**Introduction:**

*Anaplasma phagocytophilum* is a tick-borne, intraerythrocytic bacterium capable of causing anaplasmosis in humans and animals (Bakken 1994; Chen et al. 1994; Dumler et al. 2001; Rikihisa 1991). In the United States, *A. phagocytophilum*-infection is primarily a concern for humans and is spread by the ticks *Ixodes scapularis* in the east and *I. pacificus* in the west (Eisen, Eisen, and Beard 2016). Anaplasmosis has been the second most frequently reported tick-borne disease in the United States, where nearly 40,000 cases were reported between 2004 and 2016 (Rosenberg, Lindsey, and Fischer 2018). Notably, *A. phagocytophilum* is considered a host-generalist, however, analysis and characterization of its genetic variants over the last two decades indicate that specific genetic variants have varying host competences (Dugat et al. 2014; Stuen, Granquist, and Silaghi 2013). Further, the distribution of *A. phagocytophilum* genetic variants differ across spatial scales and are likely maintained in nature through different epidemiological and ecological cycles (Stuen, Granquist, and Silaghi 2013). In the United States, cases of anaplasmosis are not endemic nation-wide, and their heterogeneity is partly attributable to the distribution of genetic variants of *A. phagocytophilum* (Massung et al. 2002; Teglas and Foley 2006).

Within the United States, New York State (NYS) holds a particularly high burden of anaplasmosis, and cases have increased in the last two decades (Dahlgren et al. 2015; O’Connor et al. 2021; Rosenberg, Lindsey, and Fischer 2018; Russell et al. 2021). Recent tick-borne disease (TBD) research in NYS has identified an area of increased risk for anaplasmosis which grew in total area from 2010 – 2018, likely attributable to the geographic delineation and spatial expansion of two primary *A. phagocytophilum* variants, the pathogenic “human-active” variant (Ap-ha) and the non-pathogenic “Variant-1” (Ap-V1) (Massung et al. 2002; Massung, Mather, et al. 2003; Massung et al. 2005; M. Prusinski et al. 2023; Russell et al. 2021). Despite being present within the same sub-national boundary, each genetic variant exhibits a distinct epidemiological cycle; the white-footed mouse (*Peromyscus leucopus*) is the natural reservoir of Ap-ha, and the white-tailed deer (*Odocoileus virginianus*) is the natural reservoir of Ap-V1 (Massung et al. 2002). Previous research has shown that each variant is unable to infect the other’s primary host, adding another layer of separation between these epidemiological cycles (Massung et al. 2005; Massung, Priestley, et al. 2003). As Ap-ha *A. phagocytophilum* expands into locations with historically low incidence of anaplasmosis, understanding how the epidemiological cycles of both genetic variants will impact anaplasmosis epidemiology will remain an important topic for scientific research and public health mitigation efforts.

One framework used to describe the establishment and spread of *I. scapularis* and its pathogens is the pathogen-vector-host system (Killilea et al. 2008). As much of tick-borne disease research focuses on Lyme disease, the pathogen-vector-host system has historically been used to describe how *Borrelia burgdorferi* (the causative agent of Lyme disease) is spread between its primary reservoir hosts (white-footed mice) and how *I. scapularis* uses reproductive-stage hosts (white-tailed deer) to aid in reproductive success (Mather et al. 1989; Piesman and Spielman 1979). Notably, white-tailed deer are poor reservoirs for *B. burgdorferi*, which has prompted continued debate about the mammal’s role in spreading the pathogen (Telford et al. 1988). Two competing hypotheses are the dilution-effect and the amplification-effect (Ogden and Tsao 2009). The dilution effect suggests that increasing biodiversity decreases the relative number of pathogen-competent hosts available to harbor a pathogen, thus decreasing pathogen-prevalence (Norman et al. 1999; Ostfeld and Keesing 2000a, 2000b). Meanwhile, the amplification-effect suggests that increasing biodiversity increases the reproductive success of *I. scapularis*, allowing for pathogens to spread more easily (Huang et al. 2019; Ogden and Tsao 2009). The exact role of white-tailed deer in the spread of *B. burgdorferi* as it pertains to dilution or amplification remains unclear, partly because of the inability to separate white-tailed deer hosts from the downstream results in the pathogen-vector-host system, i.e., *B. burgdorferi* prevalence and *I. scapularis* density. The epidemiological cycles of Ap-ha and Ap-V1 *A.* phagocytophilum may provide insight into the role of white-tailed deer as dilution or amplification hosts given the pathogen’s differing natural reservoirs (Figure 1).

