Differential effects of multiplex and uniplex affiliative relationships on biomarkers of inflammation

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Abstract

Social relationships profoundly impact health in social species. Much of what we know regarding the impact of affiliative social relationships on health in nonhuman primates (NHPs) has focused on the structure of connections or the quality of relationships. These relationships are often quantified by comparing different types of affiliative behaviors (e.g., contact sitting, grooming, alliances, proximity) or pooling affiliative behaviors into an overall measure of affiliation. The influence of the breadth of affiliative behaviors (e.g., how many different types or which ones) a dyad engages in on health and fitness outcomes remains unknown. Here we employed a social network approach to explicitly explore whether the integration of different affiliative behaviors within a relationship can point to the potential function of those relationships and their impact on health-related biomarkers (i.e., pro-inflammatory cytokines) in a commonly studied non-human primate model system, the rhesus macaque (*Macaca mulatta*). Being well connected in multiplex grooming networks (networks where individuals both contact sat and groomed), which were more modular and kin biased, was associated with lower inflammation (IL-6, TNF-alpha). In contrast, being well connected in uniplex grooming networks (dyad engaged only in grooming and not in contact sitting), which were more strongly linked with social status, was associated with greater inflammation. Results suggest that multiplex relationships may function as supportive relationships that promote health. In contrast, the function of uniplex grooming relationships may be more transactional and may incur physiological costs. This complexity is important to consider for understanding the mechanisms underlying the association of social relationships on human and animal health.

Keywords: affiliation, *Macaca mulatta*, cytokines, inflammation

Introduction

For decades, research has shown that social relationships impact individual health and fitness in a variety of animal species, with estimates of the magnitude of the association with mortality in humans on par with other well recognized mortality risks (e.g., smoking, alcohol consumption) [1]. While the importance of social factors for health and fitness are widely recognized, the mechanisms by which social life exerts its influence are still not well understood [2,3]. One reason is that social life is complex; it encompasses both agonistic and affiliative interactions that vary across a range of dimensions such as frequency of interaction, symmetry, tenor, predictability, and stability [4–6]. As such, new approaches addressing this complexity are needed to better understand the biological mechanisms by which social relationships influence health.

Traditionally, two approaches taken to unravel this complexity in humans are to examine the structural and/or functional aspects of social relationships. Structural studies frequently concentrate effort on quantifying relationships by calculating the number of social partners, the frequency of interactions, or the higher order structuring of social relationships using social network analysis [1,3,7–13]. Functional studies attempt to examine what purpose or role a relationship serves and whether it meets the needs of the individual. In humans, functional measures of social relationships include surveys of perceived social support, informational support, emotional support, and tangible support [1]. Both have been associated with health outcomes where some studies have found that the quantity of relationships (structural) have health benefits and others have emphasized that the types or quality of relationships (functional) are what matters (see Holt-Lunstad et al., 2010 for a meta-analysis). In comparison, for nonhuman animals, assessing the structural aspects of social relationships is common [3,14–16], but

68 examining the functions of different relationships is far more challenging due to the fact we
69 cannot directly ask animals about the value or perceptions of their relationships. Instead, research
70 on social relationships in animals has more often relied on metrics designed to indirectly assess
71 the quality rather than directly query the function of their relationships [6].

72 As such, studies of animal affiliation have not explicitly attempted to differentiate
73 between structural and functional aspects of social relationships. Instead they tend to characterize
74 the quantity and quality of relationships by measuring various affiliative behaviors, and, in doing
75 so, these behaviors are either analyzed separately (e.g., grooming *or* proximity) or lumped
76 together giving them roughly equal weight [3,6]. Social network analysis is one technique well
77 suited to studying the structure of social relationships. Typically, researchers examine the effects
78 of individual network centrality metrics (e.g., eigenvector, betweenness, and closeness centrality)
79 and their impact on a variety of health-related metrics. While the general pattern seen across
80 these measures is that greater connectedness or centrality in specific behavioral networks is
81 associated with lower risk for gastrointestinal pathogens, increased reproduction and longevity
82 (Balasubramaniam et al., 2016; Brent et al., 2013; Cheney et al., 2016; Ostner & Schülke, 2018),
83 there is little consistency across studies in identifying which specific social role or network
84 metric is important, and some studies find no impact of social network position on fitness at all
85 (Ellis et al., 2019; Ostner & Schülke, 2018; Snyder-Mackler et al., 2020). Notably, many of
86 these networks metrics are highly correlated and, in practice, measure similar roles making the
87 study of the underlying mechanisms challenging [17,18]. Indeed, recent perspectives on network
88 analysis suggest that certain metrics such as betweenness centrality only become interesting
89 when they deviate from other network metrics such as degree centrality because if the structure
90 of the network is a result of a few highly central individuals high betweenness is likely due to

high degree [19–21]. Thus, it is difficult to ascertain which specific metric to use and thus a suite of metrics is often employed instead [22].

