33rd Annual INCOSE international symposium

hybrid event

Honolulu, HI, USA
July 15 - 20, 2023

MBSE Application to a Medication Auto-Injector Design

Bridging Systems Engineering Models and Multi-Fidelity Analytical Models

Meeting Challenges by 2035

- Multiple Delivery Challenges
- Many Physics Involved
- Strong Regulations
- MBSE as a Solution?

Applications

1. Systems engineering contributes innovative solutions to major societal challenges.
2. Systems engineering demonstrates value for projects and enterprises of all scales, and applies across an increasing number of domains.

Practices

3. Systems engineering anticipates and effectively responds to an increasingly dynamic and uncertain environment.
4. Model-based systems engineering, integrated with simulation, multi-disciplinary analysis, and immersive visualization environments is standard practice.
5. Systems engineering provides the analytic framework to define, realize, and sustain increasingly complex systems.
6. Systems engineering has widely adopted reuse practices such as product-line engineering, patterns, and composable design practices.

”By 2035, systems engineering will leverage the digital transformation in its tools and methods, and will be largely model-based using integrated **descriptive and analytical** digital representations of the systems.

Systems design, **analysis, and simulation models**, immersive technologies, and an **analytic framework** will enable **broad trade-space exploration**, rapid design evolution, and provide a shared understanding of the system throughout its life cycle.”

* Source: INCOSE SE Vision 2035

Agenda

- Challenges and System Context Definition
- Enabling Analytics in the System Model
- Need for Multi-Fidelity Analytical Models
- Integrating Analyses with the System Architecture Model
- Design Space Exploration, from Conceptual to Detailed Design
- Benefits & Challenges
- Conclusion

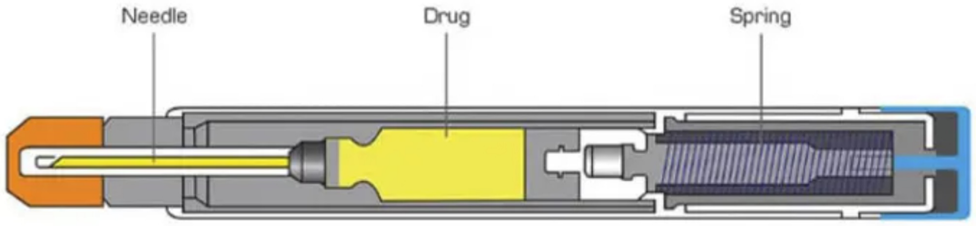
Challenges and System Context Definition

Auto-Injectors - Background

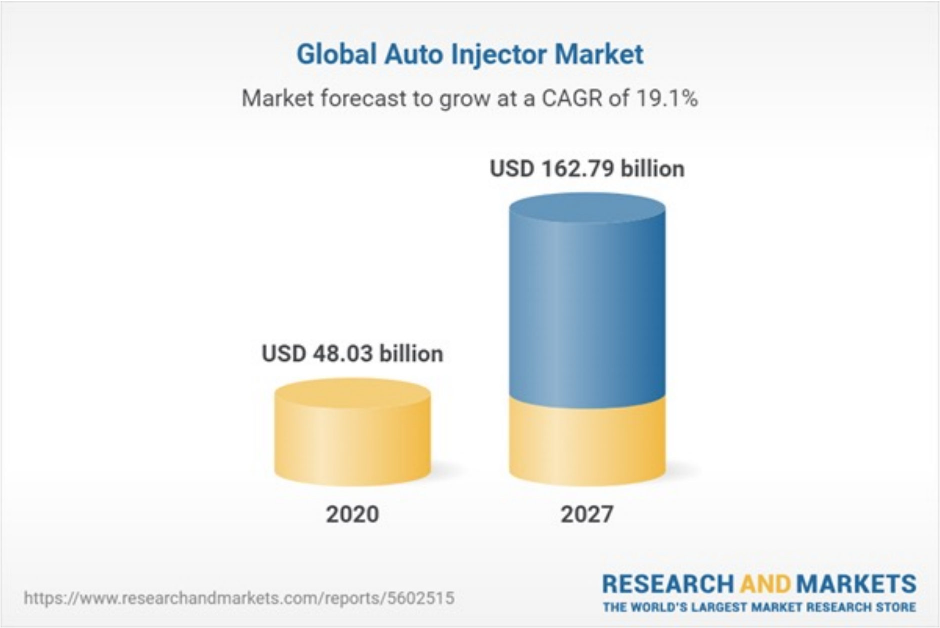
Auto-injector devices are used to treat a variety of diseases

Highly convenient as they support patient independence

Increased drug effectiveness and reduced percentage of errors vs syringes



With pen injectors, the patient actuates the needle and subsequent flow of medication through the engagement of the push-button. This design is commonly used for patients with chronic diseases. (Credit: Instron)



Auto-Injectors - Delivery Challenges

Figure 3: Complex molecules of biotherapeutics and biologics.

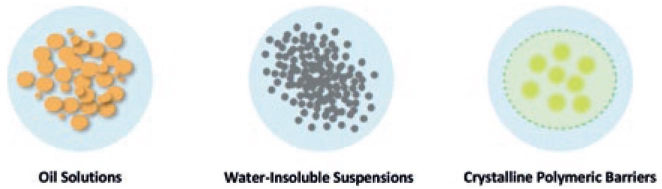
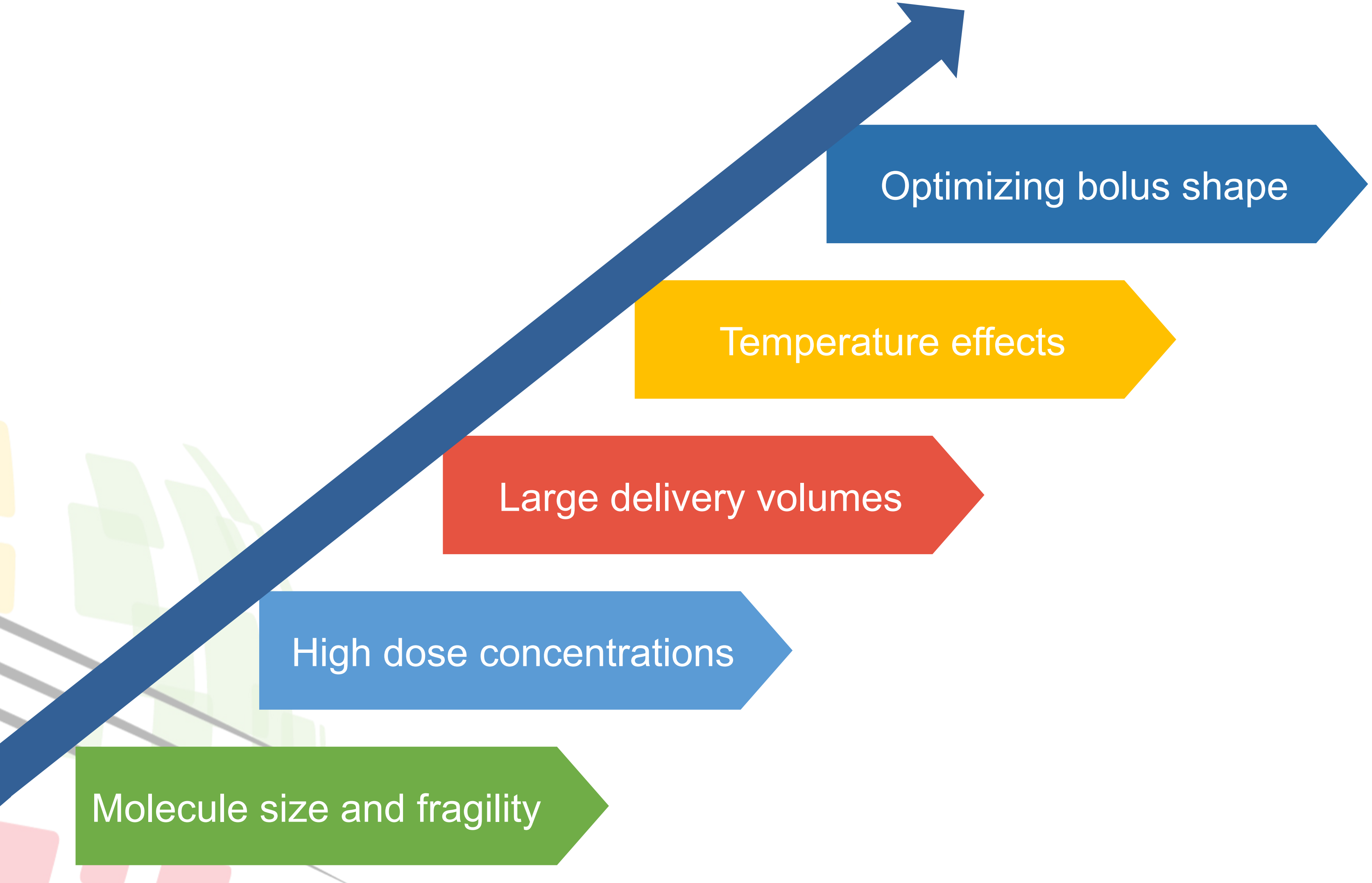


Figure 4: Formulation vehicles for LAIs.

