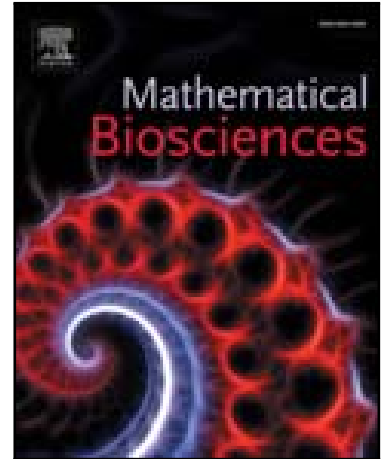


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The dual role of autoimmune regulator in maintaining normal expression level of tissue-restricted autoantigen in the thymus: A modeling investigation

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Highlights

- Mathematical models are developed to study the effect of AIRE binding affinity on negative selection.
- We show that the models exhibit bistability with a healthy (successful negative selection) and autoimmune (failure of negative selection) states.
- We demonstrate that bistability is a reflection of the dual role of AIRE in the transcriptional regulation of tissue-restricted antigens.
- We predict that AIRE-mRNA expression level is lower in the healthy than in the autoimmune states.
- We conclude that negative selection is extremely sensitive to parameter perturbations in T-cell avidity.

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