit Sociality and Health in Primates (SoHaPi); PI Julia Ostner

2014 Research scholarship of the Gerhard-Mazurczak Foundation, Schwabach, Germany

2011 Travel grant of the Gerhard-Mazurczak Foundation, Schwabach, Germany

Fieldwork

2014 - 2015 **Affenberg Salem, Southwest Germany,** 12 months
Behavioural data and non-invasive faecal and urine sample collection in semi-free ranging **Barbary macaques** (*Macaca sylvanus*)
Laboratory work: Preparation of larval cultures, faecal egg counts (McMaster flotation)
Supervisors: Dr. Julia Ostner, Dr. Oliver Schülke, Dept. of Behavioural Ecology, University of Göttingen, Germany

2011 **Ifrane National Park, Morocco,** 1.5 months
Behavioural data collection on wild **Barbary macaques** (*Macaca sylvanus*)
Supervisors: Dr. Julia Ostner, Dr. Oliver Schülke, Dept. of Behavioural Ecology, University of Göttingen, Germany

Estacion Biologia Quebrada Blanco, Peru, 1 month
Behavioural data collection on wild **Saddleback tamarins** (*Sanguinus fuscicollis*)
Supervisor: Dr. Eckhard W. Heymann, Dept. of Sociobiology and Anthropology, University of Göttingen, Germany

Laboratory experience

2016 - 2017 **Genetic parasite analyses,** 3 months
Polymerase chain reaction, gel electrophoresis, Sanger sequencing
Supervisor: Dr. Christina Strube, Institute for Parasitology, University of Veterinary Medicine, Hannover, Germany

2016 **Field endocrinology workshop,** supervised by Dr. Tobias Deschner, Dept. of Primatology, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany,

Molecular genetics and epidemiology workshop, supervised by Dr. Fabian Leendertz, Epidemiology of Highly Pathogenic Microorganisms Group, Robert Koch Institute, German National Institute of Health, Berlin, Germany

2015 - 2016 **Microscopic parasite analyses**, 7 months
McMaster flotation, morphological identification of L3 larvae from larval cultures
Supervisor: Dr. Christina Strube, Institute for Parasitology, University of Veterinary Medicine, Hannover, Germany

2012 ***MHC-DRB* genotyping** of Assamese macaques (*Macaca assamensis*), 6 months
Polymerase chain reaction, gel electrophoresis, microsatellite analysis, Sanger sequencing
Supervisors: Dr. Lutz Walter, Dr. Christian Roos, Primate Genetics Laboratory, German Primate Centre, Göttingen, Germany

2009 - 2010 **Electrophysiology**, 6 months
Cell culture, transfection, patch clamp
Supervisors: Dr. Timothy Plant, Dr. Frauke Kepura, Pharmacological Institute, Philipps-University Marburg, Germany

Data analysis skills

R	**Advanced:** Data processing and visualization, linear mixed modelling, social network analysis
	Basic: Patch occupancy modelling & information theory based model selection (collaboration with Dr. Mathias Franz, Dept. of Wildlife Diseases, Institute for Zoo and Wildlife Research, Berlin, Germany),

Teaching

2014 - 2015	**Training and supervision** of master students and international field assistants
2013	**Teaching assistant** "social behaviour and communication" course

Further qualifications

Organization	Coordination of team of 6 field assistants (Ph.D. project), 2014 - 2015
&	Organization of "SoHaPi" meetings, retreats and student workshops, 2014 – 2017
administration	Organization of the CRC Evolution of Social Behaviour Ph.D. workshop, 2014

Languages	German, native
	English, fluent (Cambridge Certificate in Advanced English Level C1)
	Latin, advanced (5 years)

Memberships

Primatological Society (Gesellschaft für Primatologie)
International Primatological Society
Ethological Society (Ethologische Gesellschaft)

Göttingen, 2nd of July 2018

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Nadine Müller

Declaration

I hereby declare that all parts of my thesis titled "The costs and benefits of sociality in semi-free ranging Barbary macaques (*Macaca sylvanus*)" were written by myself. Assistance of third parties was only accepted if scientifically justifiable and acceptable in regards to the examination regulations. Assistance or contributions to the individual chapters are indicated and all sources have been quoted.

Göttingen, 2nd of July 2018

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Nadine Müller