CLINICAL LABORATORY OPTIMIZATION

Ph.D. Dissertation Defense

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PROJECT CONTEXT

Research Collaboration

The Most comprehensive research study done on clinical laboratory (CL) optimization







- Develop a decision support tool to ease decision making of large laboratory organization design
- Develop a customized simulation tool for clinical laboratory analysis, evaluation and decision making

PROJECT MOTIVATION & SIGNIFICANCE

- Cost and reimbursement constraints drive concentration of laboratories
 - Larger organizations are more complex to manage
- Healthcare demand is growing
 - Bring more works to laboratories
- Comprehensive mastering of laboratories organization becomes too complex to be handled manually
- Manageable simple solutions adopted could be distant from efficient solutions



An essential need for an efficient decision support tool is highly appreciated

PROJECT CHALLENGES

Lack of comprehensive reference on clinical laboratory organization

	Project main activities						
Sources of information	CL understanding	CL components understanding	Problem identification & description	Modeling & validation			
Expert knowledge	×	×	×	×			
Laboratory visit	×	×	×				
'LabSim' simulation tool		×		×			
Machine manufacturer website		×		×			
Laboratory database				×			

Poor literature on clinical laboratory optimization

Mostly simulation studies for a specific problem on a specific case

CLINICAL LABORATORY



Clinical analysis laboratory is an organization gathering human and machinery resources to analyze human fluid samples such as blood.



Collection site and Examination site

With standalone sorter



EXAMINATION SITE: MAIN PROCESS



Rack making

Rack Transport

MAIN DECISION PROBLEMS IN CL DESIGN & PLANNING



PROPOSED FRAMEWORK

Systematic, top-down, stepwise framework with recursive loop



CASE STUDY: REAL LABORATORY IN FRANCE



Immunology and Chemistry disciplines



Daily Demand characteristics

		Total Number of tubes	3,847
		Number of Chemistry tubes	1,657
Demand - Tube		Number of Immunology tubes	458
		Number of Imm-Ch tubes	1,732
	י ו		
Test types	•	Total number of test type	73
		Chemistry test type	40
		Immunology test type	32
	l		
		Total number of test requested	28,632
Demand - Test	•	Total number of chemistry tests	24,041
		Total number of Immunology tests	4,591

RESOLUTION APPROACHES AND TOOLS

- MIP models solved with Cplex solver in GAMS
- Multi-objectives models tackled by weighted sum method
- Heuristic developed in Java
- Data management tool developed in Excel





FOR CLINICAL LABORATORY

PROBLEM DESCRIPTION AND DEFINITION

- Type of machines in a laboratory
- Analyzers: Immunology (e.g. DxIs), Chemistry (e.g. AUs), etc.
- Non-analytical machines: Centrifuge, Sorter, etc.
- Problem definition



RESOLUTION APPROACHES FOR MACHINE SELECTION



PROPOSED MATHEMATICAL MODEL

$$\begin{array}{lll} \textit{Min} & \sum_{j \in M} FC_{j}u_{j} + \sum_{h \in H} \sum_{s \in Q} \sum_{j \in M^{A}} RC_{hsj}x_{hsj} + \sum_{h \in H} \sum_{j \in M^{A}} CC_{hj}y_{hj} & & \text{Total machines fixed cost,} \\ & \text{Total configuration cost} \\ & \text{S.t.} & AOC_{j} \leq \tau_{j}g_{j}u_{j}; \ \forall j \in M^{A} & & \text{Analyzer operational capacity} \\ & AOC_{j} \leq \sum_{h \in H} \sum_{s \in Q} \delta_{hsj}x_{hsj}; \ \forall j \in M^{A} & & \text{Demand satisfaction for all tests} \\ & \sum_{j \in M^{d}} AOC_{j} \geq \sum_{h \in H^{d}} \left(F_{h} + \sum_{j \in M^{d}} \alpha_{hj}y_{hj}\right); \ \forall d \in D & & \text{Demand satisfaction for each} \\ & \sum_{j \in M^{A}} \sum_{s \in Q} \delta_{hsj}x_{hsj} \geq F_{h} + \sum_{j \in M^{A}} \alpha_{hj}y_{hj}; \ \forall h \in H & & \text{Demand satisfaction for each} \\ & \sum_{h \in H} \sum_{s \in Q} \lambda_{hs}x_{hsj} \leq RK_{j}u_{j}; \ \forall j \in M^{A} & & \text{Analyzer reagent capacity constraint} \\ & y_{hj} \leq HM_{hj}; \ \forall h \in H, j \in M^{A} & & \text{Analyzer test capability constraint} \end{array}$$

