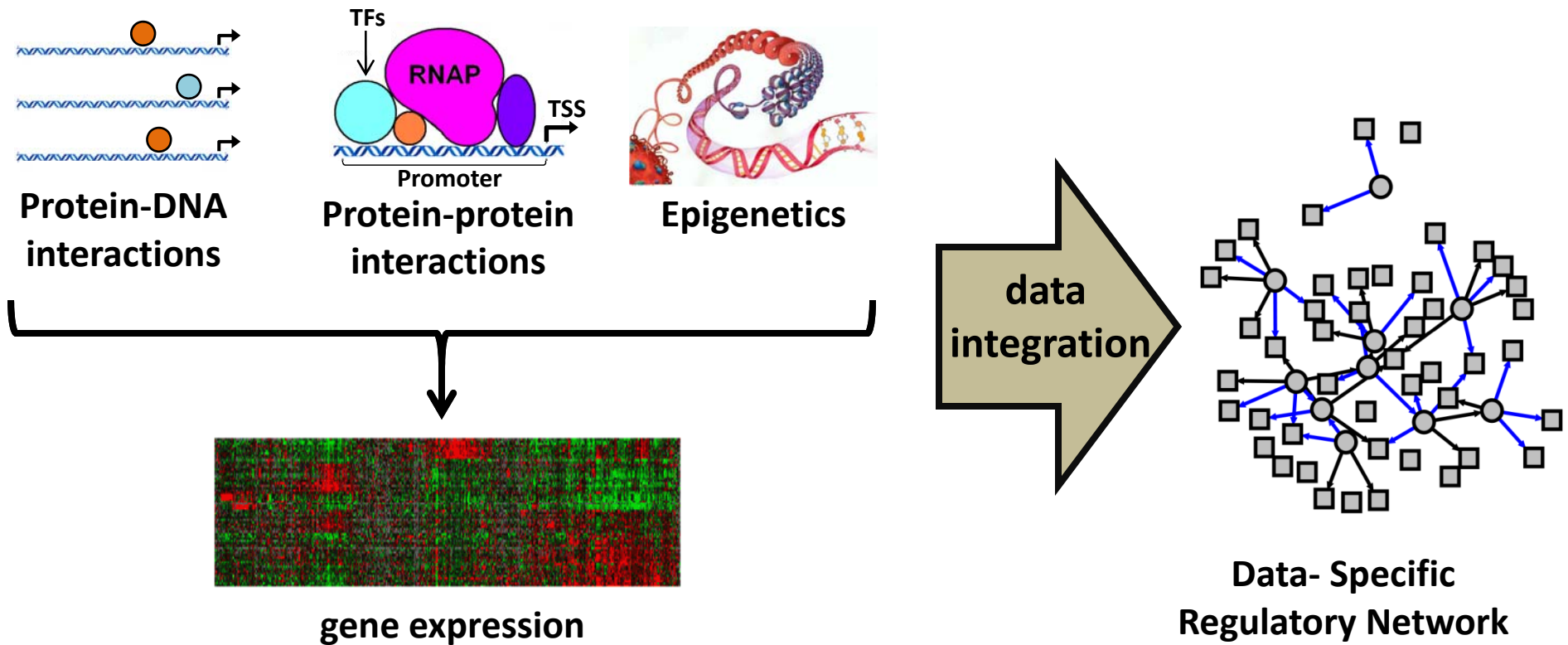


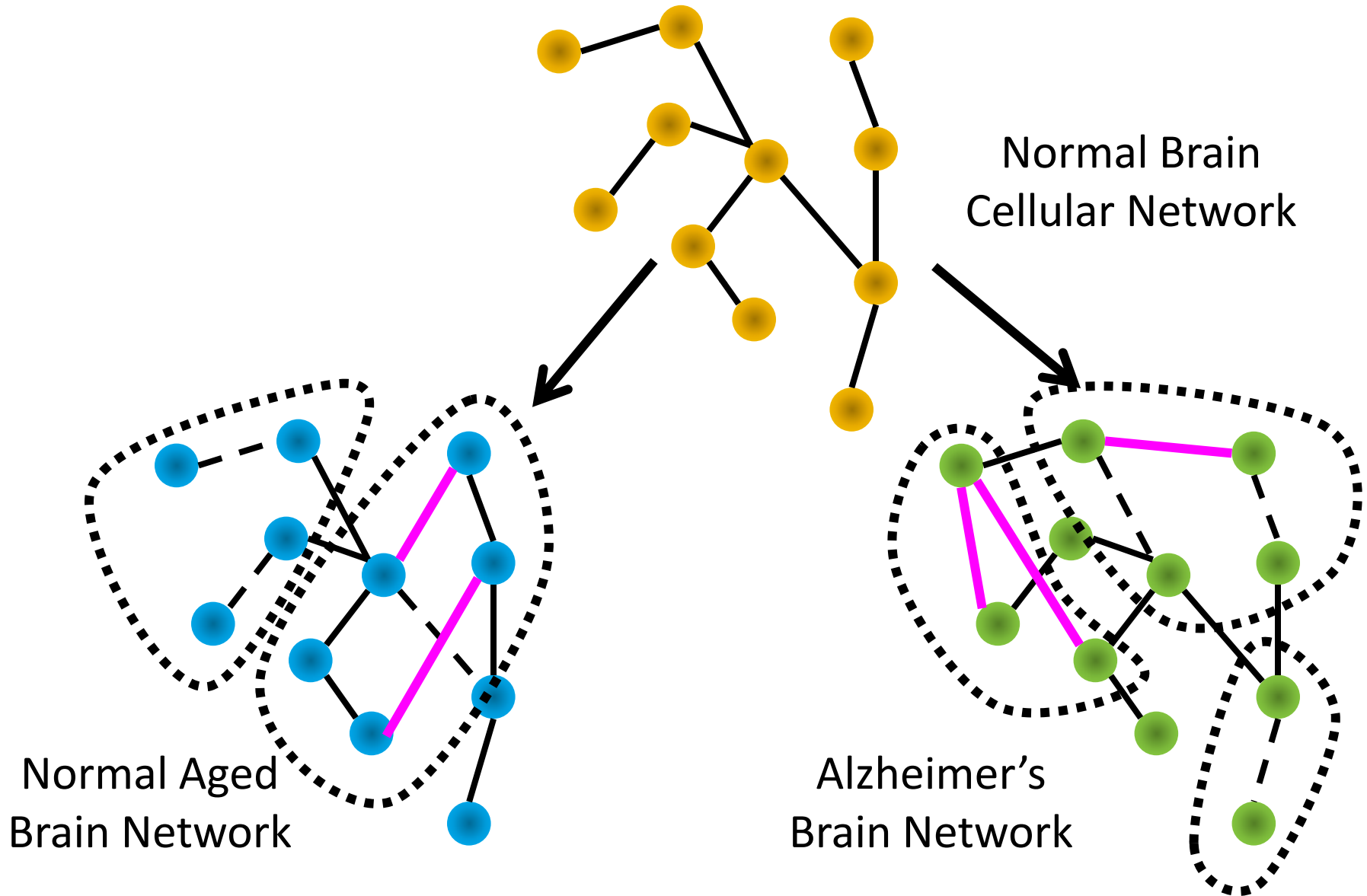
Sex-specific Differences in Alzheimer's Disease are Characterized by Unique Alterations in Cellular Network Structure

