Modern genetic studies using DNA-based “invasion forensic” approaches provide unique information about sources and pathways of biological invasions, typically, at continental spatial scales and broader. Zebra mussels have invaded over 900 water bodies in North America, costing industries and municipalities hundreds of millions USD annually, and causing extensive ecologic damage, including local extinction of native mussels and population declines of other native taxa, and dramatic restructuring of aquatic food webs with unknown impacts to higher trophic levels. We asked whether invasion genetic studies focused at the scale of a US state (MN) would provide information on routes and vectors of spread that could focus prevention. We genotyped 9 microsatellite DNA markers in > 2250 mussels collected from > 50 waterbodies across MN and the Great Lakes, analyzed genetic structure and diversity, and contrasted invasion scenarios using Approximate Bayesian Computation (ABC). Population genetic diversity is strikingly high across all MN water bodies (regardless of their size). This suggests that colonization events trace to large numbers of mussels, questioning how often they result from larvae spread by fishing boats. ABC analyses confirm that Mille Lacs Lake (infested since 2005), despite heavy boat traffic connecting it to waters throughout the state, has not infested any of 35 lakes invaded more recently. This is evidence that watercraft inspection and decontamination efforts are effective and should be continued on Mille Lacs and other high traffic lakes. Clustered invasions in Detroit Lakes, Alexandria and Brainerd Lake regions each result from dispersal into the region and short-distance spread of mussels that are genetically endemic to each of these 3 regions. This indicates that state and local prevention programs are failing to block vectors that spread mussels from lake to lake over short distances.