PROPOSED MATHEMATICAL MODEL



MACHINE SELECTION PROBLEM NUMERICAL RESULTS

	7 hours	8 hours	9 hours
Selected Immunology analyzers	2 Dx1800	1 DxI600	1 DxI600
		1 DxI800	1 Dx1800
Selected Chemistry analyzers	1 AU480	1 AU480	1 AU480
	1 AU5822	1 AU5822	1 AU5822
Selected Centrifuges	5 CentrifugeT1	5 CentrifugeT1	4 CentrifugeT1
Selected Automates	2 AutomateT1	1 AutomateT1	1 AutomateT1
Objective function value	51.766	51.071	50.983

Laboratory daily working hours



FOR CLINICAL LABORATORY

PROBLEM DESCRIPTION







Instruments with different attributes







Optimization + Design

PROBLEM DEFINITION



PROBLEM ASSUMPTIONS: LABORATORY AREA

Single floor with any structure (simple or complex polygon)

Given location for entrance and pre-occupied places (e.g. pillars)



PROBLEM ASSUMPTIONS: FACILITY

All facilities are considered rectangular with known dimensions



A clearance is defined for each facility. This clearance is simply added to the size of the facility



PROBLEM ASSUMPTIONS: FACILITY

Distance between two facilities: Rectilinear



Relationship between each pair of facilities: quantitative asymmetric flow matrix

average number of tubes transported from one point to another

Average number of time that an operator travels between two points

PROBLEM CONSTRAINTS



RESOLUTION APPROACH

NP-hard problem

Structure of the proposed hybrid heuristic approach



RESOLUTION APPROACH: GREEDY HEURISTIC

- Used to generate initial solution
- Quantitative CORELAP algorithm
- Made of two steps: (1) Sorting and (2) Placement
 - Sorting rules
 - 1. Facility 'registration desk' is always the first
 - Facility with the most connections (from and to) with the previous added facility
 - 3. Facility with the highest total closeness rating (TCR)



RESOLUTION APPROACH: GREEDY HEURISTIC + B&B

- Used to generate multiple initial solutions
- B&B manipulates in placement phase
- Branches are bounded regarding some rules



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RESOLUTION APPROACH: SELECTION PHASE

- Select best diverse solutions through comparing the obtained solutions
- **Diversity measure**: Distance between gravity centers of same-discipline facilities in 2 solutions
- Aims at providing plenty of diverse design alternatives for designers



Selected Solutions

RESOLUTION APPROACH: LOCAL SEARCH PHASE

- Improving the selected solutions through 2-opt algorithm
 - 2-opt algorithm involves swapping facilities with equal sizes
- An acceptable swap leads to a solution with better value for objective function respecting constraints
 - Feasible and infeasible swaps:



CASE STUDY:LABORATORY AREA



CASE STUDY: FACILITIES

Selected machines + other necessary instruments

Facility	Number	Length (cm)	Width (cm)	Clearance (cm)
Registration desk	2	150	110	50
Rack-making desk_C	1	150	100	50
Centrifuge	5	100	100	70
Re-racking desk_A	1	1 180 100		50
Automate	1	1 450 170		100
AU480	1	145	77	100
AU5822	1	366	158	100
Dx1600	1	171	97	100
Dx1800	1	171	97	100
Validation station_I	1	150	110	50
Validation station_C	1	150	110	50
Fridge	1	200	200	100