**Kimberly Glass
John Quackenbush**

Regulation of Transcription

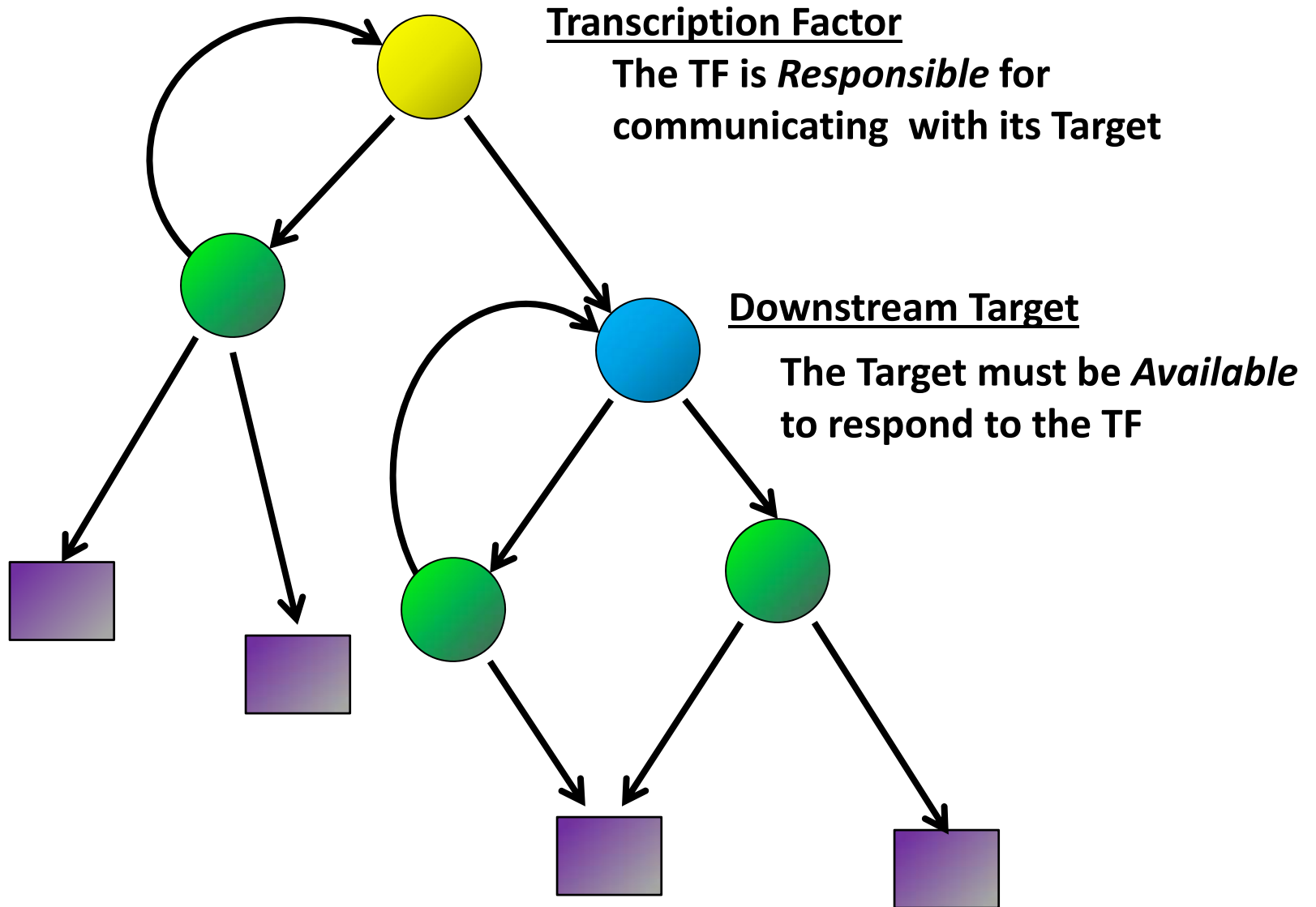


What can we learn from networks?



Message-Passing Networks: PANDA

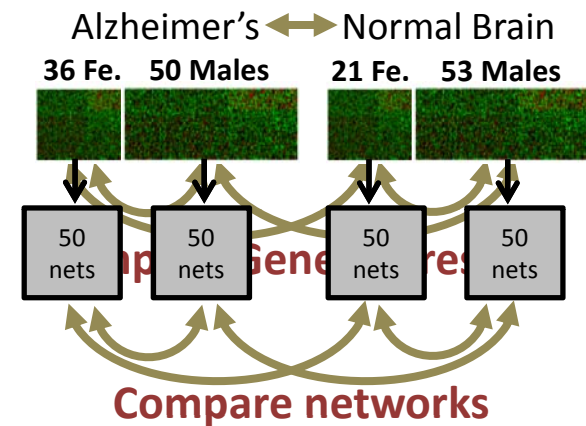
Passing Atttributes between Networks for Data Assimilation



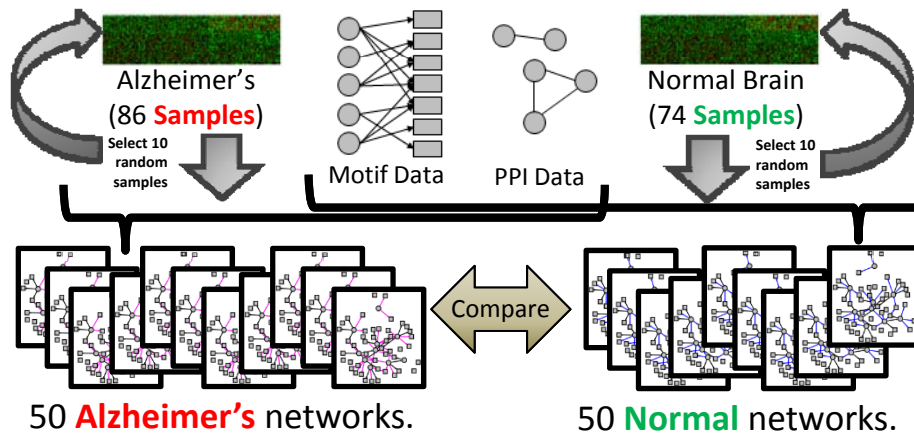
Application of PANDA to Sexual-Dimorphism in Alzheimer's Disease