* Source: ONdrugDelivery Prefilled Syringes & Injection Device, Issue 125 (2021)



Auto-Injectors - Analyses

- Determine which solutions meet our cost, safety and bolus shape (delivery time) requirements.
- Trade-offs between multiple design configurations
- Evaluate chosen solutions for robustness against temperature variation
- Analytic framework that supports the integration of simulation models from conceptual to detailed design phases

Auto-Injectors - System Problem Focus and Assumptions

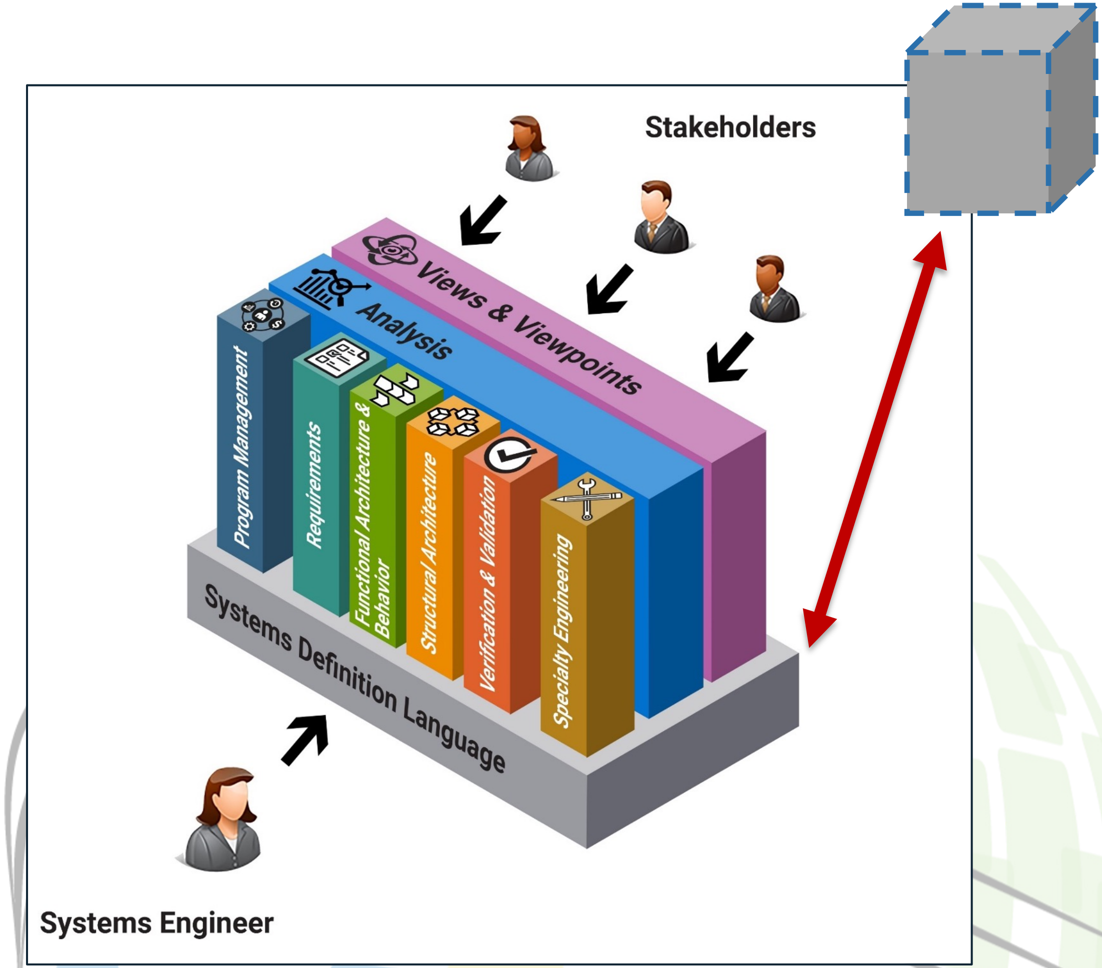
Cost — The focus is on the cost of the force delivery system (spring) and drug containment system (drug barrel). All other costs are maintained to be constant.

Safety Factor — The focus is on the drug containment system and preventing loss of the drug (highest cost of overall product).

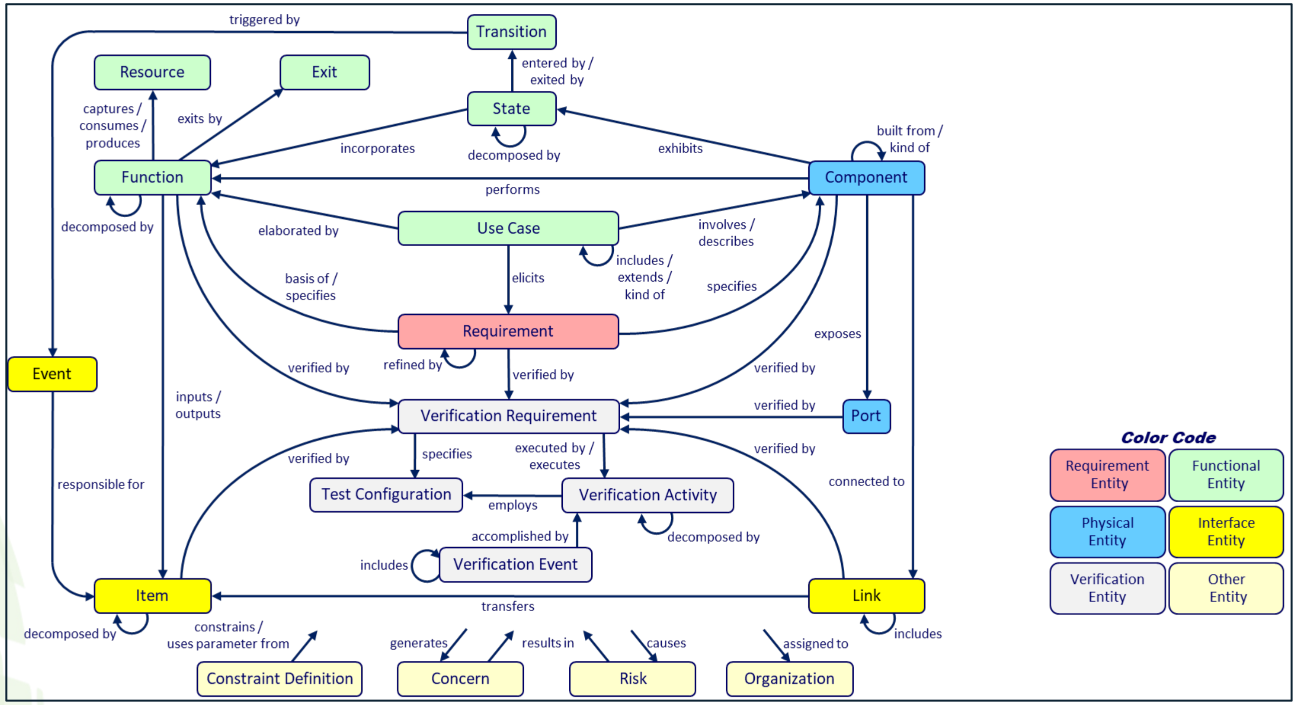
Injection Time — This design parameter is a surrogate for bolus shape. For simplification, a single drug variant and fixed injection volume is assumed.

Drug Temperature — The focus is on the effect on the proper bolus shape (injection time) and determining if the solution can delivery it robustly across expected temperature variation.

A Systems Engineering Modeling Framework



Digital Engineering Tools



Natural Language Modeling – the Systems Definition Language

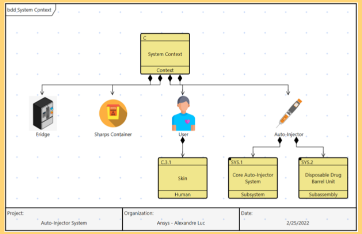
Enabling Analytics in the System Model

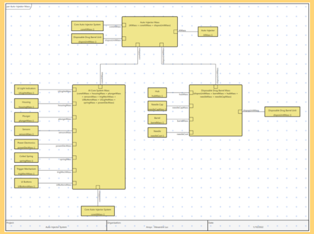
Step 1: Enabling Analytics in the System Model

