A Computational Platform for Gene Expression Analysis

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Outline

Domain Problem I

Introduction

- Molecular biology is a young field of study, with a lot of unknowns and partial knowledge.
- Studying gene expression is crucial to understand the mechanisms that control living organisms.
- We focused on two different areas:
  - differential expression analysis;
  - RNA-binding protein (RBP) discovery and analysis.

Domain Problem II

Introduction

Three distinct problems:

- Read alignment against a reference genome and differential expression analysis on the aligned data.
- RBP discovery, analysis and information enrichment.
- Further result analysis using data mining techniques.

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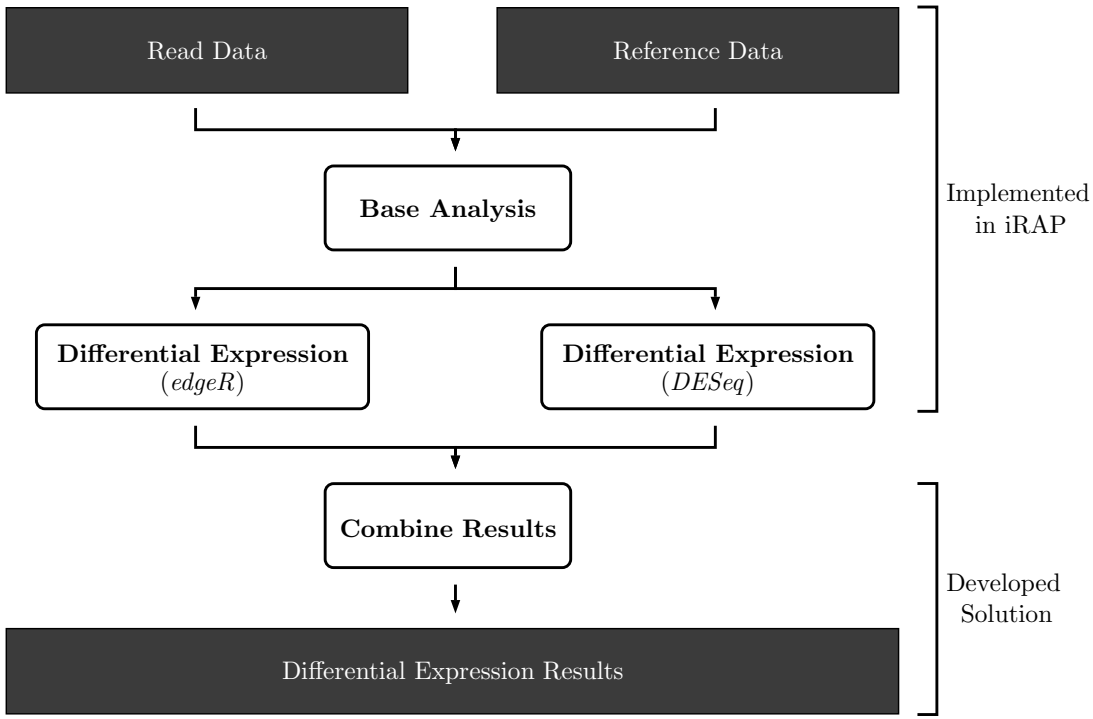
Gather information
Information should be contextually aggregated, allowing for quick access of relevant information.

- Two distinct problems warrant two different solutions.
- The developed system should be available anywhere, through the internet.
- The system should be as modular as possible, to allow future extensions.

RNA-Seq Analysis Pipeline I

Developed Solution

- Uses iRAP as the analysis pipeline.
- Conducts multiple differential expression analyses with different tools.
- Combines results from multiple tools.



