

METIS: A Case Study in the Development of a System for Tracking Protein Reagent Data from DNA Construct through Protein Purification

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ABSTRACT

In order to support large-scale proteomics, antibody, and protein engineering efforts, companies are challenged by the complexity of developing systems to track protein reagent related information, and as importantly – are challenged by implementing such a system in an environment with pre-existing data storage and tracking methods.

METIS is a web-based application developed and utilized by VLST Corp to track protein engineering, expression, and purification data. This includes information about DNA sequences, cell lines used for expression, conditioned media inventory and a catalogue of purified proteins. An important component of this application is the request system for protein expression and/or protein purification resources, which facilitates management of the downstream workflow. The system utilizes open source components, and is modular to support future expansion of functionality. It is currently being used to support the Target Discovery Platform's proteomic screening efforts and Preclinical Development programs at VLST.

METIS was incorporated into VLST's target discovery platform in a phased approach. Initial efforts were focused on supporting lab personnel by providing a system for tracking batches of purified protein. This was expanded over the course of several months to support tracking of conditioned media, cell lines and finally the DNA constructs. A step-wise, prioritized approach to enhancing the system minimized the incorporation of unnecessary features while focusing on those that provided the most immediate benefit to the users.

The modular design of the system facilitated the addition of features such as report generation, search functionality, data security, inventory, auto-calculation of protein parameters, QC information, real-time user notifications and integration with external applications.

METIS currently tracks several thousand protein constructs and batches of purified protein. Metrics provided by the system are continually used to improve internal protein production processes.