Conceptual Phase | Preliminary Phase | Detailed Design Phase | Prototype & Test

SAM* Tool

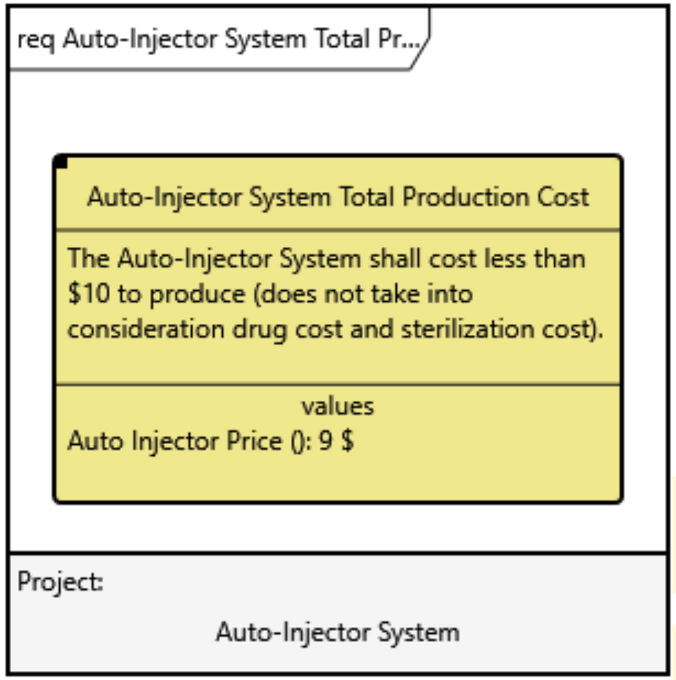
Step 1
System Model Creation

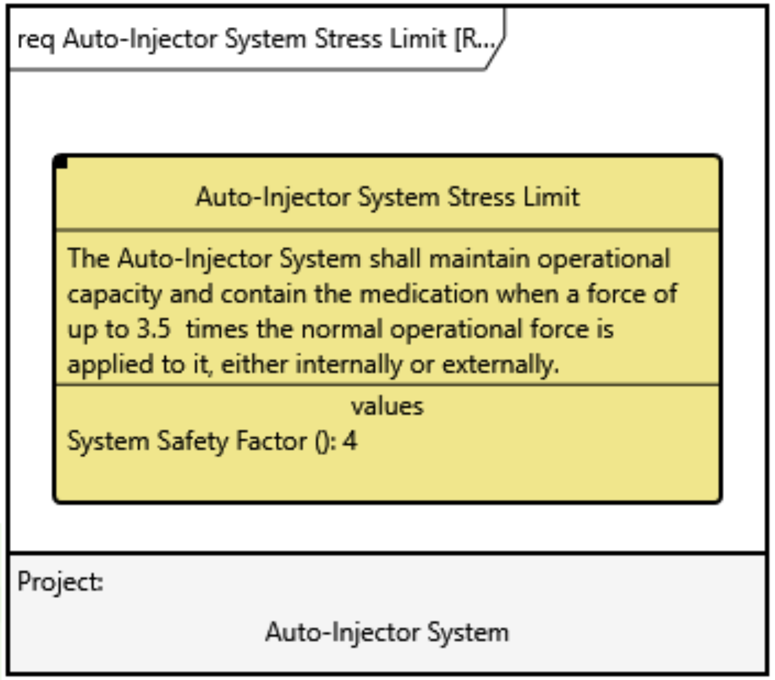


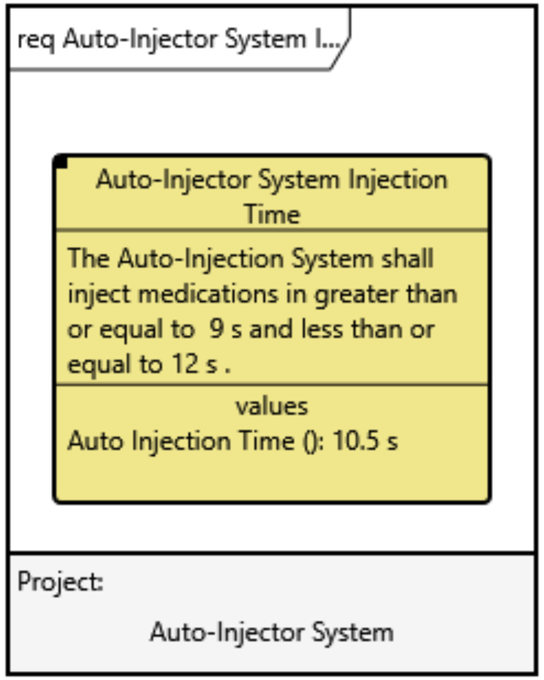


SAM = System Architecture Model*

Requirements and Parameterization

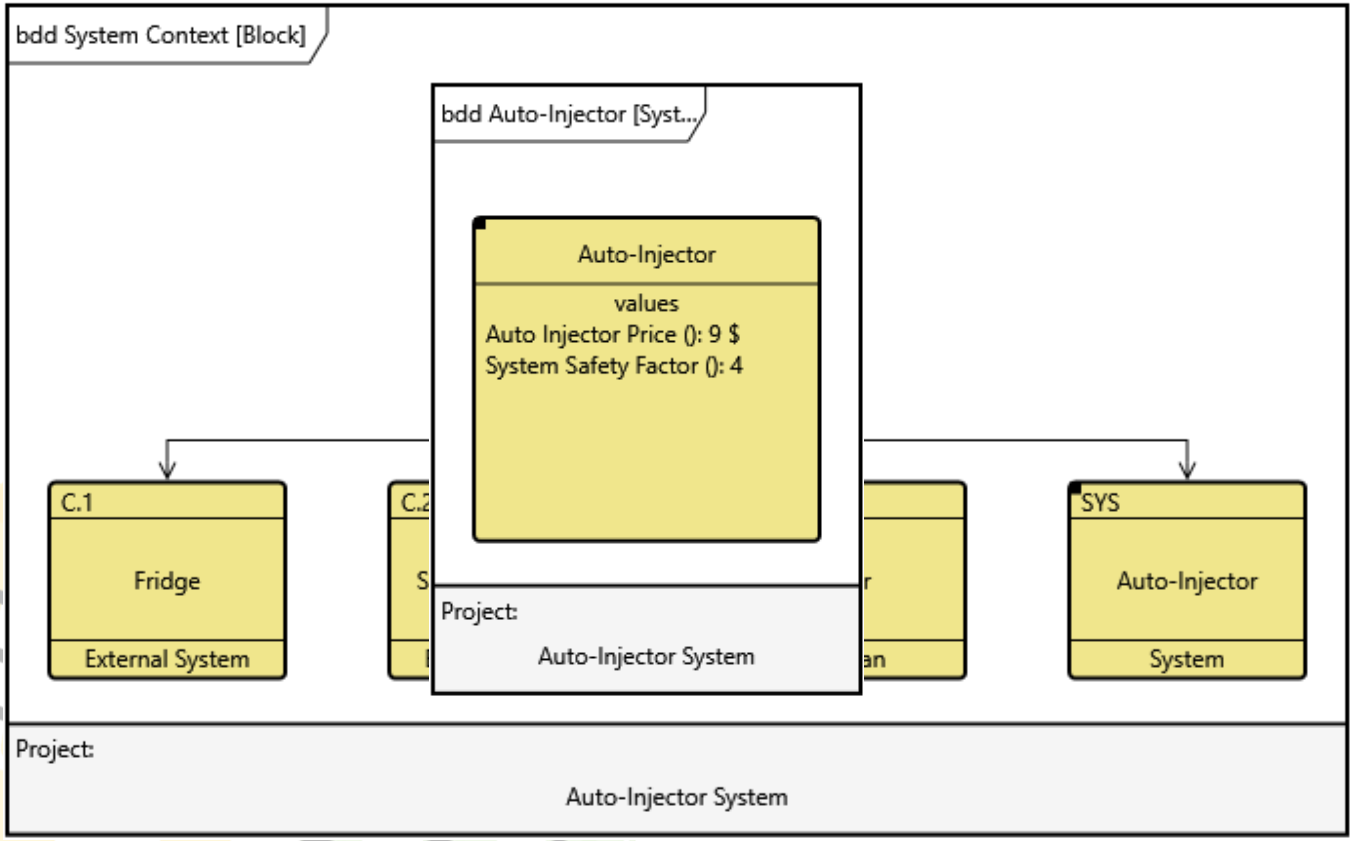




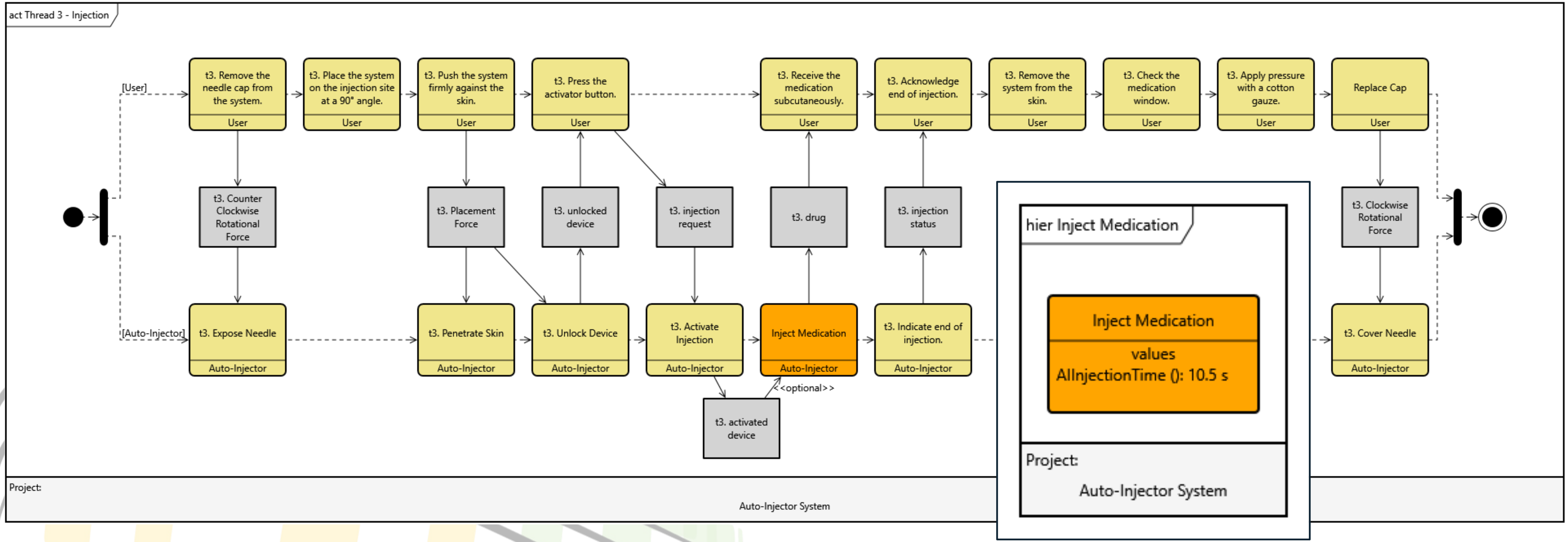


Requirements can be more than a statement. They can have values (parameters) behind them.