The dilution and amplification effect hypotheses are invariably related to the phenomenon of forest fragmentation. It is often assumed that as forest fragmentation increases, biodiversity within smaller, less connected forest patches will decrease (Diuk-Wasser, VanAcker, and Fernandez 2021). The result of decreasing biodiversity within fragmented forests leaves white-footed mice as the primary mammal by which *I. scapularis* can feed, resulting in an increase in both tick density and pathogen prevalence (Nupp and Swihart 1998). Conversely, the relationship between forest fragmentation, white-tailed deer, and entomological risk remains difficult to disentangle. The preference of white-tailed deer towards edge habitat is well described (Alverson, Waller, and Solheim 1988; Kremsater and Bunnell 1992; Leopold 1933; Miyashita et al. 2008). This behavioral preference, combined with the assumed relative increase in white-footed mice abundance in fragmented landscapes, suggests that fragmented landscapes result in increased entomological risk. Previous research has linked forest fragmentation to entomological risk; however, other research indicates that the connectivity of fragmented forests also plays a role in the propagation of tick populations and thus, tick-borne disease risk (Allan, Keesing, and Ostfeld 2003; Brownstein et al. 2005; Keesing et al. 2023, 2023; Tran and Waller 2013; VanAcker et al. 2019). It appears the relationship between white-tailed deer density and forest fragmentation and land cover type can be modulated by several factors. Studies in New York City have indicated white-tailed deer are more likely to use natural land cover, while forest connectivity was positively related to nymphal *I. scapularis* prevalence (VanAcker et al. 2019, 2023). Conversely, studies in wildlife preserves, and suburban and rural areas may present conflicting evidence on the relationship between deer presence and natural land cover (Harveson et al. 2007; Hinton et al. 2022; Maurer et al. 2022, 2022; Peterson et al. 2005; Urbanek and Nielsen 2013). In NYS, the Adirondack park is a mountainous region of nearly 25,000 km2 and consists of large connected forests but generally low estimates of deer density, tick-borne pathogen prevalence and tick-borne disease (Foley et al. 2023; Hinton et al. 2022; Hurst and Porter 2008; Khatchikian et al. 2012, 2015; O’Connor et al. 2024; M. Prusinski et al. 2023; M. A. Prusinski et al. 2014; Russell et al. 2021). The effect modification of urbanization on the relationship between connectivity and white-tailed deer density is summarized in O’Connor, Aldstadt, and Wilson (in review), where geographically weighted regression models indicate positive relationships between deer density and connectivity in some regions of NYS, and negative relationships in others. Together, these results describe a scale-dependent and complex relationship between white-tailed deer, forest fragmentation, and land use.

To better define the role of white-tailed deer in the pathogen-vector-host system, this paper investigates the following:

1.) The role of white-tailed deer as they pertain to the dilution and amplification effects, or more specifically, how white-tailed deer impact entomological risk for pathogens which they are not a reservoir for, despite increasing *I. scapularis* density and reproductive success.

2.) How the relationship between white-tailed deer functional connectivity and pathogen prevalence is modulated by land cover and spatial scale.

An improved understanding of these systems can help entomologists, tick-borne disease researchers, forest managers and landscape planners in preventing tick-borne disease and the proliferation of *I. scapularis* populations in the future.

**Methods:**

**Tables and Figures:**

A diagram of a disease risk

Description automatically generated

Figure 1: A simplified causal diagram depicting the role of white-tailed deer in the Lyme disease and Ap-ha/Ap-V1 *Anaplasma phagocytophilum* risk systems.