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Abstract

From User to DNA, CADMAD's libraries construction poses complex problems, tackled on many different fronts and sometimes with entirely different systems. Here we present a full, smart, LIMS system for manufacturing combinatorial DNA libraries, integrating the user design, planning, automation, and other LIMS (Laboratory information management system) features.

Keywords[7]:

DNALD, LIMS, DB, database, CAD, Robotics, Automation, webUI, Django

In many ways, CADMAD is a LIMS project. Many challenges are addressed with novel algorithms, systems and protocols, urging for a unified simplistic system for its users.
Our goal is to create a project management system that will tie together most of the functionality developed in CADMAD, with a user friendly interface.
We now support importing libraries from DNALD, exporting and importing to and from the automation module, managing the logical construction plan, managing the physical reagents, and automatically piping the library through optimization, planning and validation all the way to production.

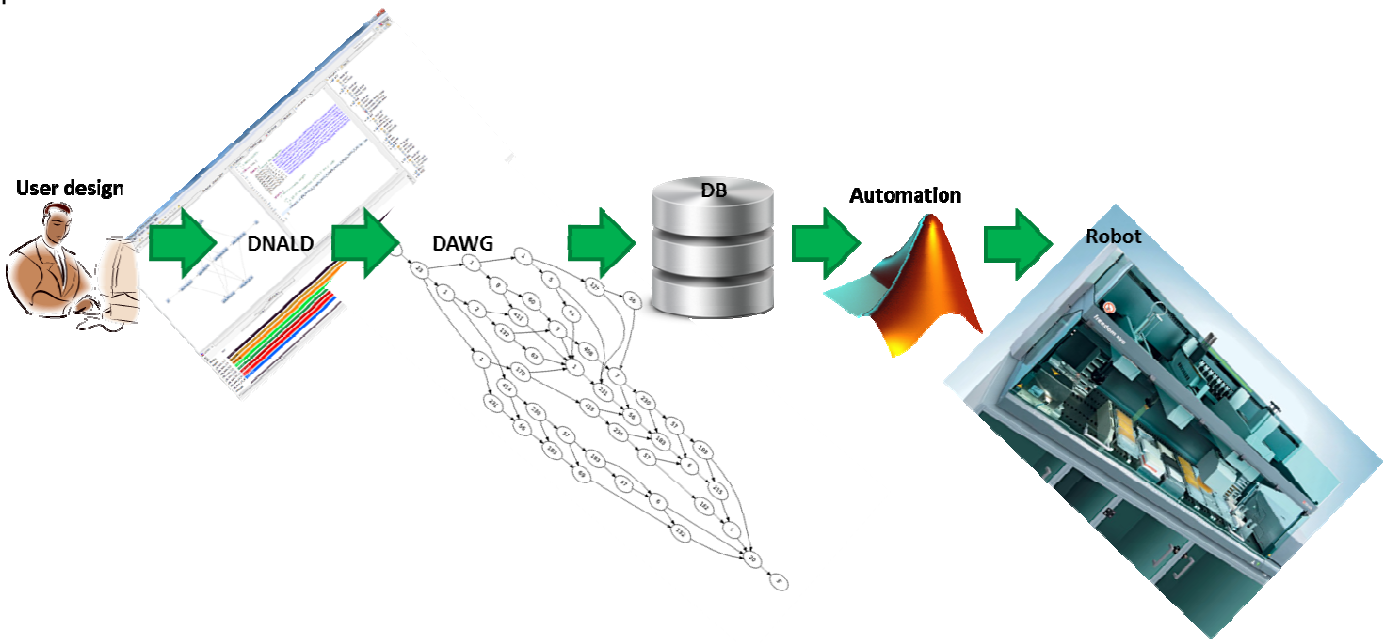

Figure A: global workflow of the various systems

[7] Keywords that would serve as search label for information retrieval

1. Implementation

DNALD integration (integrating WP1)

The user designed library is accepted from the DNALD IDE as a JSON file, representing the library as a graph similar to a DAWG (Directed Acyclic Words Graph) and is then parsed to a corresponding data model (see report 2.4).

Planning (integrating WP2)

The planning module is responsible for devising a biochemically viable construction plan to a given library. The library design (WP1) is parsed in its graph representation to a corresponding data model. It is optimized by the planning module, analysed by the pairing part of the planning algorithm and transformed into a binary tree of concatenations. The library, now a binary construction tree, is compatible with the database's data model and after passing through the primer designing algorithm and revalidation of the construction plan, it is saved to the DB.

Automation (integrating WP3)

The automation module is responsible for the execution of biochemical steps on Tecan's Evoware robotic platform. It is comprised of a LIMS like backend support for managing reagents and plates and of computationally flexible biochemical protocols.
A library's construction plan is viewed by the automation as parallel set of logical concatenations that can be dissected into a series of biochemical steps performed in parallel for the entire library and even for multiple libraries at once. The construction plan progresses by moving back and forth between database and the automation. When the automation performs a step, the reagents data (volumes, locations, etc.) is updated and can be then outputted for the next automation step. When a full concatenation is completed the plan is updated as well and the next tree layer of concatenation starts its progress through the automation.

Expanding the automation module with Gibson assembly support

Gibson assembly is a DNA assembly method which allows for the joining of multiple DNA fragments in a single, isothermal reaction. Integrating the Gibson assembly allows for a quicker, more efficient libraries assembly as well as more resilient when altering between the Y assembly method and Gibson.

LIMS (WP4)

The LIMS (Laboratory information management system) part of CADMAD holds the users' hand all the way from the completed library design (done externally using DNALD IDE) to finalizing the manufacturing process of the library's targets.
To do that, we support the manufacturing process with a database designed to hold both the implicit logical workflow of the construction process and the explicit physical biochemical reagents, protocols and plates.
The data and functionality is presented to the user through a Django+Dojo webUI frontend that allows monitoring, manual interference, and feedback.

2. Results

We have a system that accepts DNALD's libraries descriptions as a JSON file representing the library as a DAWG like graph, pipes it through the optimization and planning algorithms and writes the resulting construction plan to the supporting DB. Our system can then export the logical plan and the involved physical reagents and plates to files, processed by the automation module. New reagents, plates, etc. that result from the automation runs, are parsed by our main system and the DB is updated accordingly.
Throughout the process, the user is updated and can interfere with the processes using the Django+Dojo webUI frontend.

3. Conclusions

Our system is functional and optimal in certain aspects. The next step in its development will be to incorporate the automation module tightly within the LIMS backend.
Additional work is expected on adapting the automation to ALL's (Advance liquid logic) microfluidics platform.

4. Abbreviations

List all abbreviations used in the document arranged alphabetically.

DAWG	Directed Acyclic Words Graph
LIMS	Laboratory information management system