SYSTEM COMPONENTS

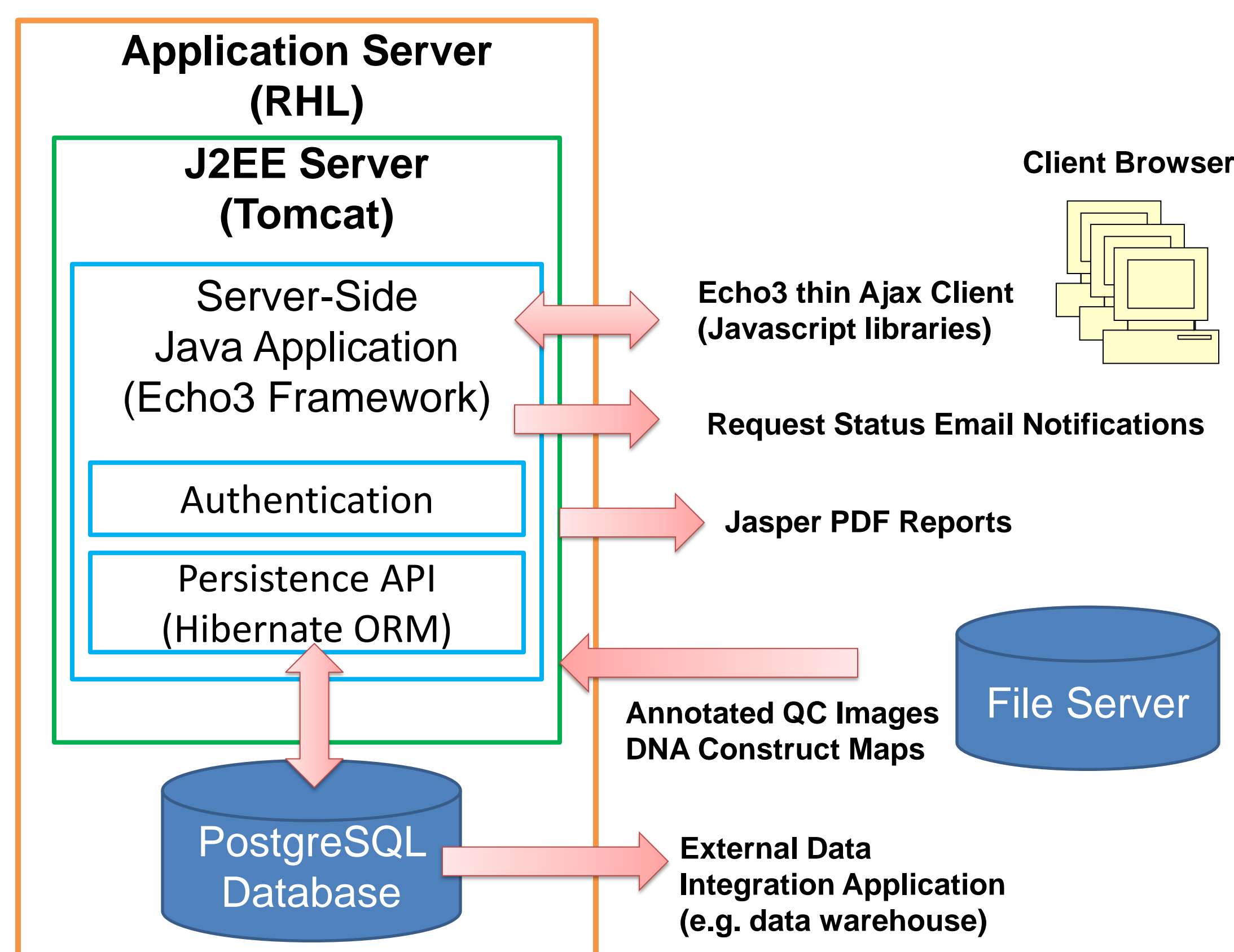


Fig. 1 Schematic of METIS components, which consists primarily of Open-Source framework components, including Java+Echo3 for the Ajax client-server framework, Apache Tomcat for the application server, PostgreSQL for the relational database, Hibernate for the object-relational mapping (ORM) layer, Jasper Reports for generating PDF reports, and JavaMail API for sending emails. Reagent data in METIS serves as a critical reference data source for additional screening-related applications at VLST.