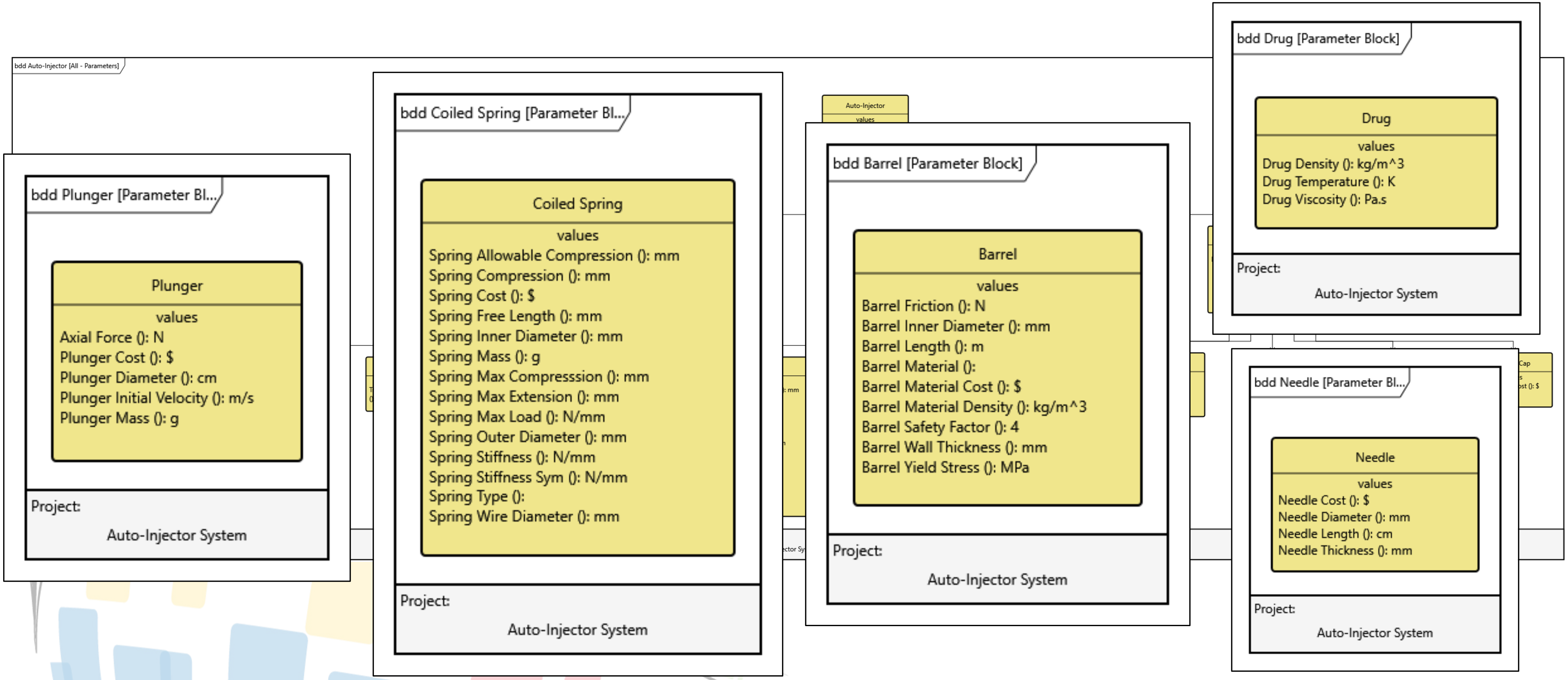
Structural Architecture – System Parameterization



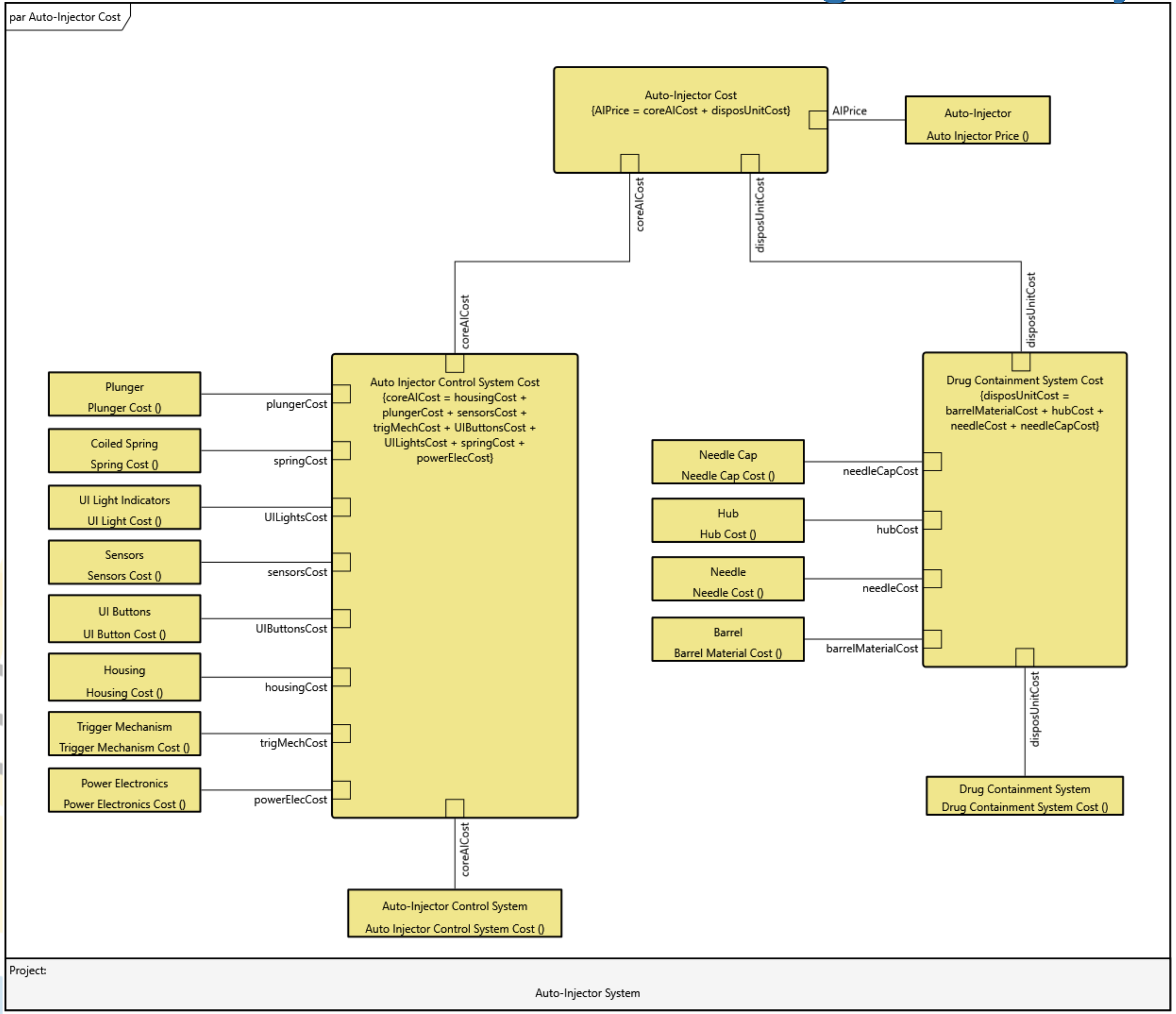
Functional/Behavior Architecture – Functional Parameterization



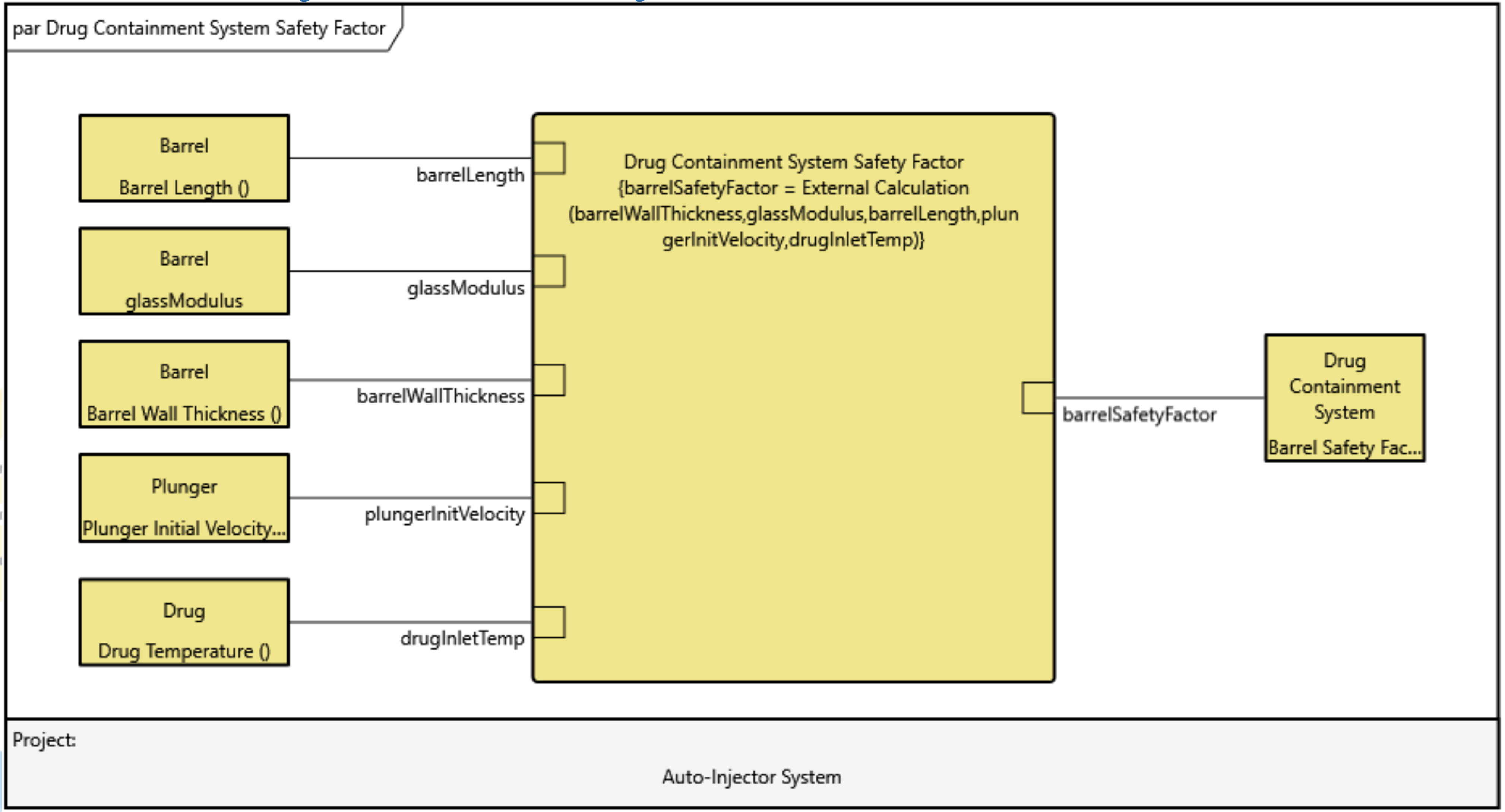
Architectural Decomposition/Derivation – Parameterization



