Much of the modern highway system duplicates the routes of ancient Native American trails. Their foot-friendly trade routes stayed close to water and often followed direct but steep routes through the mountains. For the highways and motor vehicles that followed, some changes were necessary. For example, to protect them from floods and to farm the rich soils of the valleys, the two major highways in the Central Valley are located away from the Sacramento and San Joaquin Rivers. Likewise, roads across the Sierra Nevada often follow along ridge tops because the canyons below are too steep and narrow for cars.

Interstate Highways in California are built and maintained by the federal government. They stretch across multiple states and always keep the same highway number. For example, Interstate 5 runs for 1,260 miles between the Mexican border south of San Diego and the Canadian border north of Seattle. State highway numbers often change when the road extends into a neighboring state. Odd numbers designate highways that run in a north-south direction. Even numbers designate highways that run in an east-west direction. The highways in California carry some of the highest traffic volume in the world.