Expression Data

	<u>Alzheimers</u>			<u>Normal Brain</u>		
	Overall	Female	Male	Overall	Female	Male
Number Samples	86	36	50	74	21	53
Average Age	79.2	81.4	77.54	79.5	86.3	76.8
Entorhinal Cortex	9	6	3	13	3	10
Medial Temporal Gyrus	16	6	10	12	4	8
Posterior Singulae	9	3	6	13	4	9
Primary Visual Cortex	19	7	12	12	3	9
Superior Frontal Cortex	23	10	13	11	4	7
hippocampus	10	4	6	13	3	10



Building Ensembles of Networks with PANDA

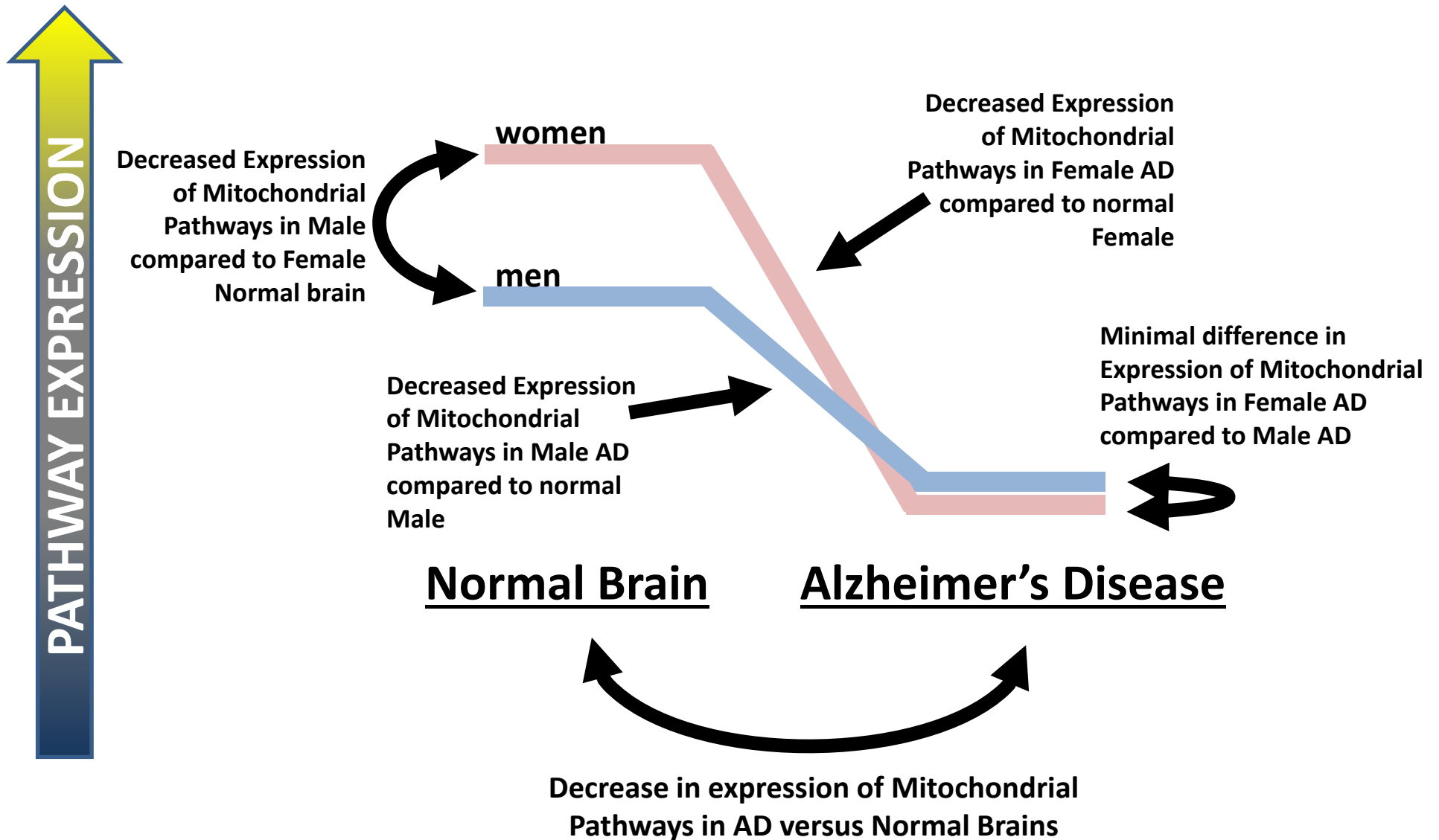


Finding 1: sex-related differential expression of gene pathways

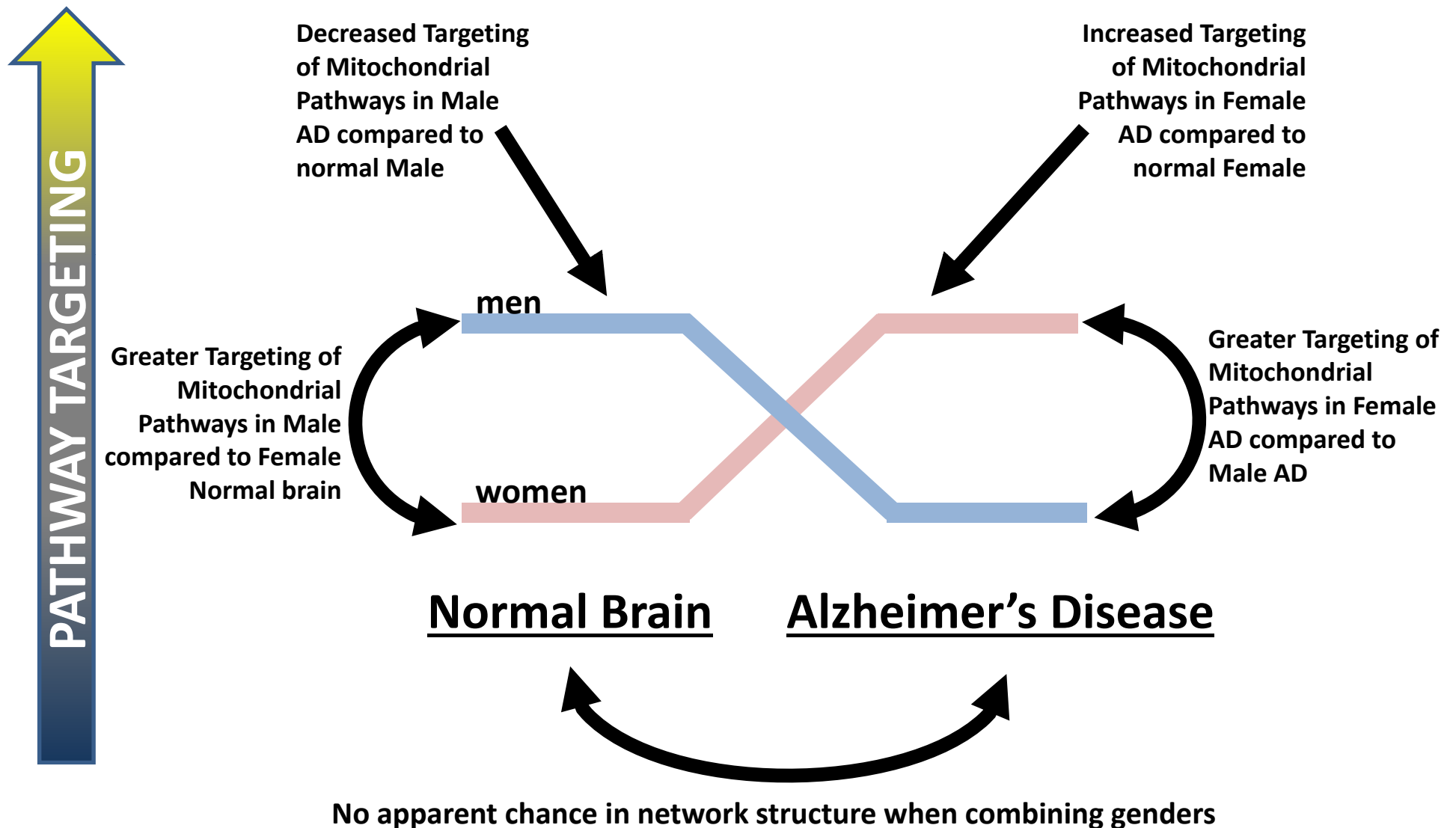
Finding 2: sex-related differential regulation of gene pathways