Another commonly used metric to assess the quality of affiliative social relationships in nonhuman primates is the dyadic sociality index (DSI) which aggregates information on the quantity (frequency) of multiple, correlated affiliative behaviors (e.g., grooming and proximity). Relationships with high DSI scores are commonly referred to as strong bonds and tend to be equitable, stable, involve frequent interaction, and are most common between kin and peers [3,23,24]. From a health perspective, higher number or quality of these strong bonds has been associated with acute hormonal responses (e.g., oxytocin or cortisol levels), increased reproduction, and longer survival [3,9,12,25]. However, these strong affiliative bonds make up only a small fraction of the affiliative relationships an individual has [12,23,26–28] with weaker affiliative bonds comprising the remainder. The function of these other, weaker bonds has been hypothesized to increase social flexibility (e.g., social connections can shift with environmental demands), allowing general social integration and indirect connections that might provide access to others who may have resources or information [3,26]. Yet, evidence for an association between weak bonds and health and fitness is mixed [12,26]. As helpful as these metrics are, such approaches may overlook key information on the degree to which the diversity or breadth of affiliative interactions in which a dyad engages are *integrated* [4,6]. For example, a relationship in which a specific dyad engages in multiple types of affiliation (e.g., contact sitting, grooming, *and* proximity) may differ from one in which a dyad engages in only one single behavioral domain (e.g., contact sitting only, grooming only, *or* proximity only), even if the rate of interaction is the same.

113 Recent advances in social network analysis and theory, and specifically multilayer or
114 multiplex networks, ([29]; e.g., multiple types of interactions among the same set of individuals)
115 may eventually provide a solution with tools to address such issues and, most importantly, to
116 disentangle the impact of structural and functional social relationships. However, currently,
117 these analytical methods (e.g., metrics like versatility and multiplex PageRank) are not
118 sufficiently sophisticated to account for the many structural differences that exist between
119 behavioral networks of different types (e.g., proximity networks are often dense and undirected,
120 contact networks may be more sparse and undirected whereas grooming networks are directed)
121 [29]. Yet, given mounting evidence for the importance of multidimensionality in social
122 relationships, the integration of diverse affiliative behaviors at this dyadic level may provide
123 important additional information (1) as to the nature of those relationships, (2) on how their
124 structure points to their potential function(s), and (3) on their downstream impacts on health and
125 fitness (Balasubramaniam et al., 2016). Indeed, in many past studies, multidimensional measures
126 often are the strongest predictors of health and fitness [1,8,13]. Yet, again, few animal studies to date
127 (except see [27]) have examined whether the integration of that diversity of interactions in a
128 relationship provide clues as to the nature of those social relationships. One exception, conducted
129 by Balasubramaniam and colleagues [14] representing one type of integrated approach, found that
130 highly connected rhesus macaques (i.e., high outdegree or eigenvector) in a grooming network
131 were less likely to have *Shigella*, a gastrointestinal pathogen, *but only if they were also well*
132 *connected in a huddling network* (i.e., high betweenness), suggesting that the presence of
133 multiple affiliative behaviors across an individual's dyadic connections (e.g., integration) confer
134 a social buffering effect on individual health (Balasubramaniam et al., 2016).

135 Here we employed a social network approach to explicitly explore whether the
136 integration of diverse affiliative behaviors within a relationship can point to the potential
137 function of those relationships and their impact on health-related outcomes in a commonly
138 studied non-human primate model system, the rhesus macaque (*Macaca mulatta*). We use
139 rhesus macaques as a group-living, nonhuman primate (NHP) model because their social
140 relationships are highly differentiated, exhibit a high degree of complexity and individual
141 variability, and have been linked to a variety of health and fitness outcomes [30–33]. Affiliation in
142 rhesus macaques, as in many primate species takes many forms, including grooming, contact
143 sitting, proximity, embracing, and less commonly coalitionary support [34–36]. In macaques,
144 grooming is commonly used to indicate the presence of an affiliative relationship [37,38]. Grooming
145 has been proposed to serve multiple social functions including: to maintain social bonds [37] and
146 social cohesion [39], and in exchange for tolerance from dominants, for agonistic support, or for
147 access to resources [40–42]. Although less commonly studied, contact sitting behavior (similar to
148 huddling) may also be an important indicator of strong affiliative relationships [43], particularly
149 those that may offer social buffering [14].
150 Therefore, in this study, an integration of affiliative behaviors was conducted by filtering
151 these behavioral networks (grooming and contact sitting) into "multiplex" and "uniplex"
152 networks. We use the term "multiplex" to refer to networks in which edges are represented by
153 the co-occurrence of multiple affiliative behaviors and the term "uniplex" to refer to networks in
154 which edges represent only one specific type of interaction (e.g. grooming *or* contact sitting, not
155 both)[4,8]. Our multiplex networks were defined as the set of dyads who engaged in both grooming
156 and contact sitting with edge-weights reflecting grooming (multiplex grooming) or contact
157 sitting (multiplex contact sitting) frequency, while our uniplex networks were defined as the set

158 of dyads who engaged solely in one behavior with edge weights reflecting the frequency of
159 interaction (uniplex grooming or uniplex contact sitting). Our rationale for constructing
160 multiplex and uniplex networks in this manner was inspired by Balasubramaniam [14] which
161 identified the combination of grooming and huddling behavior to be especially protective against
162 Shigella infection. Further, this distinction could also be hypothesized to relate to the different
163 functions of grooming (social bonding/cohesion vs. exchange for tolerance and resources).
164 Therefore, our primary focus for this study was to examine the differences between multiplex
165 grooming and uniplex grooming networks. However, we also present results comparing
166 additional complementary networks (multiplex contact sit vs. uniplex contact sit and grooming
167 vs. contact sitting) to fully explore the impact of filtering networks in this way. Our analysis had
168 two main goals: 1) determine if the network structure of related networks differed, and 2) the
169 effects of individual network centrality on health. To this end, differences in global network
170 structure of multiplex and uniplex or grooming and contact sitting networks were compared and
171 individual-level centrality metrics from these networks were examined for their association with
172 biomarkers of inflammation (i.e., serum pro-inflammatory cytokines), which are common, well-
173 established indicators of individual health status [33,44]. As such, our prediction was that
174 individuals exhibiting more central roles in multiplex (socially cohesive) networks would show
175 lower levels of inflammatory cytokines than those exhibiting more central roles in uniplex
176 networks.
177

