The multiplicity of land-use/cover changes in reducing the areas covered by vegetation is of growing concern in Uganda today. Consequently, the study intended to determine the magnitude and transition potential of land-use/cover changes in a trans-boundary river Sio catchment. The magnitude of land-use/cover changes was determined by an application of unsupervised image classification on the ortho-rectified Landsat TM/ETM images of 1986 and 2000 using ILWIS 3.3 software; whereas an ArcGIS 9.2-based Land Change Modeler was used for both change analysis and transition potential modeling. The results showed that in the period of 1986 to 2000, wetlands and bushlands largely reduced by 21% and 5%, respectively, whereas small-scale farming and grasslands increased by 14% and 12%, respectively. The multilayer perceptron attained an accuracy of 97.03%, which is a higher percentage for the possible occurrences of land-use/cover changes in Sio catchment. The major drivers of land-use/cover changes are land ownership and household size. The study therefore recommends that the awareness of land-use/cover changes is extremely important for the Sio catchment’s planning and management of the natural resources.