RNA-Seq Analysis Pipeline II

Developed Solution

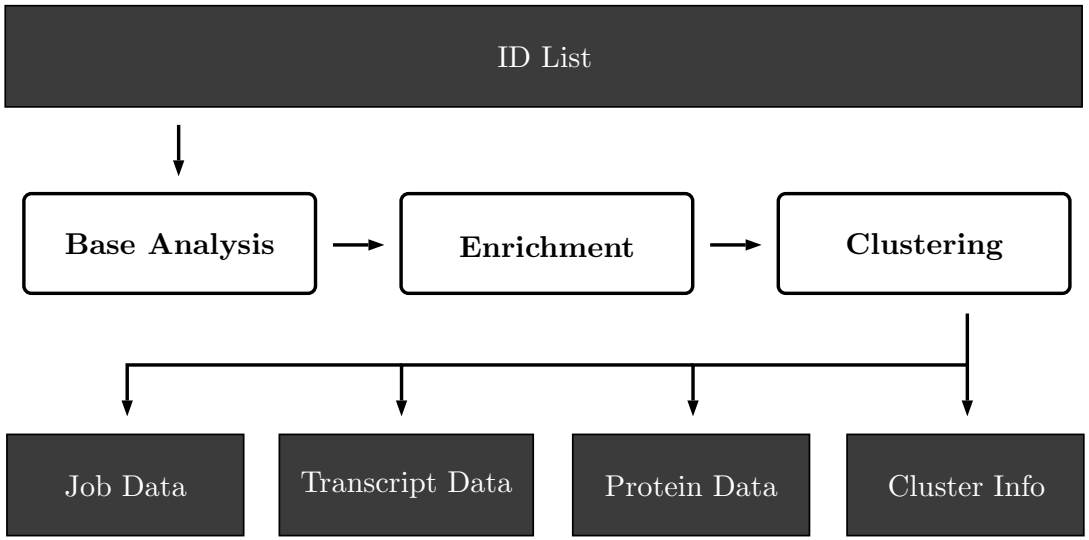
Additional features:

- Access to iRAP's web reports and gene browser, along with result visualization in the web interface.
- Synchronization with Ensembl's reference genome repositories.
- Graphical job configuration.
- Possibility to easily include other differential expression tools.

RBP Analysis Pipeline (PBS Finder) I

Developed Solution

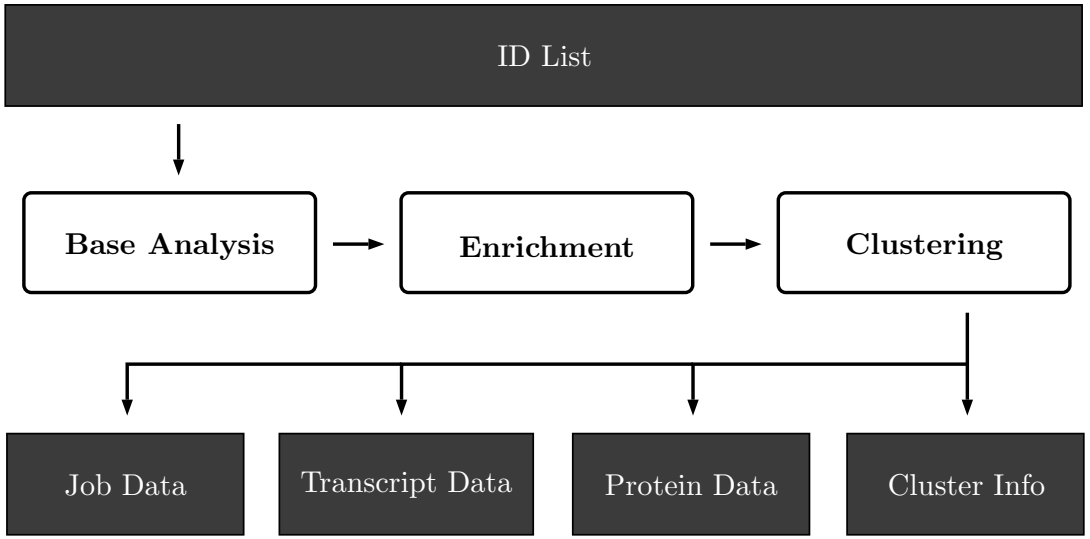
- Uses Ensembl and NCBI to identify gene species, obtain basic information and extract genetic sequences (5' UTR, 3' UTR, 3' UTR downstream).