178 ## Materials and Methods

179 **Study system**

180 Rhesus macaques live in large multi-male, multi-female social groups organized by rank
181 and kinship [45]. For females, rank is inherited from their mothers and generally all members of a
182 matriline hold adjacent ranks [46] (although see [47]). In contrast, males generally immigrate into a
183 new social group and may enter at the bottom of the hierarchy, queueing for rank, or attain rank
184 through direct competition [48]. Rhesus macaque females form the core of the social group with
185 affiliation between both kin and non-kin playing a key role in maintaining group stability [45,49].
186 Although male social bonds have important fitness outcomes in macaques generally [50], male
187 rhesus macaques engage in social affiliation far less frequently [51] and tend to be more socially
188 isolated than females [52]. Therefore, we focused our study on females, which we predict will be
189 more strongly impacted by social bonds than males. We use rhesus macaques as a group-living,
190 nonhuman primate (NHP) model because their social relationships are highly differentiated,
191 exhibit a high degree of complexity and individual variability, and have been linked to a variety
192 of health and fitness outcomes [30–33].

193 **Subjects and housing**

194 Subjects were 248 breeding age (3 years and older) female rhesus macaques (*Macaca*
195 *mulatta*) that were born at the California National Primate Research Center in Davis, California
196 (Table 1). Subjects lived in one of four large multigenerational and matrilineal social groups
197 containing 100-200 mixed-sex individuals (Table 1), each housed in a 0.2 hectare outdoor
198 enclosure. Subjects were fed commercial monkey chow and foraging enrichment twice daily.
199 Fruits or vegetables were provided weekly. Water was available ad libitum.

200

201 **Table 1: Group Demographics**

Group	Group size (adults)	N (adult females)	# of Matrilines[a]	Mean Matriline[a] size (SD)
Group A	131 (101)	74	13	5.7 (3.6)
Group B	204 (101)	67	33	2.0 (1.0)
Group C	125 (55)	39	6	6.5 (3.9)
Group D	185 (96)	68	13	5.2 (2.3)

202 [a] Number of matrilines and matriline size statistics include only breeding age females.
203 Individuals were considered part of the same matriline if they could be traced back to the same
204 female common ancestor at the time of group formation.
205
206 **Behavioral data collection**

207 Subjects were part of a larger study on the associations between social networks and
208 health. Groups A and B were studied for six continuous weeks during the birthing season from
209 March to April 2013 and 2014, respectively. Groups C and D were studied for six continuous
210 weeks during the breeding season from September to October 2013 and 2014, respectively.
211 Behavioral data were collected six hours per day, four days per week from 0900-1200 and 1300-
212 1600 each day by three observers (inter-rater reliability, Krippendorff's alpha ≥0.85). Affiliative
213 behavior was collected by one observer via scan sampling every 20-minutes (maximum 18 scans
214 per day), where identities of all adult female dyads affiliating (i.e. grooming or contact sitting)
215 were recorded[14]. All animals had tattoos and fur markings that allowed accurate individual
216 identification. All observers demonstrated animal ID reliability of > 95%. Grooming was
217 defined as cleaning or manipulating the fur of another animal and contact sitting included ventral
218 contact, embrace, or side by side sitting for at least 3 seconds. During each scan, these behaviors
219 were mutually exclusive for a dyad (an individual grooming another was not contact sitting with
220 that individual). Affiliation scans produced 1637 scans (Group A: N=418, Group B: N=410,
221 Group C: N=378, Group D: N=431) and a median of 38 grooming interactions per female (group
222 range 23 – 49) and 28 contact sitting interactions (group range 13-52). This sampling scheme has

223 been shown to produce sufficiently sampled grooming and contact sitting networks[38]. Aggression
224 data (threats, chases, bites) were collected via an event sampling protocol for six hours per day,
225 four days per week by two other observers (average of 42.5 interactions per individual, group
226 range 36.2 – 51.9). Because social status has been shown to impact inflammation[31] (although
227 see[30]), dyadic aggression data was used to calculate dominance ranks and dominance certainty
228 via the R package *Perc*[30,53]. Dominance rank was expressed as the percent of animals in the
229 group outranked and therefore ranged from 0 (low) to 1 (high).