DEVELOPMENT PROCESS SUMMARY

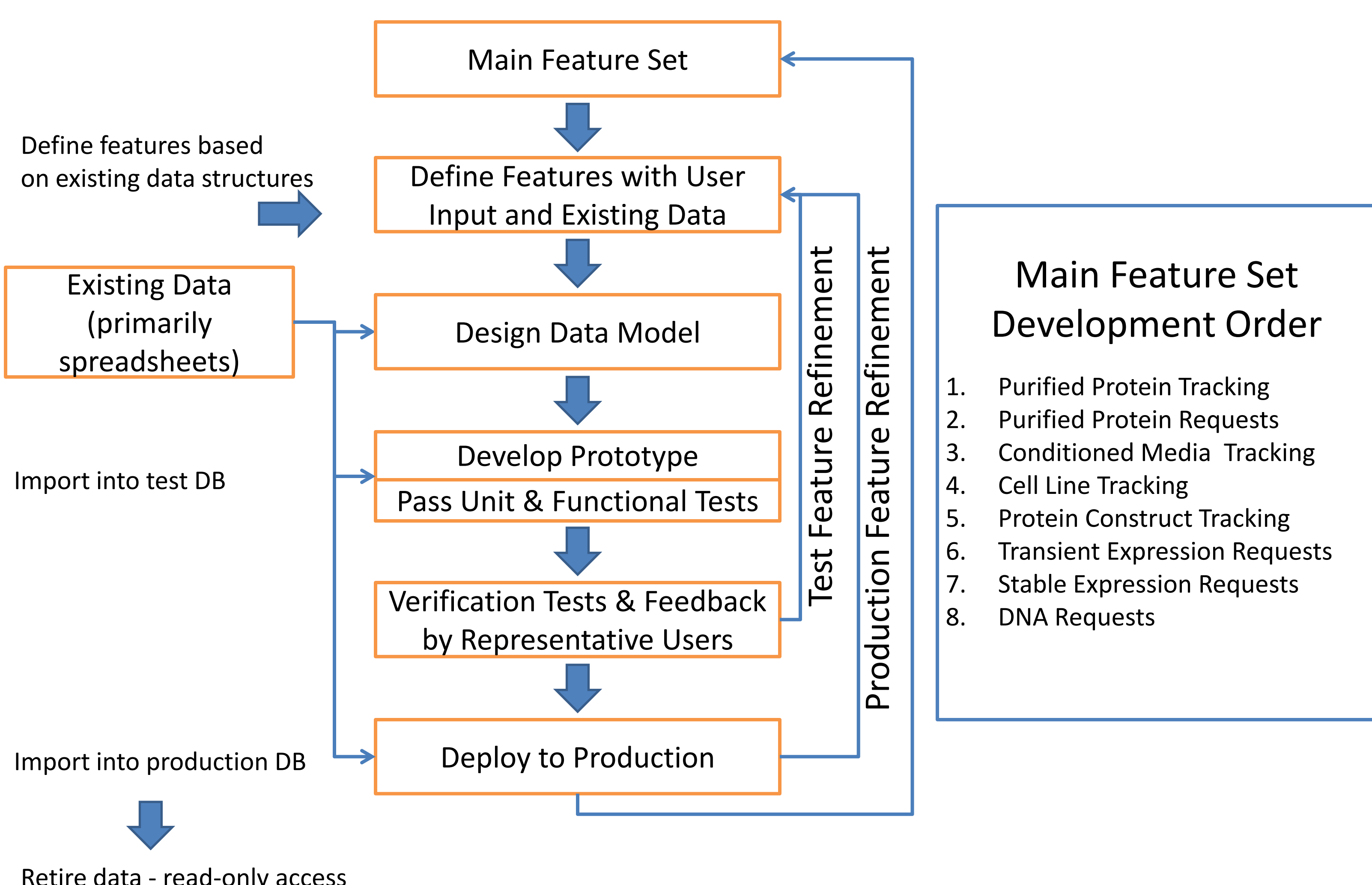


Fig. 2 Illustration of the staged development process. Key application users were identified to serve as testers, and to review features and usability with developers. Development cycles were kept short and iterative, with full input from the users. At the end of the development cycle for each main feature set, data from existing spreadsheets was imported into the database and retired. Initial development was focused on providing support for tracking and requesting purified protein. Additional tracking for conditioned media, cell lines and DNA constructs were sequentially. The final feature set focused on providing support for requesting conditioned media and DNA and prioritizing these requests.

APPLICATION FUNCTIONALITY



Fig. 3 Core reagent tracking components. Purified protein, conditioned media, and cell line records are created and maintained by individuals within the Protein Sciences group that are responsible for cell culture and protein purification. Records for DNA used in transient transfections and stable cell line protein production are maintained by individuals within the Target Discovery group. Records are entered and inventory updated as reagents are generated. Full relational links are maintained from DNA constructs to purified proteins. For quality control, links to SDS-PAGE and Western Blots are associated with the purified protein batch records and conditioned media; protein concentrations by MSD, endotoxin and protein expression level are tracked for conditioned media; and Mycoplasma test results are tracked for each cell line.

