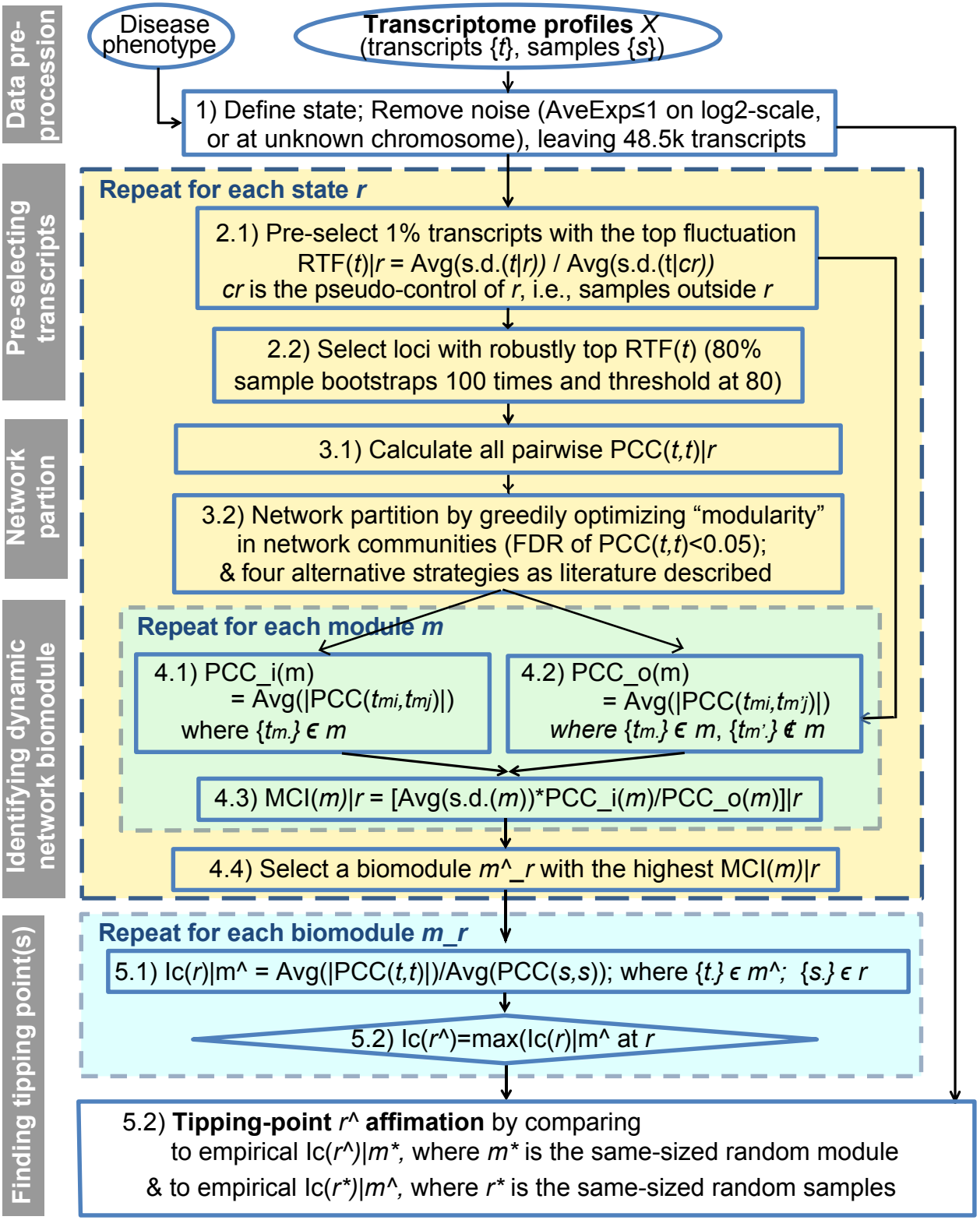
Data pre-procession
Disease phenotype
Transcriptome profiles X (transcripts {t}, samples {s})
1) Define state; Remove noise (AveExp≤1 on log2-scale, or at unknown chromosome), leaving 48.5k transcripts
Pre-selecting transcripts
Repeat for each state r
2.1) Pre-select 1% transcripts with the top fluctuation RTF(t)|r = Avg(s.d.(t|r)) / Avg(s.d.(t|cr))
cr is the pseudo-control of r, i.e., samples outside r
2.2) Select loci with robustly top RTF(t) (80% sample bootstraps 100 times and threshold at 80)
Network partion
3.1) Calculate all pairwise PCC(t,t)|r
3.2) Network partition by greedily optimizing "modularity" in network communities (FDR of PCC(t,t)<0.05); & four alternative strategies as literature described
Identifying dynamic network biomodule
Repeat for each module m
4.1) PCC_i(m) = Avg(|PCC(tmi,tmj)|) where {tm.} ϵ m
4.2) PCC_o(m) = Avg(|PCC(tmi,tm'j)|) where {tm.} ϵ m, {tm'.} ∉ m
4.3) MCI(m)|r = [Avg(s.d.(m))*PCC_i(m)/PCC_o(m)]|r
4.4) Select a biomodule m^_r with the highest MCI(m)|r
Finding tipping point(s)
Repeat for each biomodule m_r
5.1) Ic(r)|m^ = Avg(|PCC(t,t)|)/Avg(PCC(s,s)); where {t.} ϵ m^; {s.} ϵ r
5.2) Ic(r^)=max(Ic(r)|m^ at r
5.2) Tipping-point r^ affimation by comparing to empirical Ic(r^)|m*, where m* is the same-sized random module & to empirical Ic(r*)|m^, where r* is the same-sized random samples