230 **Affiliative network analysis**

231 First, weighted networks were constructed from grooming and contact sitting interactions
232 (Figure 1A). Each of these networks (i.e., grooming or contact sitting) were then separated into
233 two more networks, a multiplex network where edges between dyads that both groomed and
234 contact sat were retained (Figure 1C or 1E), and a uniplex network in which edges were retained
235 for dyads that only groomed (Figure 1D) or only contact sat (Figure 1B). Edge-weights in
236 contact sitting networks (all contact sitting, uniplex contact sitting, multiplex contact sitting)
237 reflected the number of unique scans in which a dyad was observed contact sitting over the 6-
238 week period. Edge-weights in grooming networks reflected the number of unique scans a dyad
239 was observed grooming (Table S1). For each of the 6 networks (all grooming, multiplex
240 grooming, uniplex grooming, all contact sitting, multiplex contact sitting, uniplex contact
241 sitting), centrality and cohesion measures for each individual were calculated in R (ver. 4.0.5)
242 using iGraph (ver. 1.3.0). The effects of the direct connections for individuals were measured
243 using degree centrality and strength. The effect of an individual's indirect connections in the
244 network was evaluated using eigenvector, betweenness, and closeness centralities [3,14,16]. In
245 addition, the degree to which individuals were part of cohesive local communities was measured

by the local clustering coefficient (i.e., triadic closure). Multiple metrics were chosen to reflect the different ways social integration can manifest (e.g., bridging, cohesion, embeddedness, etc. Table 2).

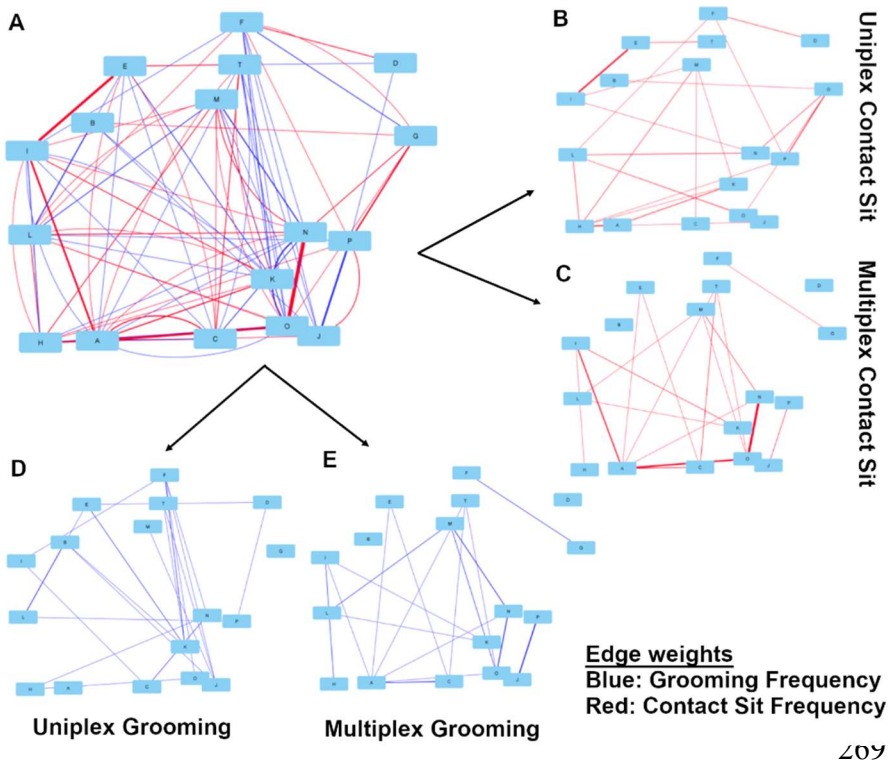

Figure 1: A network example using a subset of animals from Group XX. Edge weight is represented using line thickness and behavior is indicated by color. Network filtering started with networks consisting of (A) all observed grooming (blue) and contact sitting (red) interactions. Edges from these networks were then filtered into multiplex grooming (E) or multiplex contact sitting (C) networks if dyads engaged in both behaviors. Dyads that only groomed were filtered into a uniplex grooming network (D) and dyads only engaged in contact sitting were filtered into a uniplex contact sitting network (B).

Table 2: Network Metric Definitions

Measure	**Description**
Degree/Strength	measures the *number* (unweighted) of partners or *frequency* of interaction (i.e., strength) for each node.[54]
Eigenvector	measures whether individuals are well connected to others that are also well connected, a measure of *social capital*.[54]
Betweenness	measures the number of times a node lies on the shortest path between other nodes, which reflects an individual's role in connecting others in the network or acting as a *social bridge*.[54]
Closeness	measures how close each node is to all other nodes within the network, which reflects how *embedded* an individual is in the network. [55]
Clustering Coefficient	measures the extent to which a node's neighbors are also connected to each other, a measure of *cliquishness or subgrouping*.[56]

275 **Biological sample collection**

276 Blood samples were taken during the fifth week of each group's study period during
277 routine, semi-annual health checks. On a single morning, all animals in a group were lightly
278 sedated with ketamine (10 mg/kg) and given veterinary exams. Blood samples were obtained
279 from the femoral vein and serum was aliquoted and stored at −80 °C for later assay. The order in
280 which animals were processed and samples were collected was recorded to control for any
281 potential impacts of the sampling procedure on the physiological variables examined.