17 facilities

LAYOUT DESIGN OUTPUT (ENTRANCE E1)



LAYOUT DESIGN OUTPUT (ENTRANCE E2)



FINAL LAYOUT DESIGN WITH MANUPULATION





FOR CLINICAL LABORATORY

ANALYZER CONFIGURATION PROBLEM



Problem description









Problem definition

Analyzer Configuration

Problem

Specification the type and quantity of reagent bottles used in each analyzer

Objective is to minimize the total daily configuration and calibration costs as well as total tubes movement in the laboratory

Constraints:

- * Demand
- * Reagent capacity
- * Test capacity

PROPOSED MATHEMATICAL MODELS

Single objective model

Modeling idea: Machine selection model through fixing selection variables

Input data: Test-based demand

Objective: Minimizing total daily configuration and calibration costs

Bi-objective model

Modeling idea:



Input data: Tube-based demand

Objective: Minimizing total daily configuration and calibration costs as well as total tubs movement

PROPOSED BI-OBJECTIVE MATHEMATICAL MODEL





PROPOSED MATHEMATICAL MODEL: CONSTRAINTS



ANALYZER CONFIGURATION: NUMERICAL RESULTS

Existing analyzers

■ Immunology analyzers: Dxl600, Dxl800

■ Chemistry analyzers: AU480, AU5822

weight	τ - (π)	<i>F</i> ₁	<i>F</i> ₂	Relative gap (%)	Run time (sec)
	0	65.547	5,579	0	169.45
	0.3	49.191	5,602	2.38	10,800
	0.5	49.067	5,607	2.11	10,800
	0.7	48.997	5,690	2.57	10,800
	1	48.799	11,158	0	19.78

ANALYZER CONFIGURATION: PART OF OUTPUT

			Analy	yzers	
Test/Reagent type	Bottle size	AU480	AU5822	Dx1600	Dx1800
ALT	Small	1	6		
AST	Small	1	6		
UricAcidu	Small	1			
UricAcid	Small		2		
СК	Small		1		
Calcium	Large		3		
Creatinine	Small	1	2		
CRP	Large		2		
Triglyceride	Small		6		
UREA	Small	1	1		
			•••		
freePSA	small			1	1
PSA-Hyb	small			1	7
FRT3	small			1	1
FRT4	small			1	5
Testo	small			1	
GToxo	small			4	1
IgM-Toxo	small			4	1
Tropl	small				1
TSH	Small			2	10



FOR CLINICAL LABORATORY

PROBLEM DESCRIPTION



PROBLEM DEFINITION



!!! Note on load balancing!!!

Considering capacity and speed of analyzers as well as reagent availability, load balancing among

analyzers of a same discipline is defined based on:

- Number of **tubes** assigned to the analyzers
- Number of **tests** assigned to the analyzers

PROPOSED MULTI-OBJECTIVE MATHEMATICAL MODEL





PROPOSED MATHEMATICAL MODEL: CONSTRAINTS



PROPOSED MATHEMATICAL MODEL: CONSTRAINTS



ASSIGNMENT: NUMERICAL RESULTS



Existing analyzers

Immunology analyzers: Dxl600, Dxl800 ■ Chemistry analyzers: AU480, AU5822

weights + (π1	π 2	π3	F ₁	F ₂	F ₃	Relative gap (%)	Run time (sec)
	1	0	0	4.8325	13.686	17,387	0	5.02
	0	1	0	18.562	13.259	31,186	0	5.32
	0	0	1	5.985	13.542	15,987	0	6.66
	0.2	0.3	0.5	5.2	13.259	16,217	0	10.12
	0.2	0.2	0.6	5.611	13.260	16,053	0	8.08
	0.3	0.1	0.6	5.2	13.260	16,220	0	7.5
	0.3	0.3	0.4	5.161	13.26	16,242	0	7.98
	0.4	0.1	0.5	5.161	13.259	16,242	0	15.26