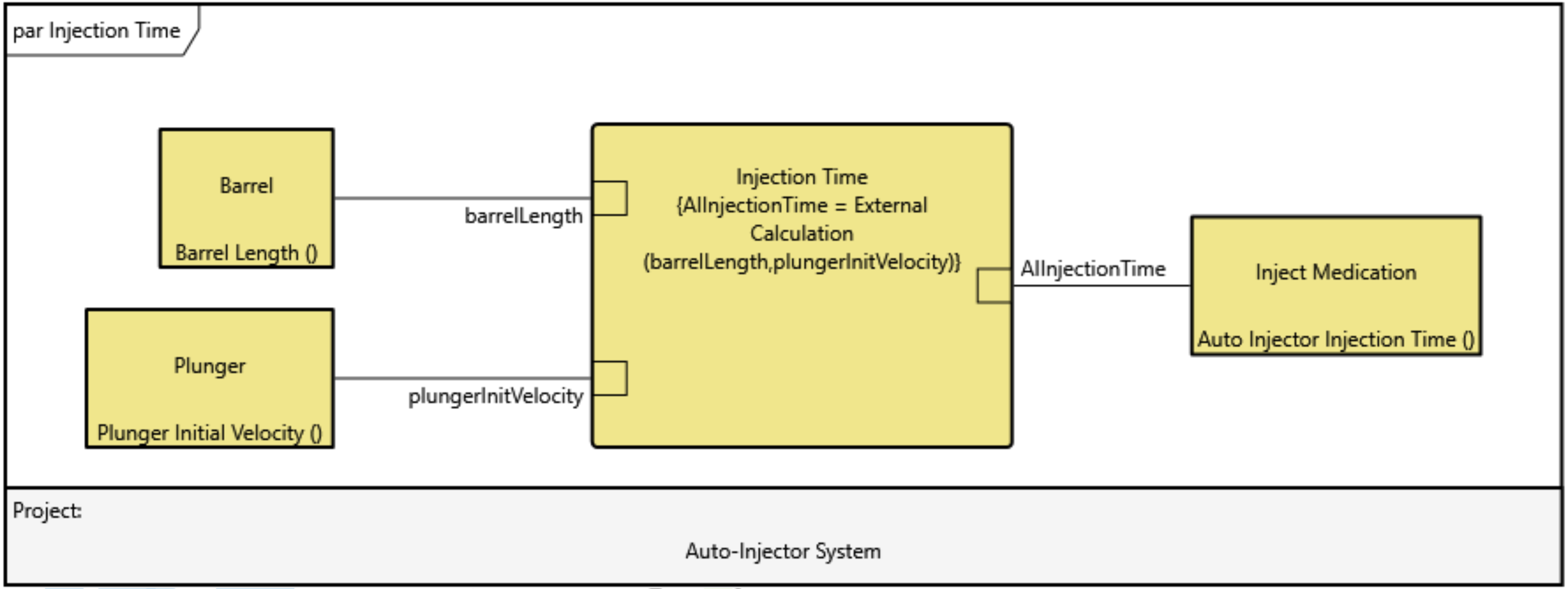
Constraint Definition – Parametric Diagram – System Cost



Constraint Definition – Parametric Diagram – Drug Containment System Safety Factor



Constraint Definition – Parametric Diagram – Injection Time



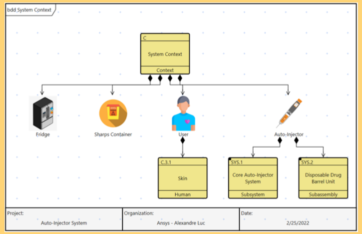
Need for Multi-Fidelity Analytical Models

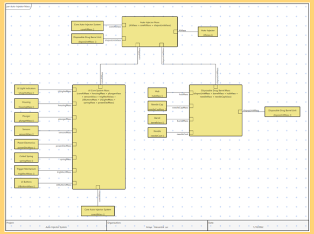
Step 2: Simulation Models Automation

Conceptual Phase | Preliminary Phase | Detailed Design Phase | Prototype & Test

SAM* Tool

Step 1
System Model Creation





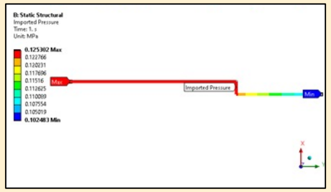
SAM = System Architecture Model*

Cost Analysis

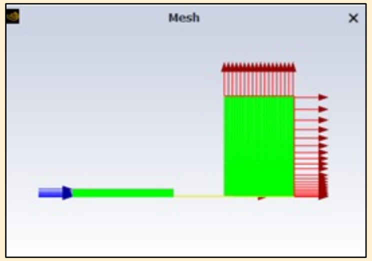
	A	B	C
1	**Barrel Design Properties**		
2	Barrel Inner Diameter	1	mm
3	Barrel Wall Thickness	0.5	mm
4	Barrel Length	0.05	m
5	Glass Volume	1.19381E-07	m^3
6			
7	**Glass Cost**		
8	Glass Volumic Cost	97.05	$/m^3
9	Barrel Glass Cost	1.16E-05	$

Step 2
Simulation Models Automation

1-way FSI Workflow



CFD Analysis

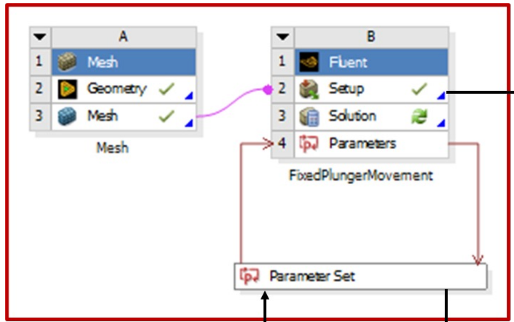


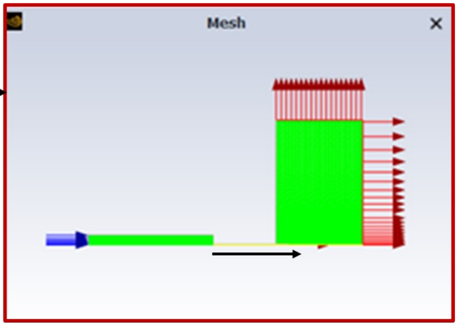
Structural Analysis

Simulation Models

Simulation Models Creation and Parametrization

CFD Analysis



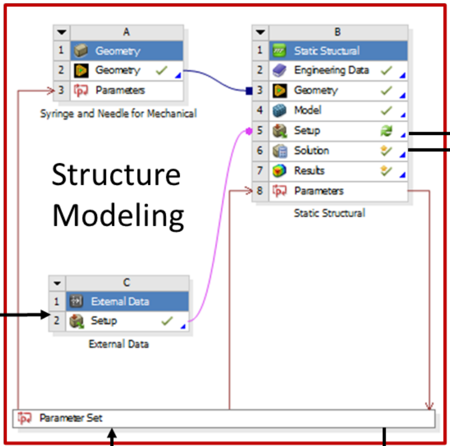


Fluid Inputs:
Plunger Initial Velocity
Drug Inlet Temperature

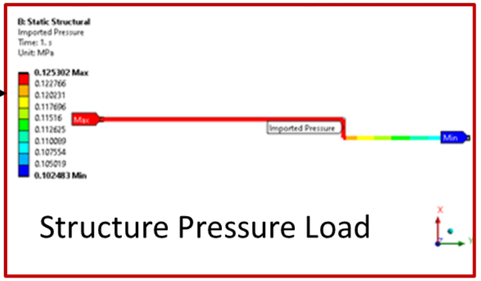
Fluid Outputs:
Barrel Wall Pressure
Drug Density
Drug Injection Time
Drug Viscosity