282 **Pro-inflammatory Cytokines**

283 Chronic inflammation is associated with a variety of diseases (e.g., diabetes,
284 cardiovascular disease, cancer) and mortality [57–59], and high levels of pro-inflammatory
285 cytokines, such as IL-6 and TNF-α, have previously been reported to be associated with social
286 variables (e.g., low social status, low social integration, poor quality relationships, loneliness) in
287 both humans and rhesus macaques [30,33,44,60,61]. Therefore, we chose to measure serum levels of
288 IL-6 and TNF-α as a general biomarker of health. Serum levels of IL-6 and TNF-α were
289 measured simultaneously using commercially available, species specific Milliplex multi-analyte
290 profiling (MAP) reagents purchased from EMD/Millipore (Billerica, MA, USA), and utilizing
291 Luminex Xmap technology (Luminex, Austin, TX, USA). Color coded polystyrene microbeads
292 coated with specific antibodies for IL-6 and TNF-α were incubated with the serum samples,
293 washed, and then further reacted with biotinylated detector antibodies followed by Streptavidin-
294 PE to label the immune complexes on the beads. After a final washing to remove all unbound
295 material, the beads were interrogated in a BioPlex dual laser (BioRad, Hercules, CA, USA). The
296 median fluorescent index for each sample was compared to a standard curve to calculate the
297 concentration (IL-6: mean = 12.55 pg/mL, sd = 46.92, range = 0 – 690; TNF-α: mean = 185.0
298 pg/mL, sd = 442.27, range = 0 – 4052; see Figure S2 for histograms). Samples were tested in

299 duplicate and had an intra-assay coefficient of variability of 15.3%. Samples were re-analyzed if
300 the CV was greater than 25% for all analytes measured. Manufacturer provided quality control
301 samples fell within recommended ranges for all assays. Samples falling below the threshold
302 sensitivity of the assay (1.6 pg/mL) were assigned a value of zero (IL-6: N = 77, TNF-α: N =
303 56).

304 **Statistical analysis**

305 Two sets of analyses were done to determine whether 1) multiplex and uniplex grooming
306 networks (i.e., Fig 1B vs 1C or Fig. 1D vs 1E) or grooming and contact sitting networks (Fig. 1A
307 red vs. blue) differ in structure and relationships to known social features of rhesus macaques
308 (e.g., kin bias, hierarchical organization), and 2) whether network metrics from these networks
309 predicted biomarkers of inflammation, with a specific focus on the relative impact of multiplex
310 vs uniplex (or grooming vs. contact sitting) network position on inflammation.

311 First, to validate this method, the structure of the multiplex and uniplex networks, which
312 were treated as weighted and directed (grooming only) networks, were compared to determine if
313 they exhibited differences in key structural features of rhesus relationships. For example,
314 evidence suggests that despotic macaques such as rhesus, particularly in large groups, are likely
315 to have grooming networks that are modular (i.e., shows subgrouping), expected to be based on
316 kinship, and have individual network positions (i.e., eigenvector centrality) that are correlated
317 with rank[62,63]. Therefore, we examined whether these two networks differed in the degree of
318 clustering (Newman's modularity, clustering coefficient), kin bias (e.g., proportion of kin (kin
319 unweighted degree/total unweighted degree)), and associations with rank (proportion of
320 grooming up the hierarchy, rank disparity among grooming dyads) for each of the four groups
321 studied. Also, because previous research has focused on bond strength, we further examined

322 reciprocity, strength of relationships (average edge weight), and distribution of grooming
323 (eigenvector centralization) across these network types. Due to the low number of groups in the
324 comparison, paired t-tests were used to evaluate if network metrics were consistently different
325 across groups. Normality of the differences was evaluated using the Shapiro-Wilk test, and if
326 significant then Wilcoxon signed rank tests were used. Grooming and contact sitting networks
327 were also compared. As a final structural analysis, we examined the correlations between
328 individual level network positions from these two network types (Table S2) to evaluate
329 multicollinearity within networks and associations between networks, including contact sitting
330 networks.

331 Next, to determine if an individual's position in the multiplex or uniplex networks was
332 associated with pro-inflammatory cytokines, we ran generalized linear models using a negative
333 binomial distribution (proc glimmix, SAS 9.4) on each biomarker separately (see [30] for details on
334 distribution choice and Figure S2 for distributions). For these analyses, networks were treated as
335 weighted but undirected because of our focus on the qualities of a relationship rather than
336 focused specifically on grooming behavior and because contact sitting is recorded as an
337 undirected behavior (i.e., information on who initiated the interaction is unavailable). One
338 animal was excluded from the IL-6 analyses because it was an outlier with influence (Cook's D
339 >1); all other outliers had a Cook's D < 0.5 and therefore were included in the analyses. A
340 second animal was excluded from all analysis due to the fact she was not included in the uniplex
341 network. Model building proceeded in five steps for each outcome (i.e., IL-6, TNF-α, see Figure
342 S2). For all steps, ΔAIC > 2 was used to identify potential predictors and candidate models. For
343 one social group, 6 animals were not present in the uniplex contact sit network (they never
344 engaged in contact sitting with someone they did not also groom). Therefore to evaluate the

