Bridging multi-omic time series data and dynamic modelling

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1. Rationale

Introduction

- MicroRNAs (miRs) control over 60% of mammalian protein coding genes [1].
- Large time course mRNA and miR data sets are being generated.
- Bioinformatic analysis of larger datasets can tell us what is going on a global scale.
- Dynamic modelling investigates complex interactions on a smaller scale.
- **AIM: Link multi-omic time series data and dynamic modelling.**

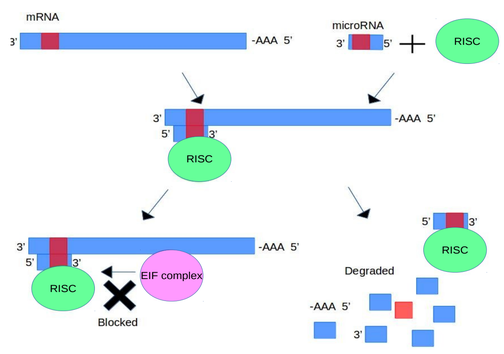

Fig. 1: Post-transcriptional modifications by mRNA-miR interactions.

Methods

- Using various tools I have constructed a pipeline, inspired by a previous method [2].
- mRNA and miR expression from MCF-7 cells were measured under normoxia and hypoxia. Downloaded from GSE47534 [3].
- 3 mRNA and miR samples were taken at 0 hours/normoxia, and thereafter under hypoxic conditions at: 16, 32 and 48 hours.
- **Our pipeline bridges multi-omic time series data and dynamic models.**

2. Pipeline

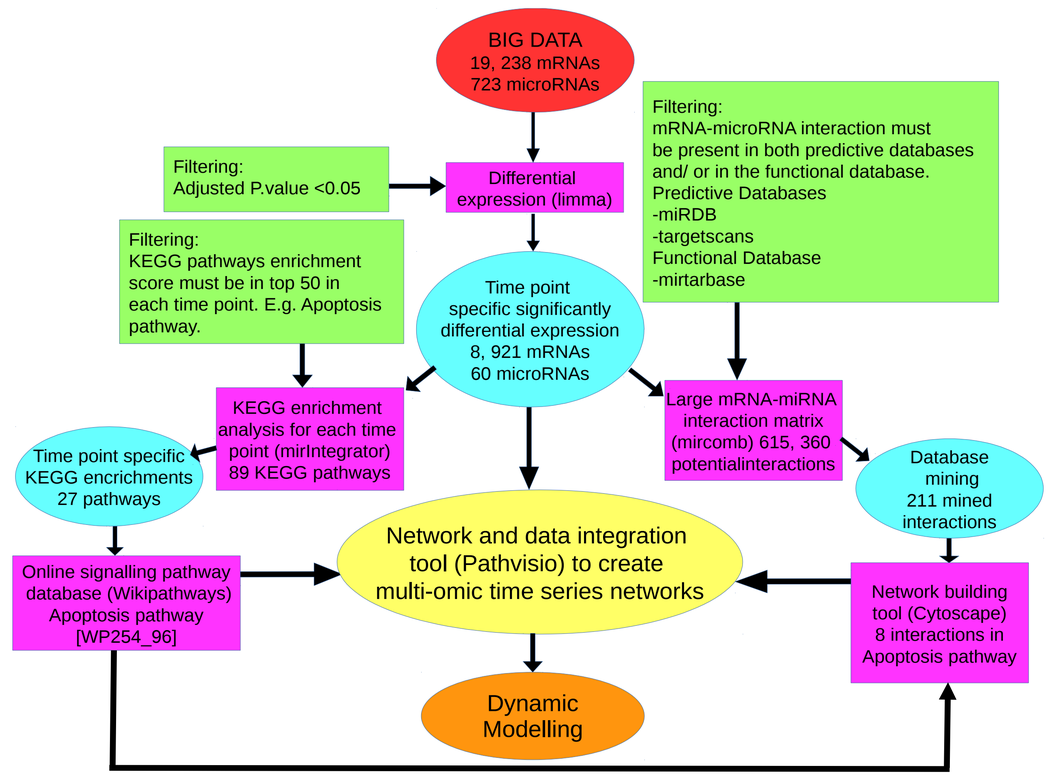

Fig 2: Pipeline for bridging multi-omic time series networks and dynamic modelling, via multi-omic time series networks.