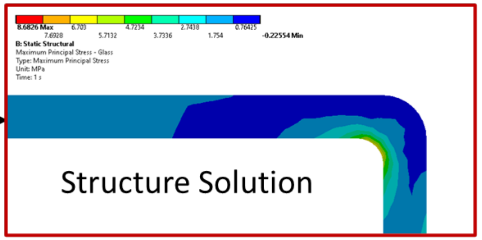
Structural Analysis

Fluid Pressure



Barrel Pressure from Fluid





Structure Inputs:
Material Modulus
Barrel Wall Thickness

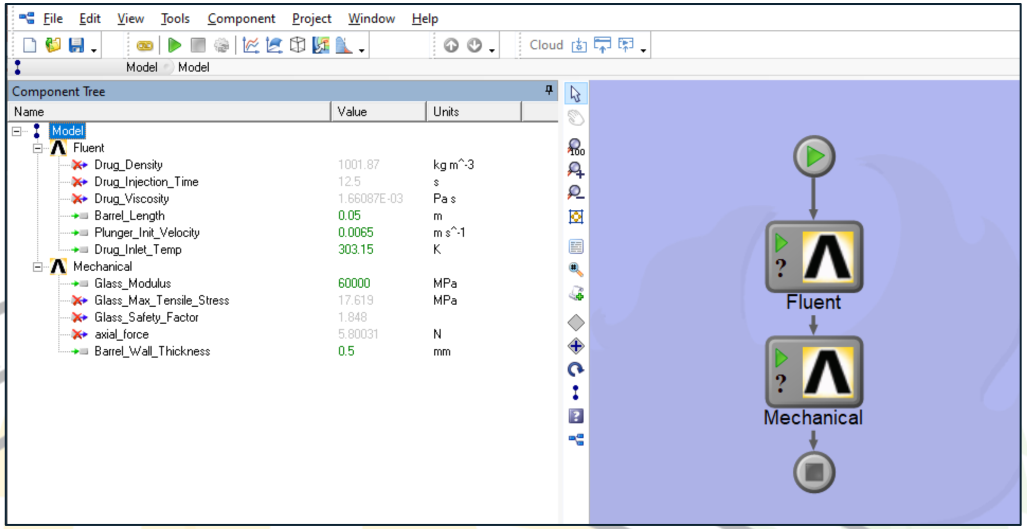
Structure Outputs:
Max Tensile Stress
Safety Factor

Cost Analysis

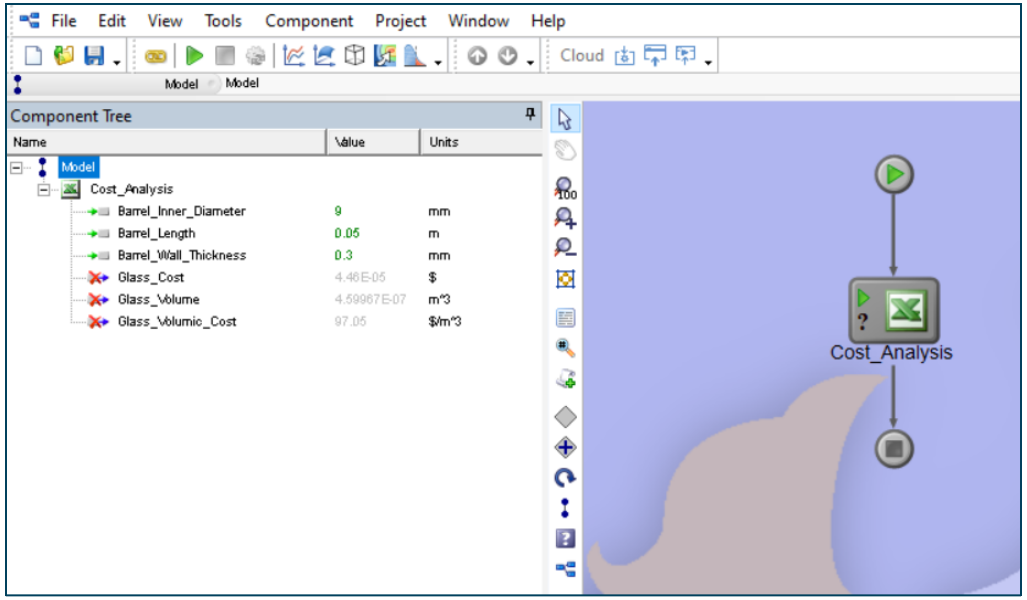
	A	B	C
1	**Barrel Design Properties**		
2	Barrel Inner Diameter	9	mm
3	Barrel Wall Thickness	0.3	mm
4	Barrel Length	0.05	m
5	Glass Volume	4.59967E-07	m^3
6			
7	**Glass Cost**		
8	Glass Volumic Cost	97.05	$/m^3
9	Barrel Glass Cost	4.46E-05	$

Simulation Model Automation

1-way Fluid Structure Interaction Workflow



Cost Analysis Workflow



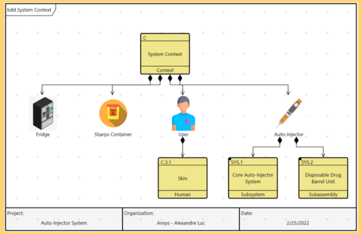
Integrating Analyses with Systems Architecture Model

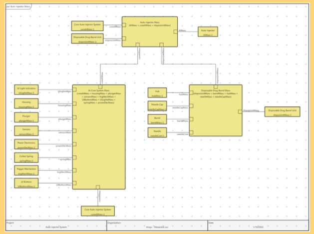
Step 3: Connect Simulation Models to the SAM

Conceptual Phase | Preliminary Phase | Detailed Design Phase | Prototype & Test

SAM* Tool

Step 1
System Model Creation





SAM = System Architecture Model*

Bi-directional Connector

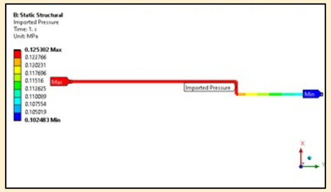
Step 3
Connect Simulation Models to the SAM

Cost Analysis

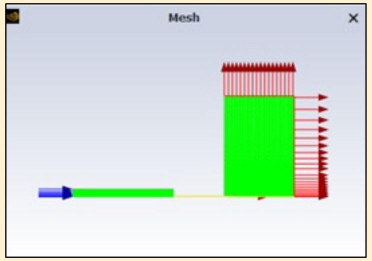
	A	B	C
1	**Barrel Design Properties**		
2	Barrel Inner Diameter	1	mm
3	Barrel Wall Thickness	0.5	mm
4	Barrel Length	0.05	m
5	Glass Volume	1.19381E-07	m^3
6			
7	**Glass Cost**		
8	Glass Volumic Cost	97.05	$/m^3
9	Barrel Glass Cost	1.16E-05	$