ASSIGNMENT: OUTPUTS (TUBE-ANALYZER ASSIGNMENT)

Tube	AU480	AU5822	Dx1600	Dx1800
T1		1		
T2		1		
Т3		1		
T4		1		
T5	1	1		
Т6	1			
Τ7		1		
		•••	•••	
T1663				1
T1664				1
T1665			1	
T1666			1	1
T1667			1	1
T1668				1
			•••	
T2116		1		1
T2117		1	1	
T2118	1			1
T2119		1	1	
T2120		1	1	
T2121	1			1

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ASSIGNMENT: OUTPUTS (TUBE TEST-ANALYZER ASSIGNMENT)

Test Name	Tube	AU480	AU5822	Dx1600	Dx1800
ALT	T1		1		
AST	T1		1		
T-Billirubin	T1		1		
Creatinine	T1000	1			
Glucose	T1000	1			
Ferritin	T3525				1
TSH	T3525				1
ALT	T3529	1			
AST	T3529	1			
HBc-Ab	T3529			1	
HBsAb	T3529			1	
HBsAgV3	T3529			1	



FOR CLINICAL LABORATORY



New laboratory process & decision problem

PROBLEM DESCRIPTION AND DEFINITION

- Miquoting
 - Simplifies the workflow and increases traceability in laboratories
 - Better scheduling; e.g. deadline satisfaction
 - Brings Extra costs and increases the number of tubes
 - Fixed policies for current laboratories

Challenges

- Aliquoting alternatives
- How many aliquots
- Test assignment to aliquots

PROBLEM DEFINITION: ILLUSTRATIVE EXAMPLE



FIRST PROPOSED RESOLUTION APPROACH Aliquoting decision process Test assignment to primary Number of aliquots Aliquoting required determination candidates selection tubes & aliquots Tube-Test matrix Tube-Analyzer & Assignment Start Tube test-Analyzer matrixes Analyzer-Test matrix Tubes Scheduling sequence No KPIs/ Termination No Simulation & Constraints rules **KPI** calculation Satisfied? triggered? Yes Yes End



OF CLINICAL LABORATORY

CLINICAL LABORATORY SIMULATION MODELING



Simulation type: Discrete-Event-Simulation



Simulation software: FlexSim





- Customized library (SimuLab): 28 objects
- Customized flow items: Tube and Racks
- Input/output Tables



EXAMPLE OF A SIMULATED OBJECT



Automate (Sorter with aliquoter)



EXAMPLE OF A SIMULATED OBJECT





MAIN CHARACTERISTICS OF CLINICAL LABORATORY

- A real-world system with complicated machine environment
- Machines with complicated operational attributes
- Several different flows through the system
 - Tubes/Racks flow through the laboratory
 - Sample flow through the analyzers
 - Information (test result) flow through the system
- Dynamicity
- Stochasticity



MAIN CHARACTERISTICS OF CLINICAL LABORATORY

- Machine eligibility restriction regarding the available reagent
- Precedence constraints between some tests of a tube for some tubes
- Aliquoting
- Backtracking or recirculation
- Tubes with different priorities: STAT or Routine
- Operators as transporters or task executers (in registration, validation, rack making)

Multiple objectives

- Turnaround Time (TAT) minimization
- Throughput maximization

CASE STUDY: GENERAL WORKFLOW



SIMULATION MODELING INPUTS



KEY PERFORMANCE INDICATORS (KPIs)



Tube time in system (TIS)