Figure 2 illustrates steps taken to reduce 19238 mRNAs and 723 miRs to 8 mRNA-miR interactions.

- Purple boxes = analysis being performed. Tool names are in the brackets [4–9].
- Blue circles = outcomes of filtering.
- Green boxes = filtering methods.
- Red, yellow and orange circle = main inputs and the outputs.

Ultimately, we created multi-omic time series networks which were then analysed to build gene regulatory networks and then perform dynamic modelling, using CellDesigner and COPASI [10, 11].

3. Multi-omic time series network

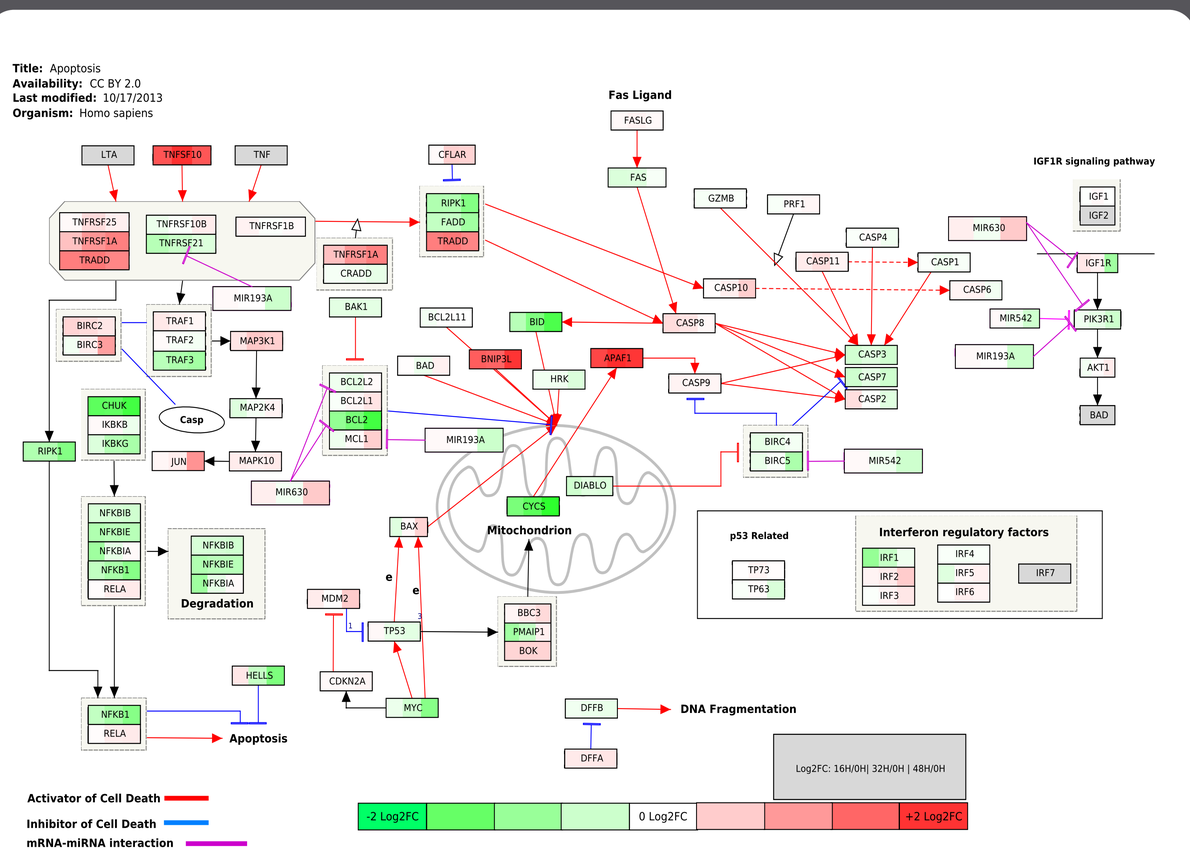

Fig. 3: Integrated mRNA-miR apoptosis pathway with time point specific differential expression results from MCF-7 breast cancer hypoxia datasets.