345 effects of uniplex contact sitting we use a subset of the full dataset for AIC comparisons. First, a
346 random effect indicating the group ID was evaluated for each outcome, and all subsequent
347 models were compared to this random effects only model. Second, variables from the literature
348 (age, dominance rank, dominance certainty, sampling order), although not of direct interest here,
349 were evaluated to determine if it was necessary to control for their effects on inflammation
350 before examining social network variables. Third, due to the large number of potential predictors
351 in our exploratory analysis, a statistical winnowing strategy was used to reduce the number of
352 social network variables under consideration [64]. This involved running univariate models for
353 each metric from each network (6 networks with 6 metrics each). Due to our goal of directly
354 comparing effects of centrality in different networks and predictions for multiplex vs uniplex
355 networks, if no metric generated improvement in model fit (i.e., $\Delta AIC > 2$) for a given network
356 all available network metrics for that network were explored in step 4. Fourth, to compare the
357 effects of uniplex and multiplex network connectivity directly, candidate predictors from step 3
358 for the uniplex and multiplex grooming (Figure 1D vs E), uniplex and multiplex contact sitting
359 networks (Figure 1B vs C) were directly compared. Additionally, effects of centrality in
360 grooming vs contact sitting networks were compared (i.e., Figure 1A red vs blue). Fifth, a final
361 set of best models was identified by comparing AIC across all models generated in steps 3 and 4.
362 Metrics from the same network were never included in the same model due to the
363 interdependence of network metrics. If no single best model emerged, candidate models (i.e.,
364 those with $\Delta AIC \leq 2$) are discussed. A log of all models tested is available in Tables S3-4.

365 **Ethical Note**

366 All procedures used in this study met all legal requirements of the United States as well
367 as guidelines set by the American Society of Primatologists regarding the ethical treatment of

368 non-human primates. This study was approved by the Institutional Care and Use Committee at
369 the University of California, Davis and was carried out in compliance with the ARRIVE
370 guidelines.
371

372 **Results**

373 *Multiplex vs. Uniplex Affiliation Networks*

374 For all groups studied, clear differences in network topology, kinship, and associations
375 with dominance rank were seen between the multiplex and uniplex affiliative networks (Table 3).
376 Multiplex grooming networks had higher average edge-weight (the average number of
377 interactions per social partner), clustering coefficient, and modularity (the degree to which the
378 network can be divided into subgroups) than uniplex grooming networks for all groups. Notably,
379 although average edge-weights in the multiplex networks were higher than uniplex networks, the
380 predominant edge weight in all networks was 1-2 interactions (Figure S1). Multiplex grooming
381 networks also consistently showed more kin bias (proportion kin) and reciprocity than uniplex
382 grooming networks. In contrast, both multiplex and uniplex grooming networks showed
383 associations between rank and affiliation (i.e., grooming was directed up the hierarchy and
384 eigenvector centrality was correlated with rank in both networks) but the disparity in the ranks of
385 the grooming partners was greater in the uniplex affiliation networks compared to the multiplex
386 networks. Results for the multiplex vs uniplex contact sitting networks were the same as for
387 multiplex and uniplex grooming networks with the exception of reciprocity and grooming up the
388 hierarchy which were not calculated for these undirected networks (Table 3). Individual
389 centrality metrics generated from the multiplex grooming networks were largely uncorrelated
390 with metrics from the uniplex grooming networks (mean correlation strength = 0.11, SD = 0.08,

Table S2). In contrast, centrality metrics from grooming and contact sitting (mean correlation strength = 0.37, SD = 0.07) and multiplex and uniplex contact sitting networks (mean correlation strength = 0.32, SD = 0.24) were moderately correlated. In contrast, the structure of the all grooming and all contact sitting networks did not differ on any examined metric with the exception of average edge-weight which was higher in grooming networks.

Table 3: Whole Network Metric Comparisons

Network	Multi vs. Uni Grooming	Multi vs. Uni Contact Sit	Contact Sit vs Grooming
Density	Multi = Uni	Multi = Uni	CS = GR
Modularity	Multi > Uni*	Multi > Uni*	CS = GR
Eigenvector Centralization	Multi = Uni	Multi = Uni	CS = GR
Avg Edge Weight	Multi = Uni[a]	Multi = Uni[a]	CS < GR*
Clustering Coefficient	Multi > Uni*	Multi > Uni*	CS = GR
Reciprocity	Multi > Uni*	-	-
Proportion Kin	Multi > Uni*	Multi > Uni*	CS = GR
Proportion Up Rank	Multi < Uni*	-	-
Rank Disparity	Multi < Uni*	Multi < Uni*	CS = GR
Rank/Eigenvector centrality correlation	Multi = Uni	Multi = Uni	CS = GR

Multi: Multiplex network; Uni: Uniplex network; GR: Grooming; CS: Contact Sit. Effect indicates the overall difference between networks for all groups using a paired t-test. [a] Wilcoxon test. * $p < 0.05$

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IL-6. There were six models that had AIC within 2 of the best fit model, all of which included metrics from both the multiplex and uniplex grooming networks. For all models, less connected individuals in the multiplex grooming network (degree, closeness, or clustering coefficient) but more connected individuals in the uniplex grooming (strength, closeness) network had higher levels of IL-6, although these effects were not significant in all candidate models (Table 4). Due to this directional consistency we present the results of the just the best fit model in Figure 3A-B. Multiplex closeness was not correlated with uniplex closeness (r = -0.04). Contact sitting degree was weakly negatively correlated with uniplex closeness (-0.13) but more strongly correlated

411 with multiplex closeness (r = 0.77) yet analysis of VIF (< 2.5) and tolerance (≥ 0.4) did not

