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This study adapted and parameterized the Ecosystem Demography 2 (ED2) model for an old-growth coniferous forest in the Pacific Northwest, USA. We validated the model using an extensive suite of forest inventory, eddy covariance, and biophysical observations, and then used the model to explore the physiological responses of the forest to climate anomalies. The calibrated model well reproduced the observed forest composition and canopy structure, and successfully estimated carbon, water and energy fluxes. The modeled water-use efficiency (WUE) was almost doubled from 1998 to 2015, because the relative decrease in carbon uptake was smaller than that in water loss. By machine-learning techniques, we found that the relative importance of climate variables on WUE showed varied patterns across different time scale in that air temperature and VPD mainly determined WUE at seasonal scale, while VPD, radiation or atmospheric CO<sub>2</sub> concentration can govern the daily or half-hourly WUE. Via the “top-flat” scheme of the current ED2 model, too much radiation transmitted through the canopy and led to over-heated leaves in the lower canopy. Higher leaf temperature with higher leaf VPD together caused substantial lower stomatal conductance through canopy, especially in the middle and lower canopy. (Received February 06, 2018)