his manuscript the authors advocate for the use of a small set of properties of animal networks, namely the spectral radius and Fiedler value (both based on eigenvalues of the network's contact matrix) as practically useful shortcuts to predict specific infectious disease outcomes, mainly the maximal prevalence of infection in the host population. According to their paper, simply knowing the structure of the contact network of individuals within a population would allow one to estimate the vulnerability of that population to disease spread, without a need for specific information about the pathogen (e.g., transmissibility) or host physiology (e.g., recovery rate of infected individuals) or other features specific to the particular disease system. So, without painstaking parameterization of models for particular populations, and with only data on spectral properties of the network, one might derive a sufficiently robust first-guess at vulnerability to disease so that appropriate actions may be taken. Thus, the main selling point for the study is its ability to provide a robust, less-data-intensive shortcut for disease prediction and hence management.  
  
They derive this conclusion via a series of steps, although I admit that I struggled to follow the structure and logic of their approach. The steps start with obtaining information on interaction networks for a set of animal species in which various observational methods are used to identify interactions between pairs of individuals (e.g., proximity, contact). Models are then used to describe the network structure, which can then be used to ask about impacts on pathogen transmission or disease spread. Of course, such approaches have been used many times in the recent (and not so recent) literature, with various conclusions regarding the importance of specific network features such as modularity, mean number of contacts per individual, network size, number of edges, etc., being drawn. What is different here is that the authors focus on certain eigenvalues (spectra) of the network rather than the more traditional measures. Further, they simulate the behavior of generic diseases by varying transmission probability (beta) and host recovery rate (gamma) to run SIR models of pathogen transmission in the network and compare select spectra against more traditional measures using machine learning algorithms to assess predictive capability. They have a short section that compares their general modeling results to two specific empirical cases of disease spread, namely bTB in badgers and DFTD in Tasmanian devils.  
  
To my mind, the authors have set for themselves a very high bar. They wish to provide a simpler, less data-hungry method for drawing both generalities about how network structure (whether spectral or more traditional features) affects disease spread in animal populations, as well as enough specific, predictive information to provide the basis for management decisions for those populations. I had considerable trouble envisioning how this research strategy would be actionable for, e.g., wildlife managers. Perhaps fewer data on pathogen behavior and host immune function would be required, but considerable data on social networks would be all the more essential, as would sophisticated expertise in multivariate interpretable machine learning algorithms. I would be more comfortable with a paper that explored the generalities in their approach without promising, e.g., that "...the spectral radius of an animal network is a powerful predictor of spread for diverse hosts and pathogens that can be a valuable shortcut for stakeholders to understand the vulnerability of animal networks to disease." I did not see this promise being validated in the paper and suspect that specific applications might not be enhanced by the modeling strategy advocated.  
  
I was concerned about the central method for obtaining information on animal social networks (which they incorrectly term "contact networks"). The data come from ASNR (ref 24), which at the time of publication included a highly biased sample of animal species. Initially 3 species of insects, 2 fish, 2 reptiles, 5 birds, and ~34 mammals were included in the data set, which has expanded a bit but without changing this bias. Of the mammals, most are large, diurnal primates. Ants are highly overrepresented in number of networks but poorly represented in number of species. Most studies were <6 months in duration, preventing detection of possible seasonal or interannual changes in contact network structure, e.g., as population density or distribution fluctuates. Half the studies had unspecified time resolution of observations. Roughly half seem to be of captive animals. Quoting from ASNR, "behavioral data span a range of social associations from direct physical contacts such as grooming and trophallaxis to indirect interactions such as spatial proximity and associations." In other words, these are social networks, not necessarily contact networks, with powerful relevance to inferring pathogen transmission. To what degree are the species that wildlife managers need to manage for disease well represented in the network data set? How important is it to have a less biased sample of species and conditions on which to base the assessment of matrix spectra? It is quite problematic that none of this is described in the Methods, and recourse to the original paper and website was required.  
  
A few problems in the Results include: the possibility that the sensitivity of PC2 to "network duration" was a methodological artifact of the great variation in the time periods over which data were collected, which could affect accuracy of network construction.  
In line 176, the authors refer to Fig 2a when they mean Fig 3a.  
Why is maximum proportion infected the central epidemiological response variable? Why not R0 or time to maximum or minimum prevalence? This prevalence variable might not be of the greatest importance to disease impacts or management.  
I was confused by the observation that the effect of spectral radius on infection prevalence depended on beta and gamma, which seems to contradict the interpretations that traditional epidemiological data can be replaced by this technique. Also, contrary to what is stated, gamma is a property of host immunity/physiology rather than a property of the pathogen.  
I was confused by the claims of strong validation of the approach with the two case studies on bTB and DFTD. For bTB, the authors state, "Our model predicted the proportion of infected badgers in the network to be 0.45, which was much lower than the average proportion infected across all networks included in our study (0.71)." This seems like poor validation, or invalidation. What follows this is something that sounds like post hoc reasoning to explain the poor fit. For DFTD, I was confused about the suitability of this disease as a validation data set given the lack of "recovered" individuals, rendering SIR models suspect. The model estimate of 89% of individuals infected indeed falls within the range of empirical estimates for mature devils of 70-100%, but does this constitute a validation? The sentence starting line 247 made no sense to me.  
  
I found the opening paragraph of the Discussion to quite strongly overstate what the authors showed and its usefulness. In Fig. 3a they show that species identity was equally strong as a predictor of epidemic outcomes as Fiedler value, but this is not addressed. I disagree that the study showed that the authors "...not only demonstrated the high predictive power of a network's spectral properties but also show that our predictions can be a useful tool for estimating spread in systems with complex disease dynamics." Maximum prevalence is not the same as spread, and actual disease dynamics were not a part of the exercise. Regarding whether the "global surrogate models provide animal health practitioners with an intuitive framework" regarding population vulnerability, I wonder how that is envisioned to work? Wouldn't large amounts of data on contact networks, plus a sophisticated understanding of beta and gamma (critical for choosing models), be essential for making quantitative predictions? And wouldn't the predictions be limited to maximum prevalence rather than population vulnerability?  
  
Line 299 appears to have an editing problem with what is inside the parentheses.  
  
  
  
Reviewer #2:  
  
Suitable Quality?:  
No  
  
Sufficient General Interest?:  
No  
  
Conclusions Justified?:  
No  
  
Clearly Written?:  
Yes  
  
Procedures Described?:  
Yes  
  
Supplemental Material Warranted?:  
Yes  
  
Comments:  
While I appreciate the intention of this manuscript, I felt that it was not a complete story and I am concerned that even with the structural concerns (below) addressed that it may not yet rise to the level that I would expect of a paper in PNAS. The general question posed, that some, possibly complex, combination of network measures may be better predictive of epidemic dynamics than any single measure, is an interesting one. However, I don't think the manuscript as currently structured can really answer this question.  
  
First, the authors only analyze simulations rather than observed epidemics (barring two empirical examples). Second, the authors only present the fit of the ML models, but do not illustrate whether these models do better than prior methods for estimating the final size of epidemics on networks (e.g. from the PGF from Newman, or the edge-based model from Miller). Given the former, I am not surprised that there are strong correlations between network properties and simulated outcomes (ML models are highly flexible), but the overall story would be more convincing if the authors quantified how much better these models do than conventional methods.  
  
I did not find the two empirical examples that are presented convincing. The authors themselves indicate that the devil facial tumor final epidemic size is well fit even by a non-network model. Overall, fitting only the final size seems limited as it is heavily dependent only on outbreak settings as opposed to the endemic disease that might be better suited to modeling prevalence.