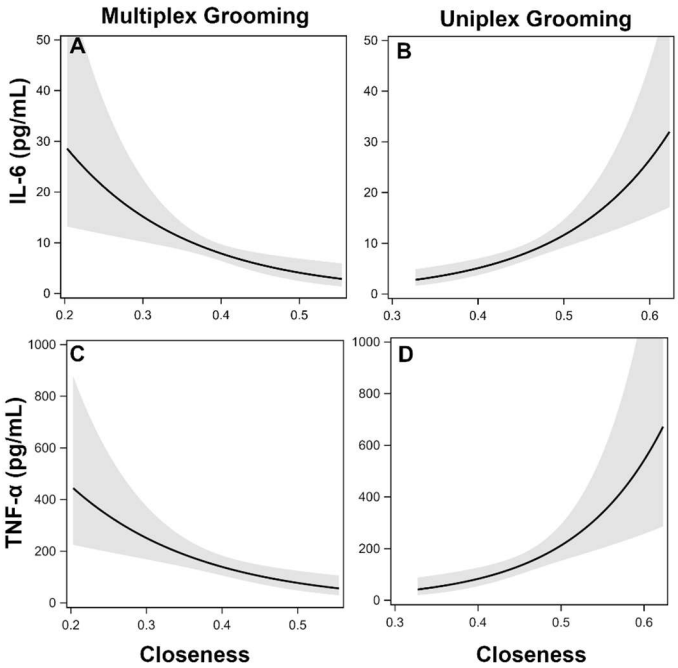
412 indicate any issues with collinearity.

413 **Table 4: IL-6 Candidate Model Outputs**

Model Parameters	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Intercept	0.03	2.8**	1.6***	-0.7	1.8***	1.8**
Uni GR Strength	-	0.05**	0.04**	-	0.04**	0.04**
Uni GR Closeness	7.6**	-	-	6.2**	-	-
Multi GR Degree	-	-	-	-	-	-0.03
Multi GR Closeness	-3.6*	-3.2	-	-	-	-
Multi GR Clustering	-	-	-	-	-0.4	-
ΔAIC	0.00	0.30	0.70	1.40	1.90	1.90

414 * p < 0.05, ** p < 0.01. Uni = Uniplex, Multi = Multiplex, GR = Grooming network. All models
415 were run using a negative binomial distribution and included a random effect of group.
416

417
418 **Figure 2.** Effects of affiliative centrality
419 on cytokines. Effects of multiplex (Multi)
420 grooming closeness (A) and uniplex (Uni)
421 grooming closeness (B) on levels of IL-6
422 with 95% confidence intervals (Model 1).
423 Effects of multiplex grooming closeness
424 (C) and uniplex grooming closeness (D)
425 on levels of TNFα with 95% confidence
426 intervals (Model 1).
427



428 **TNF-α.** There were five candidate models
429 identified; the top four of these included
430 comparisons of multiplex and uniplex
431 grooming centrality and the last included
432 centrality metrics from the grooming and contact sitting networks (see Table 5). As with IL-6,
433 lower centrality in the multiplex grooming network (degree or closeness) but higher centrality in
434 the uniplex grooming network (strength or closeness) were consistently associated with higher
435 levels of TNF-α (Table 5, Figure 3C-D). In the fifth candidate model, higher eigenvector

436 centrality in the grooming network but lower closeness centrality in the contact sitting network

437 were associated with higher levels of TNF- α.

438

439 **Table 5: TNF-α Candidate Model Outputs**

Model Parameters	Model 1	Model 2	Model 3	Model 4	Model 5
Intercept	2.9*	6.6**	4.9**	0.9	8.3***
Uni GR Strength	-	0.06**	0.06**	-	-
Uni GR Closeness	9.4**	-	-	10.4**	-
Multi GR Degree	-	-	-0.1*	-0.1*	-
Multi GR Closeness	-5.9**	-6.0**	-	-	-
All GR Eigenvector	-	-	-	-	1.7**
All CS Closeness	-	-	-	-	-8.0**
ΔAIC	0.00	0.10	1.30	1.60	1.80

440 * $p < 0.05$, ** $p < 0.01$. Uni = Uniplex, Multi = Multiplex, GR = Grooming network, CS =
441 Contact sitting network. All models were run using a negative binomial distribution and included
442 a random effect of group.
443

444 ## Discussion

445 Social primates have a complex web of differentiated social relationships, which vary in

446 their structure and function. While strong affiliative social relationships are usually associated

447 with better health, less is known on how the multidimensionality or integration of different

448 affiliative behaviors within a social relationship might impact health. We identified affiliative

449 relationships that were multiplex (animals affiliated using both grooming and contact sitting

450 behavior) versus uniplex (animals only groomed or only contact sat). Examination of these

451 networks revealed that they differed in topology, kinship, and associations with rank. Multiplex

452 networks were more modular, clustered, reciprocal, had higher average edge weights, and were

453 more strongly associated with kinship. In contrast, dyads in the uniplex networks tended to be of

454 more disparate ranks. Notably, these differences in kinship and rank between multiplex and

455 uniplex networks were not apparent when looking at all grooming or contact sitting interactions.

456 The health impacts of these two networks differed as well, with females that were *less* socially
457 embedded in multiplex grooming networks exhibiting higher levels of biomarkers of
458 inflammation (IL-6 and TNF-α), whereas females *more* socially connected in uniplex grooming
459 networks exhibited higher levels of biomarkers of inflammation. Notably, these effects were
460 primarily seen in multiplex and uniplex grooming, not in the other networks tested. These
461 results suggest that grooming which occurs in the context of multiplex affiliative relationships
462 may result in health benefits (i.e., reduced inflammation) while grooming occurring in uniplex
463 affiliative relationships may have potential costs.