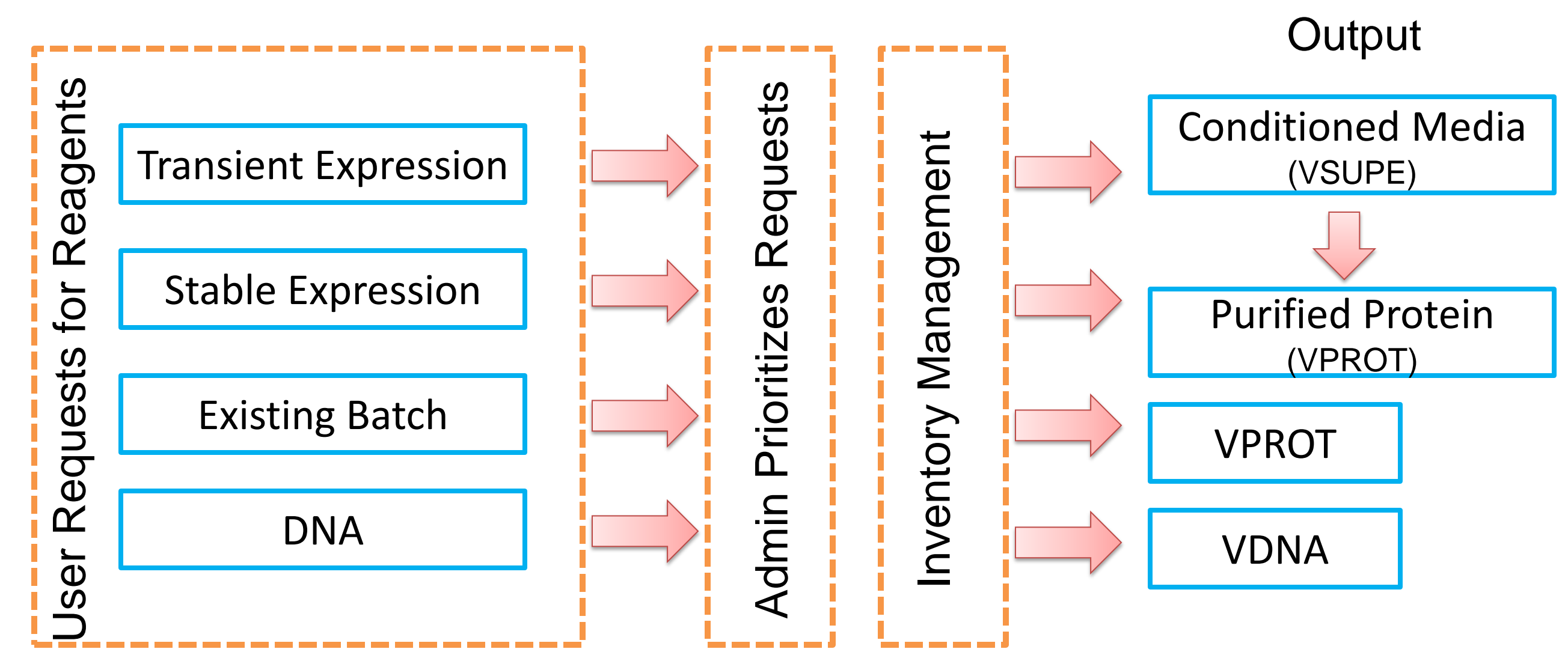


Fig. 4 Reagent request components. Requests for protein reagents are prioritized by users with administrative privileges for editing, canceling, and prioritizing requests. These requests move through pending, started and completed status. At each status change, emails are sent to the users notifying them of the status change and completion of request. Given a large volume of requests, and that all lab staff can submit requests, prioritization allows the organization to place emphasis on projects that have critical timelines.

APPLICATION SCREENSHOTS

The figure shows three screenshots of the application interface. The top screenshot is a 'TRANSFECTION REQUEST' form for request ID 1538. It includes fields for DNA ID, requester email, project name, cell type, volume, and DNA quantity. Callouts indicate it is 'Associated with DNA Construct' and provides an 'Email for Automatic Notification of Request Start & Completion'. The middle screenshot is a 'PROTEIN RECORD' for batch VPROT230. It shows a table of purification steps and associated test results. Callouts highlight 'Complete Protein History', 'Endotoxin Test Results', 'Protein Purification Steps', 'Protein Yield & Inventory', and 'Online QC Data Files'. The bottom screenshot is a 'DNA RECORD' for construct VDNA517. It shows fields for vector name, notebook, and sequence. Callouts indicate 'Links to Construct Maps', 'Calculated from Mature Sequence', and 'PDF Reports for all Records'.

Fig. 5 Example screenshots illustrating details captured for a transfection request, protein batch and DNA construct. Shown at the left of each screenshot is the overall application navigation panel, which supports submitting and prioritizing requests for proteins or DNA, viewing and editing details for batches of purified protein, conditioned media, cell lines, and the DNA constructs. Not shown are summary tables, PDF reports, search screens and the other protein-related detail screens.

SUMMARY

METIS is a web-based application developed and utilized by VLST Corp to track protein engineering, expression, and purification data from DNA construct through purified protein, and manage requests for various protein reagents. It was developed using primarily Open-Source components in an iterative fashion together with key stakeholders, to provide critical workflow and reagent data to lab staff, managers, and other screening-related software applications.