RBP Analysis Pipeline (PBS Finder) II

Developed Solution

- Uses RBPDB to discovery RNA binding proteins based on the obtained sequences.
- Uses UniProt to enrich the obtained results and performs clustering analysis on those results.



RBP Analysis Pipeline (PBS Finder) III

Developed Solution

Clustering analysis:

- Uses k-medoids and hierarchical clustering, both with Jaccard and binary distance matrices.
- Executes every possible combination of clustering setups (alternates algorithms, distance matrices, used features, etc.).
- Results are filtered (acceptable solutions must have a minimum percentage of entries per cluster, clusters must have defining features, etc.).
- Solution quality internally determined based on the average silhouette.

RBP Analysis Pipeline (PBS Finder) IV

Developed Solution

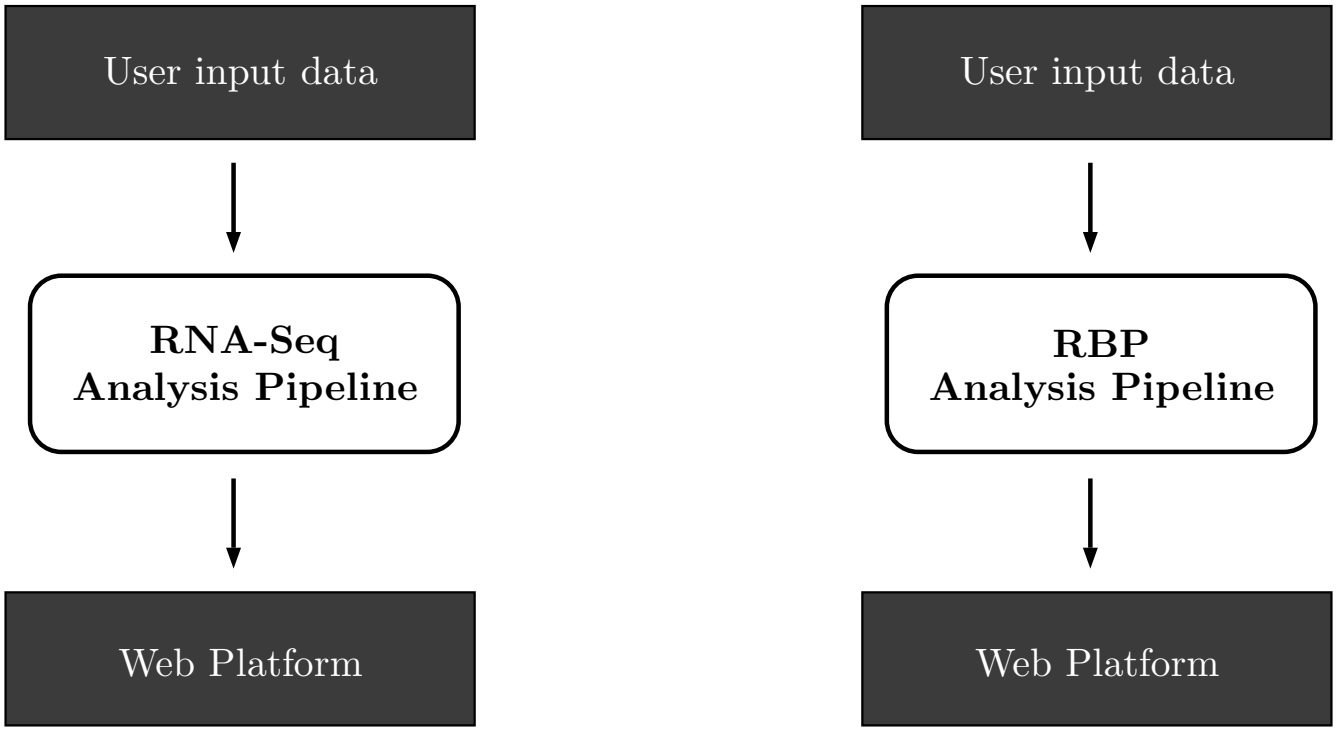
Additional features:

- User account and job management system.
- References to external platforms with relevant information based on context.
- Support for multiple identifier notations (Ensembl, Entrez, RefSeq and GenBank).
- Visualization of defining features for each cluster.
- Job completed notification system.

Integration

Developed Solution

While focusing on aggregation and quick access to information, does it make sense to separate the results into two different platforms?



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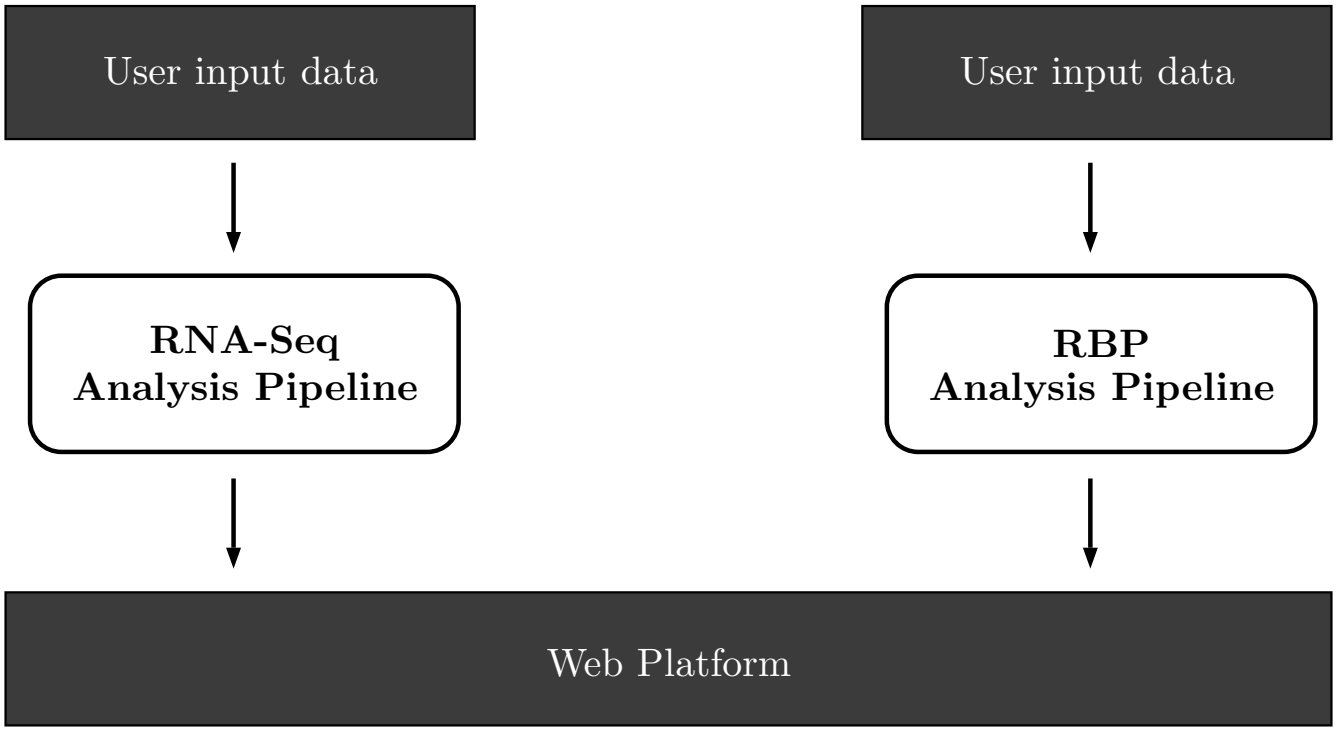
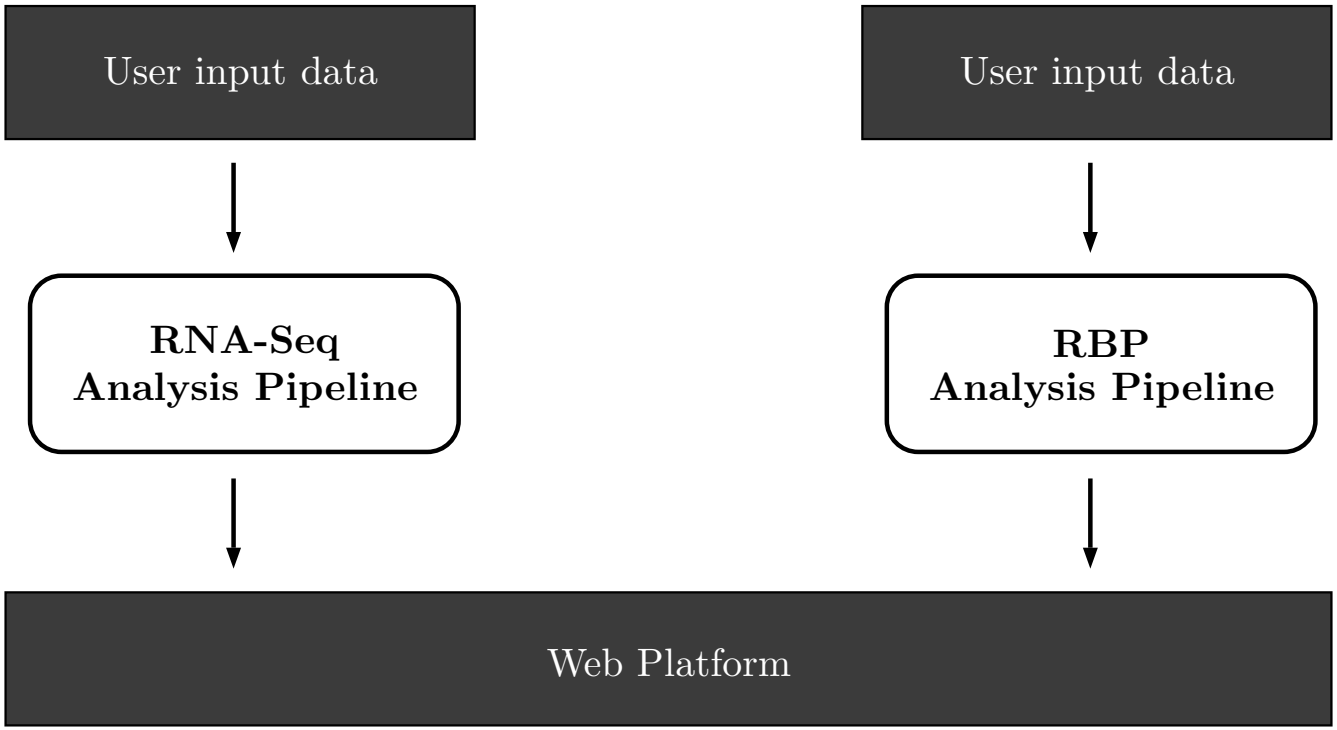


Integration

Developed Solution

A list of differentially expressed genes is not very useful without further information about those genes. Does it make sense for a user to launch a new gene enrichment task by hand?