464 Networks consisting of dyads with multiplex relationships showed differences from
465 uniplex relationships in network topology, kinship, and associations with dominance. Multiplex
466 networks had structural characteristics consistent with strong bonds or supportive affiliative
467 relationships[23,65,66]. Specifically, interactions in the multiplex networks were more likely to be
468 reciprocal, frequent (i.e., higher edge-weight), clustered, and associated with kinship, suggesting
469 they are relationships that are regularly maintained and potentially more stable across time[23,66].
470 Previous methods demonstrating that strong bonds enhance fitness, particularly those using
471 sociality indices, have also used multiple behaviors to assess relationship strength (e.g.,
472 grooming and proximity[12,26,27]). However, these methods rely on total duration or frequency of
473 affiliation to describe relationships rather than characterizing the breadth or dimensionality of the
474 relationships (e.g., dyads can have high DSI through grooming, proximity, or both). Similar to
475 strong bonds, multiplex affiliative relationships may improve health and fitness by buffering
476 individuals from the negative impacts of stress, improving predator detection, promoting
477 offspring survival, and improving social stability[14,16,67,68].

478 Also consistent with the literature on strong affiliative bonds, being well connected to
479 others was associated with biomarkers of better health. Specifically, the negative association
480 between multiplex grooming centrality (e.g., degree, closeness centrality, or clustering
481 coefficient) and biomarkers of inflammation indicated that individuals that were generally well
482 connected in the network (e.g., at the core of the group) may be at lower risk for inflammation
483 related diseases[57]. Our results add to the literature suggesting that strong bonds may improve
484 fitness by altering endocrine and immune function[13,25,69,70]. Consistent with this idea, Yang et
485 al.[71] found in humans that socially integrated individuals (i.e., those with more social
486 connections across multiple domains) exhibited lower inflammation, whereas social strain (e.g.,
487 higher levels of family criticism or demands) was associated with greater inflammation. Given
488 that familial and friend relationships tend to endure through extended periods, often persisting
489 over decades (in both humans and NHPs), these relationships may have an important and long-
490 lasting impact on health.

491 Uniplex grooming relationships may reflect relationships that are more transactional in
492 nature [72]. The fact that uniplex grooming relationships are less kin biased but likely to occur
493 between dyads of more disparate ranks suggests that these relationships may be more related to
494 grooming being used as a commodity in exchange for tolerance or support from higher ranking
495 animals. These relationships are likely more transactional in nature, reflecting a desire to
496 maintain peace/tolerance or used in a biological market exchange[40,41], rather than reflecting a
497 strong affiliative relationship. The positive association between females' connectedness in
498 uniplex grooming networks and biomarkers of inflammation suggests that uniplex grooming
499 relationships may not be supportive on their own and instead are associated with increased
500 physiological costs, at least in the short term. Specifically, predictors of inflammation in the

501 uniplex grooming networks included strength or closeness centrality. However, the various
502 network centrality metrics from the uniplex grooming network were more highly correlated with
503 each other than the other networks, and therefore it is difficult to identify which specific aspect
504 of uniplex grooming centrality might be driving these effects. However, collectively this group
505 of candidate predictors indicates that greater general connectedness (direct and indirect) in
506 uniplex grooming was associated with increased inflammation. Uniplex grooming relationships
507 were maintained through generally less frequent interactions that were more likely to occur
508 between animals of disparate ranks which may result in greater uncertainty regarding the
509 outcome of any given interaction. This uncertainty may be stressful, and therefore have at least
510 short-term physiological costs[73]. If these relationships are more transactional in nature, reflecting
511 a desire to maintain peace/tolerance or used in a biological market exchange[40,41], then
512 maintaining more of these transactional relationships may result in increased stress, which if
513 sustained can result in long-term physiological costs[13]. It is possible that these short-term costs
514 are actually investments that may manifest in future benefits (e.g., tolerance, alliance support)
515 that would offset these costs, yet this is difficult to test as the "commodities" exchanged may be
516 heterogeneous and the time-scale for market exchanges is often unclear[74]. However, other work
517 points to benefits of weak or economically based bonds to survival and reproduction[9,26]
518 (although see[12]). While these types of connections may have ultimate fitness benefits (e.g.,
519 alliance support, increased access to food), this research suggests they may also be associated
520 with proximate costs.

521 **Conclusion**

522 Both humans and many species of NHPs engage in a complex interconnected system of
523 social interactions. Understanding the mechanisms by which social relationships impact health

524 and fitness remains a challenge. Decades of research has established that affiliative social
525 relationships can benefit health, however, the complexity and multidimensionality of
526 relationships has yet to be explored. By utilizing a network approach, we were able to
527 characterize two types of affiliative social relationships that differed in their network topology,
528 kin bias, associations with rank, and importantly their associations with biomarkers of
529 inflammation. Our research has indicated that features of multiplex affiliative relationships are
530 consistent with the concept of a strong supportive relationships and may support health and
531 fitness. In contrast, more transactional affiliative relationships (e.g., uniplex affiliation) may
532 incur short-term health costs yet may result in ultimate benefits through commodity exchange.
533 Still unclear is whether these effects are specific to the combination of behaviors used here (i.e.,
534 contact sitting and grooming), or if other affiliative behaviors (e.g., proximity) might provide
535 similar information. Further research into the dimensionality of relationships might reflect
536 different qualities or functions of relationships is needed. However, this complexity is important
537 to consider for understanding the mechanisms underlying the impact of social relationships on
538 human and NHP health.
539

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