Step 2
Simulation Models Automation

1-way FSI Workflow



CFD Analysis



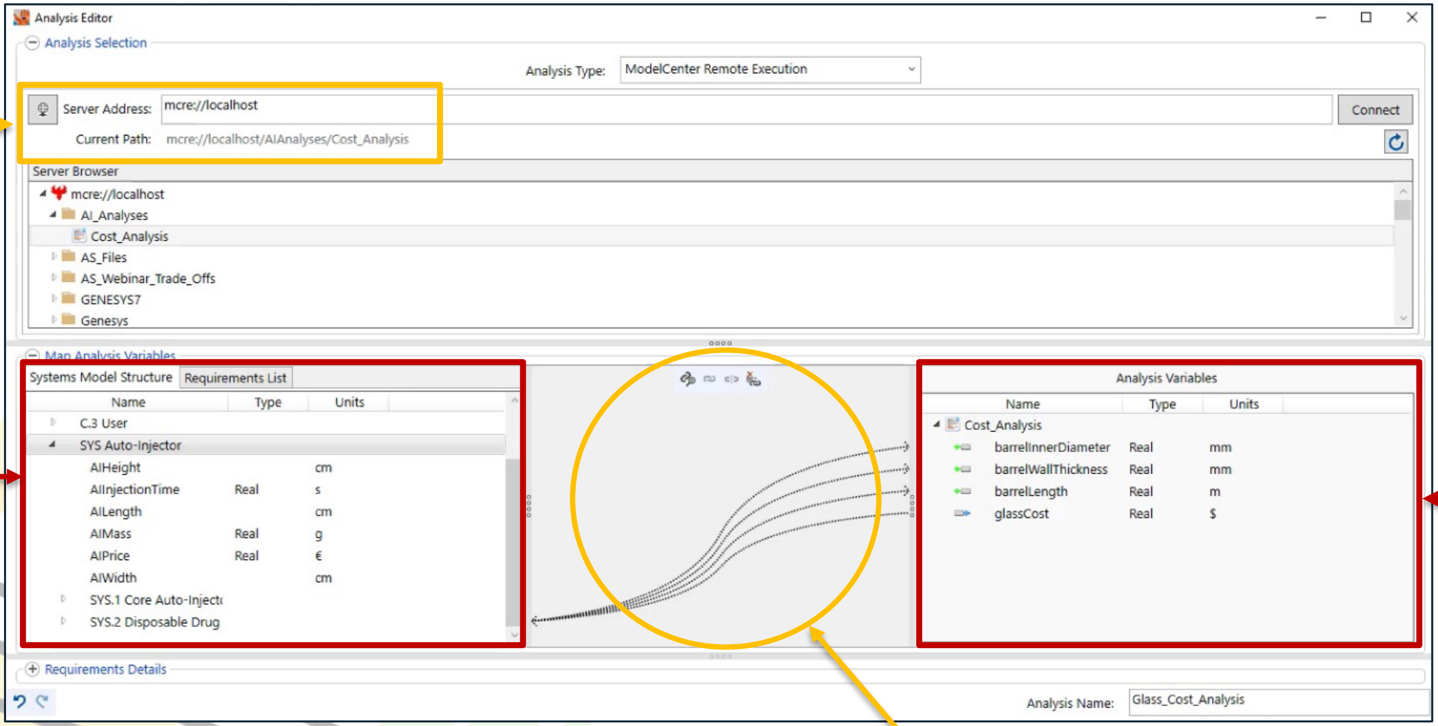
Structural Analysis

Simulation Models

Step 3: Connect Simulation Models to the SAM

Server Address to access Simulation Workflows

Parametrized Architectural Entities



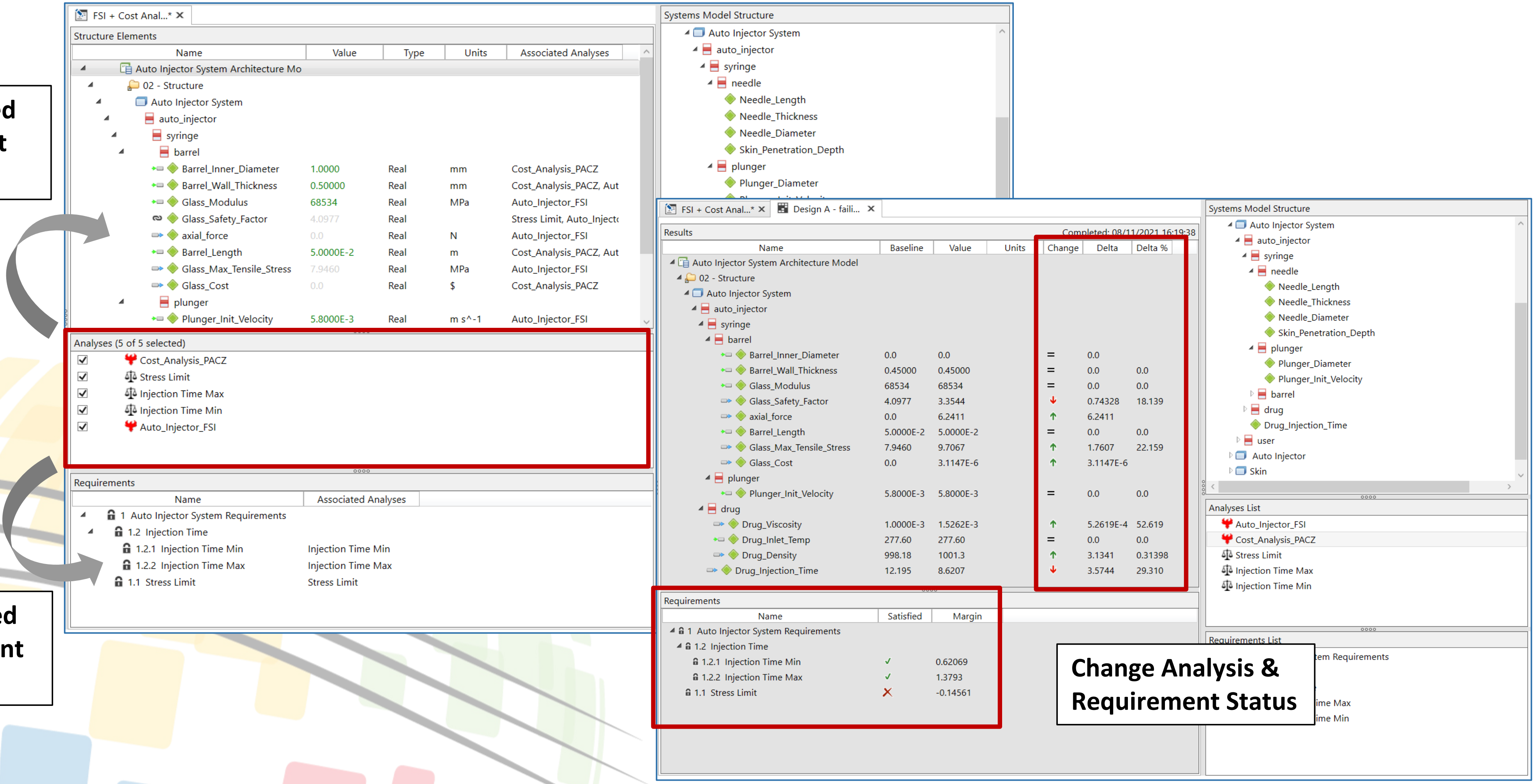
Analysis Variables

Parametric Mapping

Step 3: Connect Simulation Models to the SAM

Analyses mapped with Component Entities

Analyses mapped with Requirement Entities



Change Analysis & Requirement Status

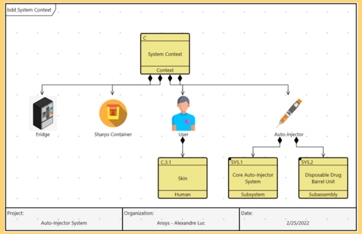
Run Trade Studies in the SAM

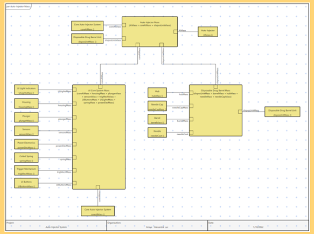
Step 4: Run Trade Studies in the SAM

Conceptual Phase → Preliminary Phase → Detailed Design Phase → Prototype & Test

SAM* Tool

Step 1
System Model Creation





SAM = System Architecture Model*

Bi-directional Connector

Step 3
Connect Simulation Models to the SAM

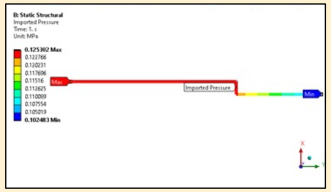
Step 4
Run Trade Studies in the SAM

Cost Analysis

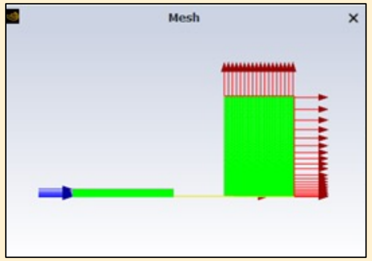
	A	B	C
1	**Barrel Design Properties**		
2	Barrel Inner Diameter	1	mm
3	Barrel Wall Thickness	0.5	mm
4	Barrel Length	0.05	m
5	Glass Volume	1.19381E-07	m^3
6			
7	**Glass Cost**		
8	Glass Volumic Cost	97.05	$/m^3
9	Barrel Glass Cost	1.16E-05	$

Step 2
Simulation Models Automation

1-way FSI Workflow



CFD Analysis



Structural Analysis

Simulation Models

Configure and Run Trade Studies in the SAM

- Design of Experiments set up in the SAM directly
- Specify Design/Response Variables and DoE method
- Results gathered in a Data Explorer Table
- Save Results back to the SAM

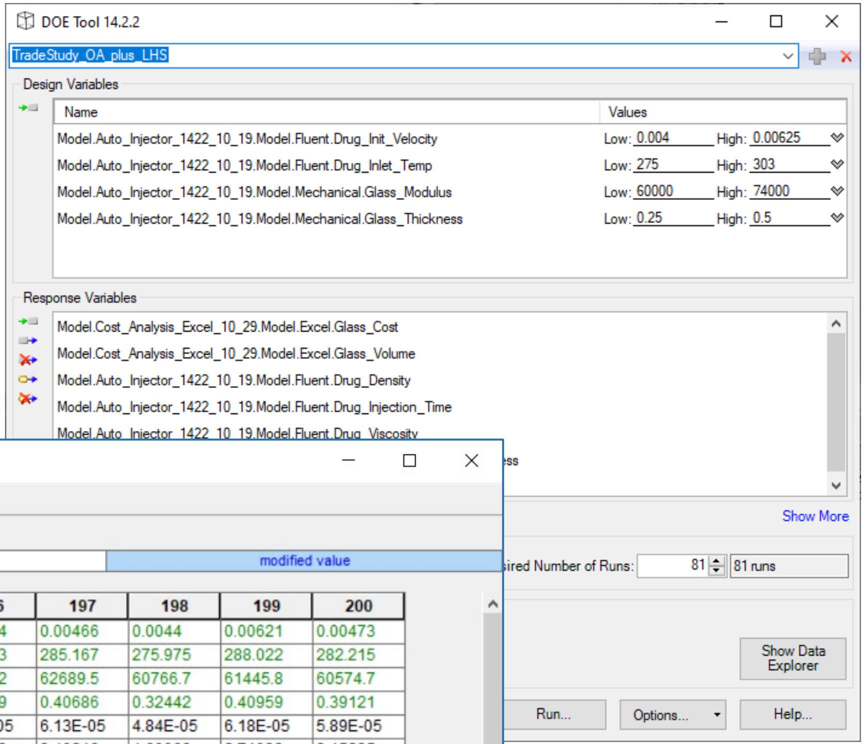


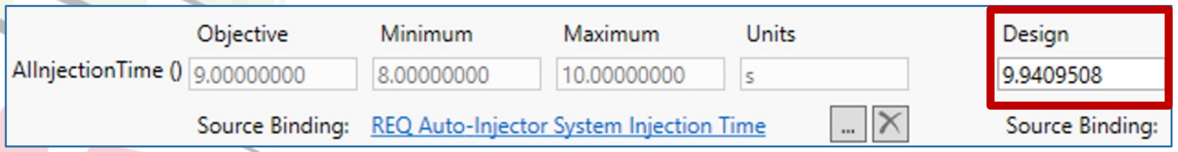
Table - LHC200_11_8.tstudy - Data Explorer