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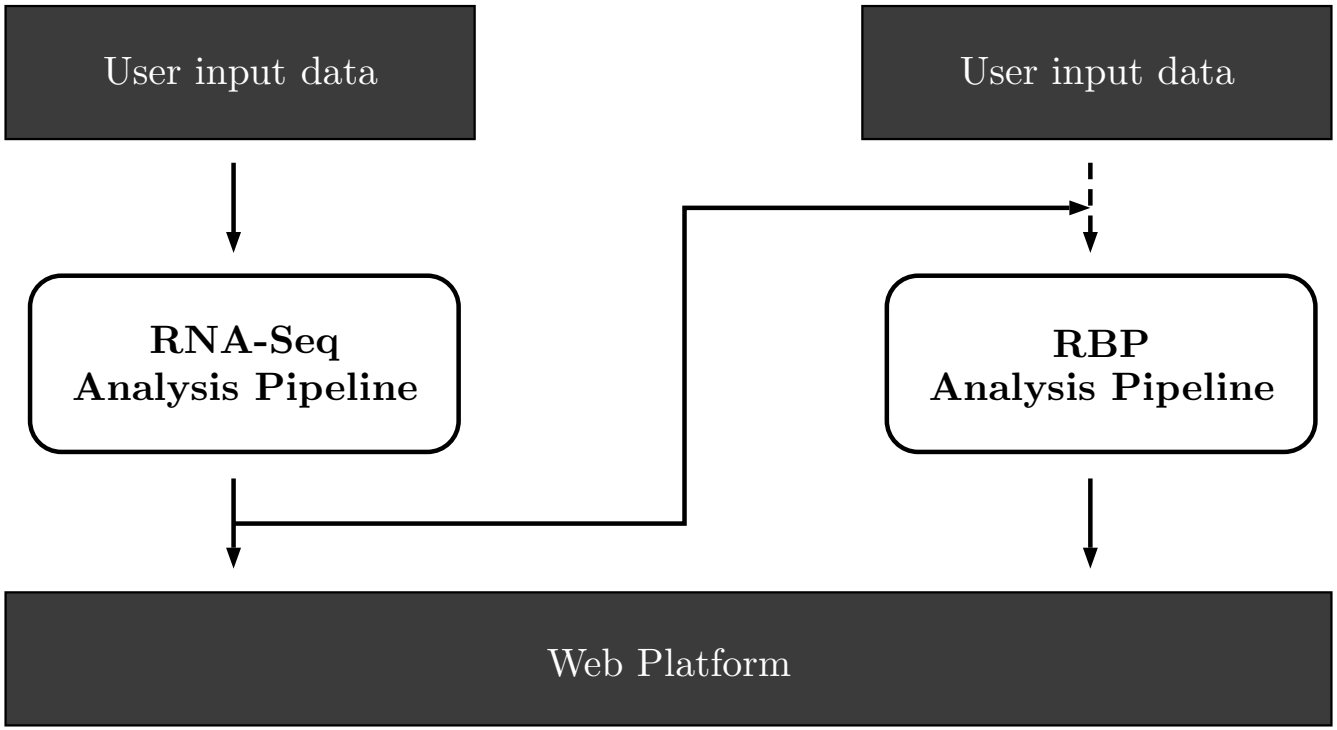
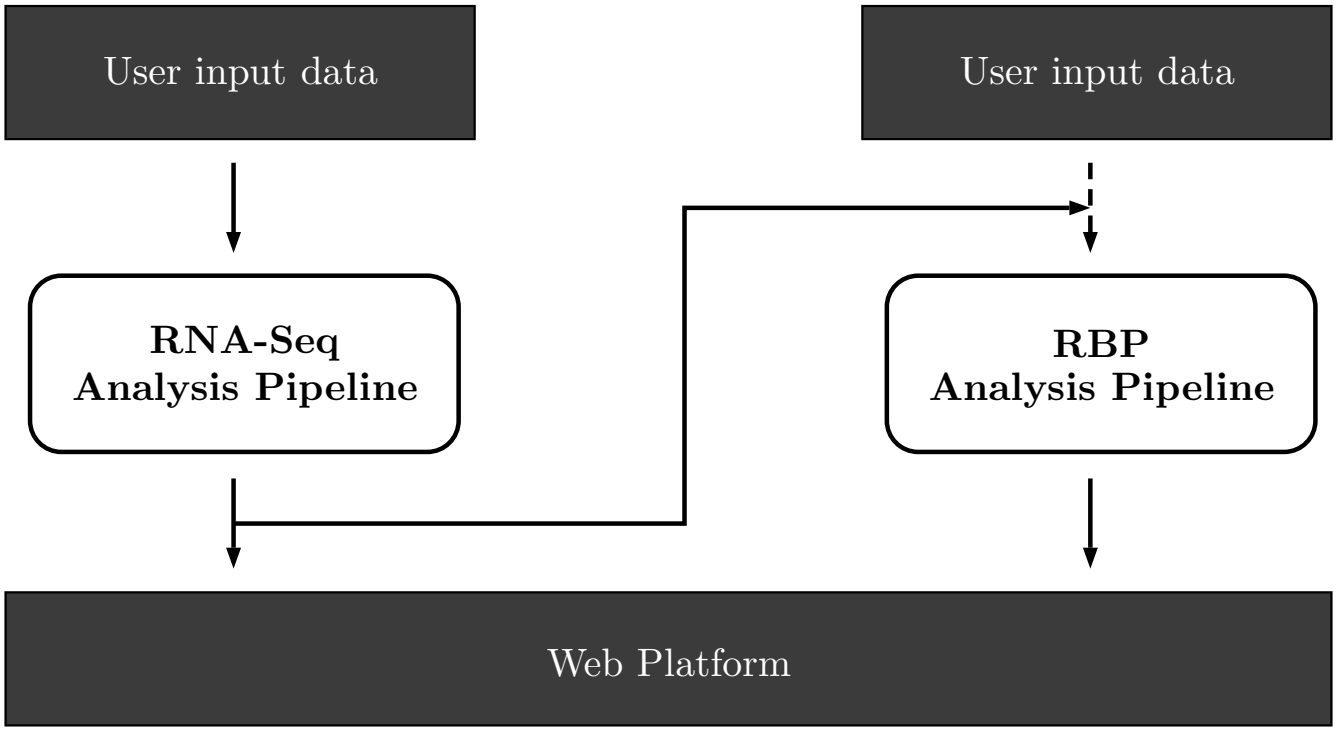


