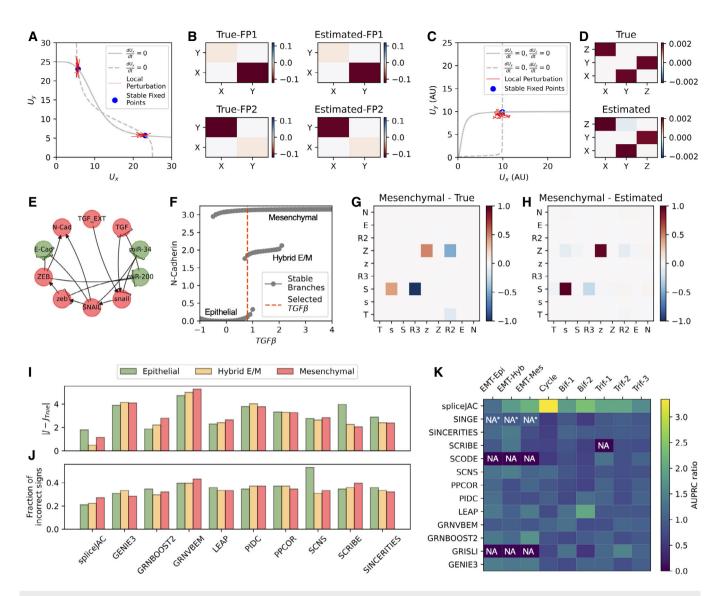**Figure 2. Benchmarking spliceJAC against *in silico* circuits and comparison with other existing GRN inference methods.**

A The phase space of a bistable toggle switch including nullclines (silver lines), stable fixed points (blue dots), and stochastic perturbation around stable fixed points (red lines). X- and y-coordinates represent unspliced mRNA counts of genes X and Y.

B Ground truth (top) and inferred (bottom) interaction matrices for the two stable fixed.

C The phase space of a monostable circuit of three genes that activate each other in a loop.

D Ground truth and inferred interaction matrix of the three genes circuit.

E The EMT circuit proposed by Tian *et al* (2013). Green and red nodes highlight epithelial and mesenchymal genes, while pointing and t-shaped arrows represent activation or inhibition, respectively.

F Bifurcation diagram showing the available attractors as a function of TGF-beta inducer. The red dotted line highlights a value leading to tristability used for spliceJAC testing thereafter.

G, H Ground truth (G) and estimated (H) interaction matrices in the mesenchymal state.

I, J Comparison with existing GRN inference methods based on the absolute difference between ground truth and prediction (I) and maximization of the fraction of correct matrix element signs (J). Green, orange, and red bars showcase results for the Epithelia, Hybrid E/M and mesenchymal states, respectively.

K The AUPRC ratio for all methods in the Beeline pipeline and spliceJAC. For each circuit state, the AUPRC scores are normalized by the average score achieved for the state. NA = no output file was generated. NA* = an output file without any predicted edge was generated.

element-wise absolute difference between the ground truth and estimated Jacobians (Fig 2I) and fraction of incorrect signs in the estimated Jacobian (Fig 2J). spliceJAC consistently performed better in both metrics and in all three states. To test diverse biological scenarios, we further used the BoolODE simulation tool to generate synthetic data for three cases: a cycling circuit exhibiting a limit cycle, a

bifurcating converging circuit with two stable states, and a trifurcating circuit with three stable states (Appendix Fig S3) previously studied in the Beeline GRN inference benchmarking package (Methods and Protocols: Simulation of *in silico* circuits). To quantify the goodness of state-specific GRN inference, we used the Beeline package to evaluate the area under the precision recall curve (AUPRC,