Multi-omic time series networks can be analysed to identify interactions for dynamic modelling. The network above shows how a miR integrated apoptosis pathway changes in MCF-7 cells at 16, 32 and 48 hours under hypoxia. Colour changes represent differential expression between the respective time points in a sequential order contrasted against normoxic condition (0 hours).

4. Gene Regulatory Network

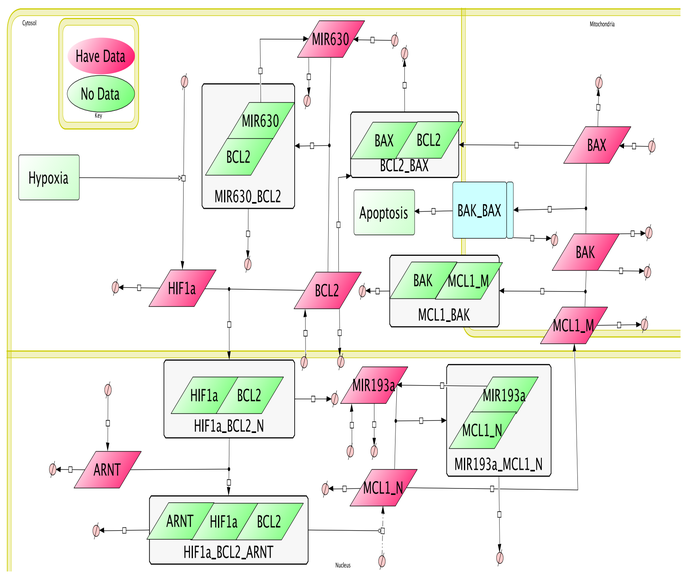

Fig. 4: GRN built around mRNA-miR interactions found by analysing mutli-omic time series network.

Interactions: BCL2-MIR630 and MCL1-MIR193a from Figure 3. This knowledge directed a literature search to build a gene regulatory network (GRN) centered around the 2 selected mRNA-miR interactions within the context of apoptosis under hypoxic conditions. Only RNA data was available, so an RNA based GRN was made. This GRN was then used as the blueprints for building dynamic models. Normalised data of these genes (shaded in red) were extracted for parameter estimations.

5. Dynamic mRNA-miR models

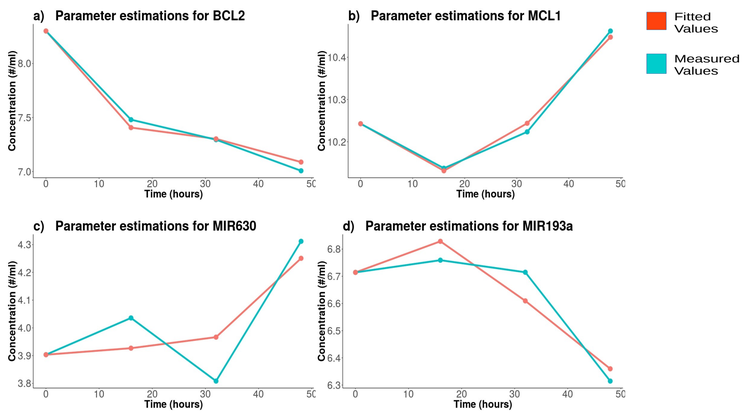

Fig. 5: Paramter estimations of mRNAs and miRs found in the muti-omic time series network.

Parameter estimations of BCL2, MCL1, MIR630 and MIR193a indicates how BCL2-MIR630 and MCL1-MIR193a could influence apoptosis under hypoxia [12, 13].

Parameter estimations are one of the tools in computational modelling. Further analysis by other modelling tools could direct *in vitro* work.

Concluding remarks

Conclusions

- **I have created a method to bridge the gap between multi-omic time series data sets and dynamic modelling.**
- **Further investigation in both BCL2-MIR630 and MCL1-MIR193a may be fruitful in breast cancer research.**

References

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