Throughput

Resource utilization



Tube/Test Tardiness



Waiting times at queues

SIMULATION MODELING PROCEDURE



Create laboratory area

Add objects from 'SimuLab' library

Connect selected objects



SIMULATION OUTPUTS



Customized output Tables + Standard FlexSim dashboard

Laboratory throughput

Average number of tests analyzed per hour	3052.65
Average number of tubes treated per hour	534.39
Test TAT from tube registration to test validation	
Average TAT	84.47 min
Maximum TAT	250.65 min
Minimum TAT	23.28 min

Tube TAT from tube registration to test validation

Average TAT	108.37 min
Maximum TAT	250.06 min
Minimum TAT	31.91 min

Tardy tubes	
Total number of tardy tubes	202
Percentage of tardy tubes	5.25%
Number of tardy Immunology tubes	37
Number of tardy Chemistry tubes	0
Number of tardy Immunology-Chemistry tubes	165

SIMULATION OUTPUTS

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Resource utilization



	Waiting	times
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Staytime at different Queues						
Object	Min	Max	Average			
Tube Generator/Tubes Q	0.00	19230.00	9612.50			
Rack builder_Centrifuge/Tube entry	0.00	36.18	1.67			
Rack builder_Centrifuge/Output	0.00	4163.71	2032.06			
Re_racking Desk/Entry point	0.00	60.93	10.49			
Re_racking Desk/Output	0.00	396.44	107.47			
Automate/Tubes_Q	0.75	247.39	142.10			
Automate/Output	0.00	83.34	14.24			
AU5822/Input buffer	0.00	0.00	0.00			
AU480/Input buffer	0.00	348.89	29.43			
Dxl800/Input buffer	0.00	105.10	14.62			
Dxl600/Input buffer	0.00	11.29	0.22			
Validation Console_I/Entry point	0.00	3.89	0.16			
Validation Console_C/Entry point	0.00	21.42	0.91			

State of Operators Idle TravelEmpty TravelLoaded Utilize							
Operator_R1	43%		5	7%			
Operator_R2	43%		5	57%			
Operator_RMC		83.3%	ó	2.9% 2.8%	11%		
Operator_RRA		62%	4.5% 4.5%	29%			
Operator_AA	32%	12%	<u>t</u>	56%			
Operator_VI		93%	6		7%		
Operator_VC		54%		36%			
0	% 20%	40%	60%	80%	100%		





CONCLUSION AND CONTRIBUTIONS

- Comprehensive study on clinical laboratory optimization
 - System identification
 - Decision problems identification and definition
- An optimization framework for efficient decision making on CL design and planning
- Customized single and multi-objective mathematical models for
 - Machine selection problem
 - Analyzer configuration problem
 - Assignment problem
- Customized hybrid heuristic algorithm for clinical laboratory layout design problem
- Address and characterize the aliquoting problem as an optimization problem
 - Customized simulation environment

PERSPECTIVES

- Clinical laboratory with automation line
- Optimizing the number of full-time employees
- Advanced optimization algorithms for multi-objectives problems

Pareto-based approachesMCDM



Evaluation on different benchmarks at different scales



Simulation integration with optimization methods

PUBLICATIONS AND SCIENTIFIC PRODUCTIONS

One published US patent entitled 'Intelligent handling of materials'

https://patents.google.com/patent/WO2018111721A1/en

- Two filed US patent entitled
- 'Laboratory instrument selection and configuration'

System and method for clinical laboratory layout design'

- Two accepted full papers in international conferences
- Sohrab Faramarzi Oghani, El-Ghazali Talbi, Martin Bué, Eric Varlet. Optimization of analyzers configuration in a clinical laboratory: a mathematical model. *MOSIM'18*, Jun 2018, Toulouse, France.
- Sohrab Faramarzi Oghani, El-Ghazali Talbi, Martin Bué, Eric Varlet. A heuristic approach for standalone clinical laboratory layout design. *META'2018*, October 2018, Marrakesh, Morocco.



One accepted and presented abstract entitled 'A mathematical model for machine selection problem in clinical laboratories' in OR2018 Conference in *Brussels*, Belgium.

Questions?

Thank You