Integration

Developed Solution

A fully integrated solution: the analysis pipelines can be used separately or automatically executed in sequence; result visualization for both pipelines is isolated.

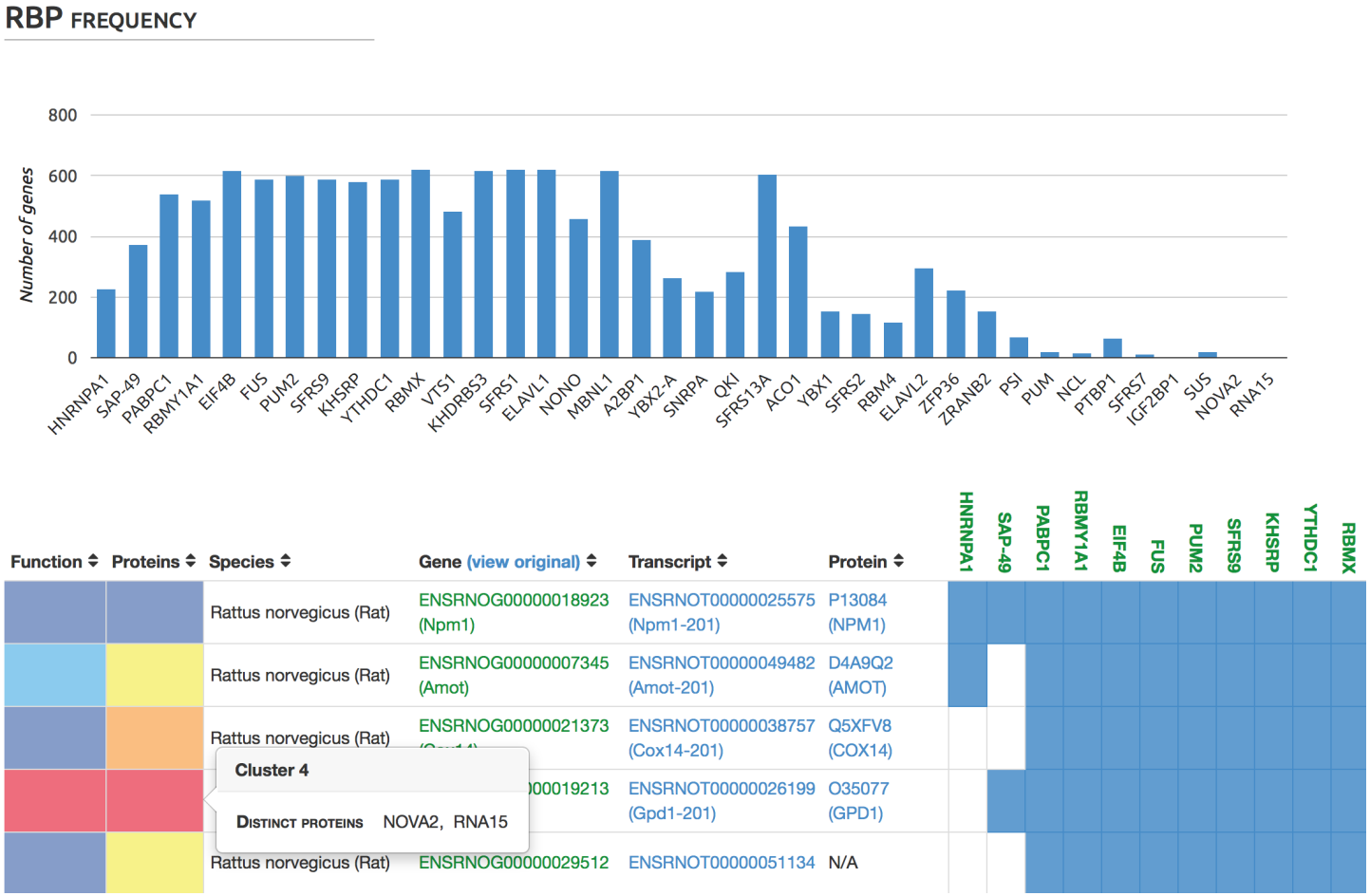


NOTES:
- Refer objectives, data and experimental method.
- Refer results.

RBP Analysis Pipeline (PBS Finder) I

Case Studies

Case study results viewed in PBS Finder



RBP Analysis Pipeline (PBS Finder) II

Case Studies

NOTES:
- Refer objectives, data and experimental method.
- Refer results.
- Show screenshot.
- Show table.

Objective Fulfilment

Conclusions

- RBP analysis pipeline and web platform (PBS Finder) implemented and tested. PBS Finder has been in production for several months; during this time it was thoroughly tested by IBMC experts.
- RNA-Seq analysis pipeline implemented and tested (iRAP deployed and result consolidation tool implemented).
- Integration of both tools could not be accomplished.

Future Work

Conclusions

- Fully integrate the RNA-Seq analysis pipeline with the web platform (automatic job configuration, result visualization, etc.).

- Study the requirements for deploying the platform in large scale, and assess the feasibility of making it available internet-wide.

Review

1. Introduction
   - Domain Problem
   - Motivation and Objectives
2. Developed Solution
   - Overview
   - RNA-Seq Analysis Pipeline
   - RBP Analysis Pipeline (PBS Finder)
   - Integration
3. Case Studies
   - RNA-Seq Analysis Pipeline
   - RBP Analysis Pipeline (PBS Finder)
4. Conclusions
   - Objective Fulfilment
   - Future Work

A Computational Platform for Gene Expression Analysis

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