Finding 3: differential-regulation of gene pathways may be connected to hormone response

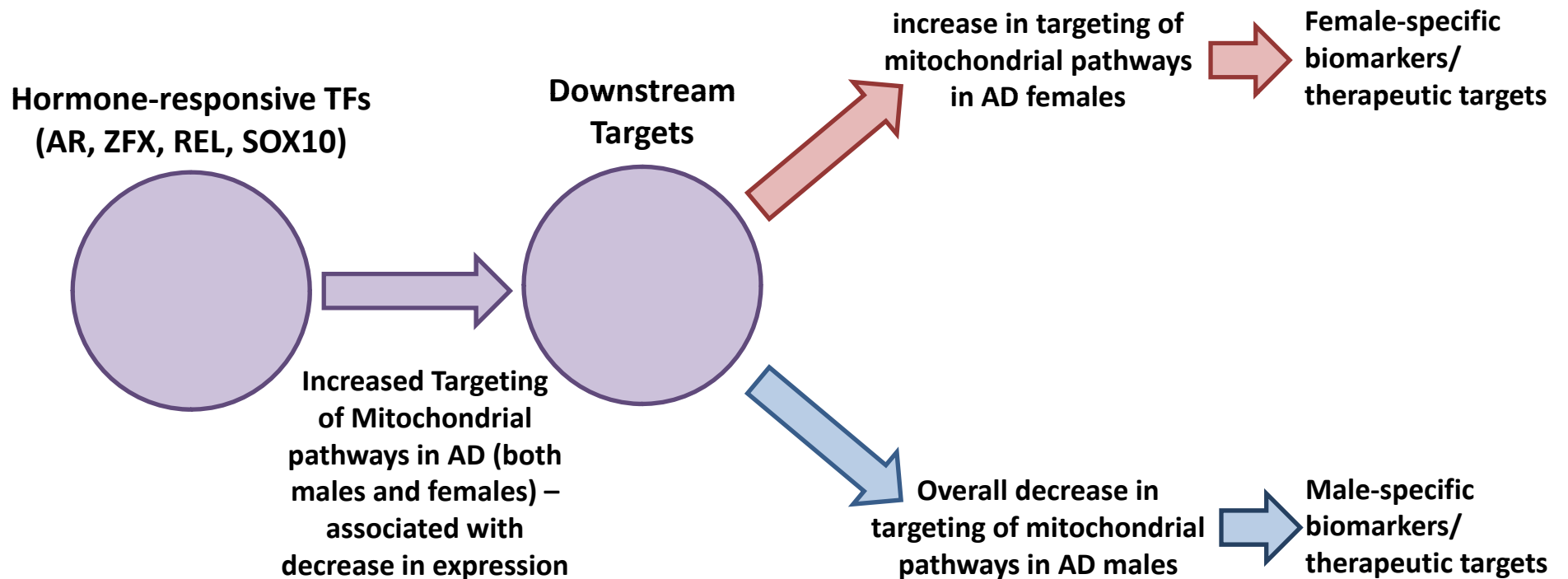
Finding 1: Sex-related Differential-Expression of Gene Pathways



Finding 2: Sex-related Differential-Regulation of Gene Pathways



Finding 3: Differential-regulation of gene pathways may be connected to hormone response



Proposed Research Plan

- **We will validate our findings by repeating the differential-expression and -regulation analysis in other Alzheimer's Disease datasets.**
- **We will investigate potential confounding factors (such as age) that might influence our predictions.**
- **We will search for independent validation of our conclusions by mining both the literature and other publically-available sources of information.**
- **We will identify potential sex-specific AD treatments, and suggest follow-up experiments necessary to verify and test their potential efficacy in model systems with an eye on application to patients.**

Feasibility and Impact

- **The tools needed to conduct our research include publically available data and a high performance computer.**
- **The insights we can provide into sexual dimorphism in the development and progression of Alzheimer's disease would likely not be possible using other data analytical methods.**
- **Our findings may suggest drugs or other interventions that would help “rewire” the molecular networks that drive the disease.**
- **Given our previous research in other diseases, we plan to use these analyses to better understand sex-specific differences in disease susceptibility beyond Alzheimer's, increasing the potential impact of this work.**