File Chart Help

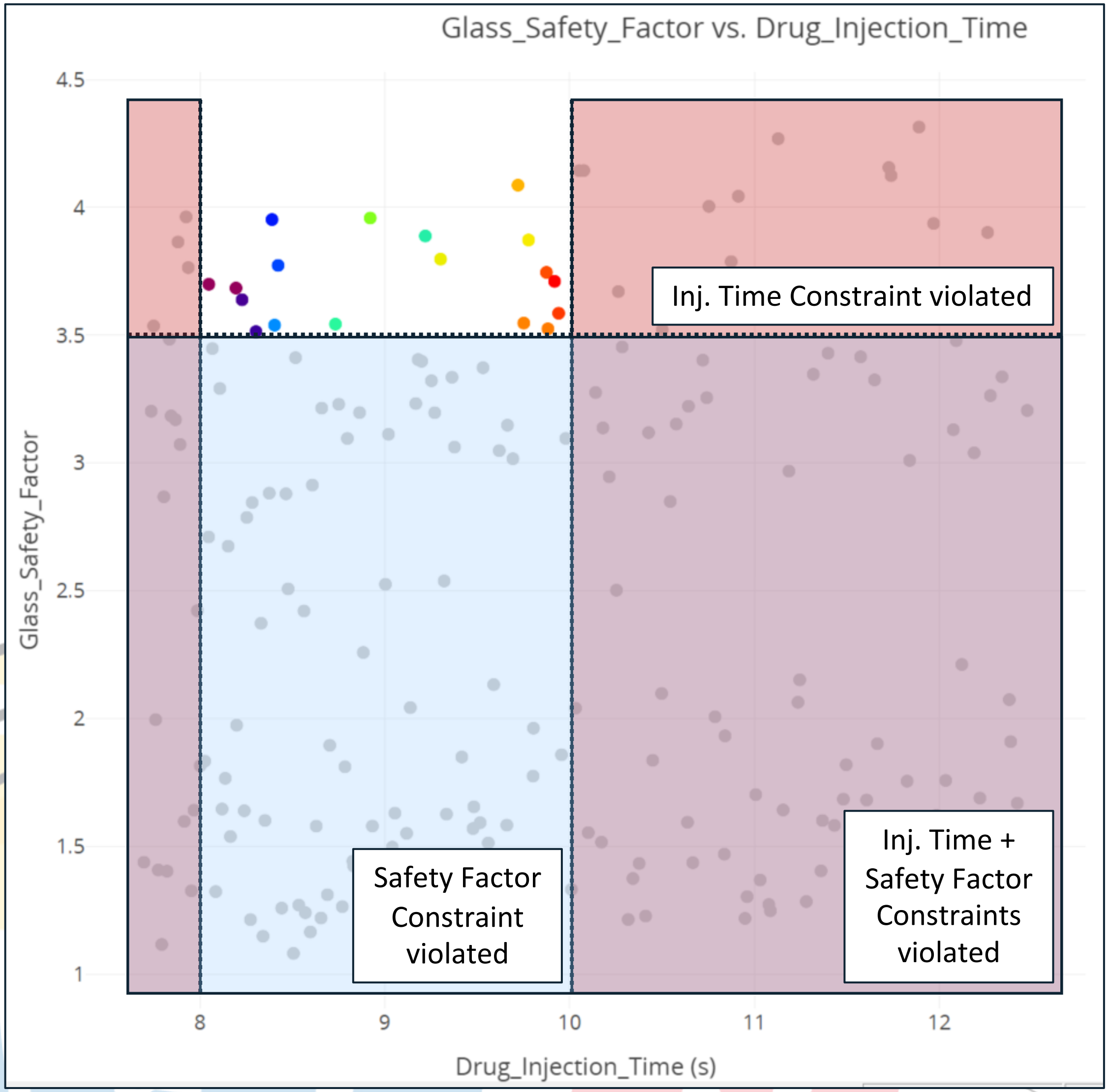
Add View Finder Plug-Ins

Legend: input | valid output | invalid output | modified value

AUTO SCROLL	188	189	190	191	192	193	194	195	196	197	198	199	200
design variable(Model.Auto_Injector_1422_10_19.Model.Fluent.Drug_Injection_Velocity)	0.00435	0.00465	0.00429	0.00402	0.00439	0.00431	0.00496	0.00451	0.00404	0.00466	0.0044	0.00621	0.00473
design variable(Model.Auto_Injector_1422_10_19.Model.Fluent.Drug_Temperature)	283.684	282.966	290.837	291.336	285.482	286.556	276.825	276.982	292.693	285.167	275.975	288.022	282.215
design variable(Model.Auto_Injector_1422_10_19.Model.Mechanical.Glass_Modulus)	60309.1	64836.8	66113.9	64280	71016.6	73374.2	72278.3	71191.8	71445.2	62689.5	60766.7	61445.8	60574.7
design variable(Model.Auto_Injector_1422_10_19.Model.Mechanical.Glass_Thickness)	0.3497	0.43337	0.43453	0.32853	0.44119	0.33143	0.49319	0.2695	0.35499	0.40686	0.32442	0.40959	0.39121
response(Model.Cost_Analysis_Excel_10_29.Model.Excel.Glass_Cost)	5.23E-05	6.55E-05	6.57E-05	4.91E-05	6.68E-05	4.95E-05	7.51E-05	4.00E-05	5.32E-05	6.13E-05	4.84E-05	6.18E-05	5.89E-05
response(Model.Auto_Injector_1422_10_19.Model.Mechanical.Glass_Safety_Factor)	1.8191	3.25549	3.32506	1.66844	3.42963	1.68108	4.14427	1.27204	1.90949	3.40216	1.60069	2.71038	3.15235
response(Model.Auto_Injector_1422_10_19.Model.Mechanical.Glass_Max_Tensile_Stress)	17.8989	10.0016	9.79231	19.5152	9.49373	19.3685	7.85662	25.5967	17.0517	9.57038	20.3412	12.0131	10.3288
response(Model.Auto_Injector_1422_10_19.Model.Mechanical.axial_force)	5.88007	5.95226	5.86686	5.8059	5.8889	5.87055	6.02699	5.91874	5.80861	5.95455	5.89155	6.35256	5.96971
response(Model.Auto_Injector_1422_10_19.Model.Fluent.Drug_Density)	1000.09	1000.24	998.662	998.562	999.733	999.518	1001.47	1001.44	998.291	999.796	1001.64	999.225	1000.39
response(Model.Auto_Injector_1422_10_19.Model.Fluent.Drug_Injection_Time)	11.4968	10.7423	11.6504	12.4226	11.3985	11.6074	10.0767	11.0782	12.3867	10.7209	11.3684	8.04705	10.5773
response(Model.Auto_Injector_1422_10_19.Model.Fluent.Drug_Viscosity)	[illegible]	1.30622E-...	1.06065E-...	1.04751E-...	1.21910E-...	1.18457E-...	1.56247E-...	1.55500E-...	1.01299E-...	1.22953E-...	1.60370E-...	1.13975E-...	1.33404E-...



Get Design Insights and Identify Solution Space



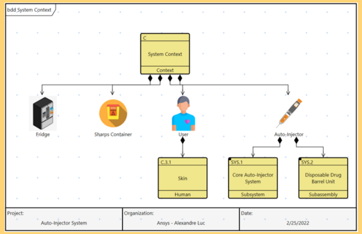
- Highly-constrained Design Space
- Useful to get Design Space Insights from the Conceptual Stage
- Help relaxing/refining requirements and narrowing down the Design Space

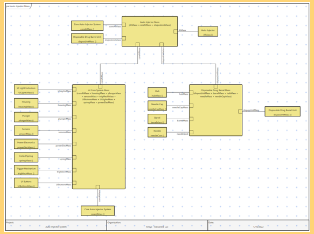
Step 4: Run Trade Studies in the SAM

Conceptual Phase | Preliminary Phase | Detailed Design Phase | Prototype & Test

SAM* Tool

Step 1
System Model Creation





SAM = System Architecture Model*

Bi-directional Connector

Step 3
Connect Simulation Models to the SAM

Step 4
Run Trade Studies in the SAM

Cost Analysis

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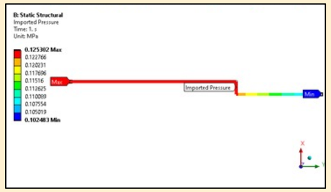
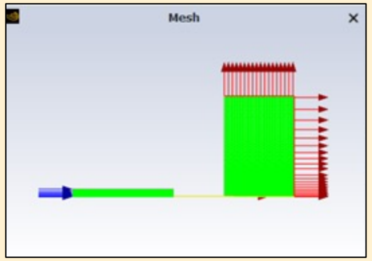
Step 2
Simulation Models Automation

1-way FSI Workflow



CFD Analysis



Structural Analysis

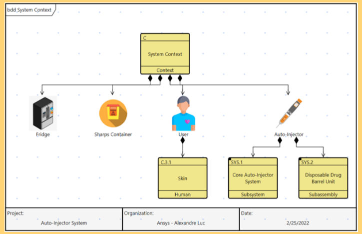
Simulation Models

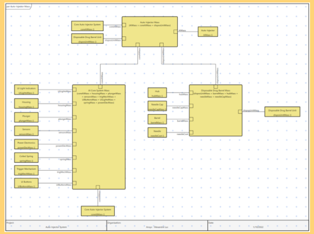
Step 5: Moving into Detailed Design

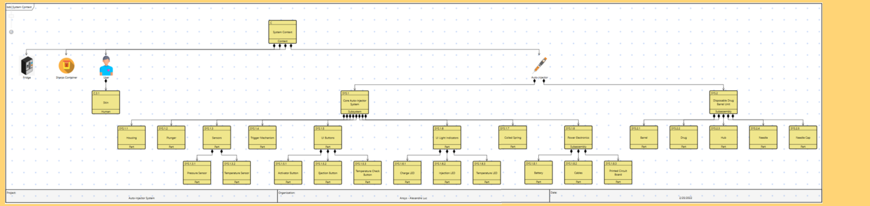
Conceptual Phase | Preliminary Phase | Detailed Design Phase | Prototype & Test

SAM* Tool

Step 1
System Model Creation







SAM = System Architecture Model*

Bi-directional Connector

Step 3
Connect Simulation Models to the SAM

Step 4
Run Trade Studies in the SAM

Step 5 - Moving into Detailed Design

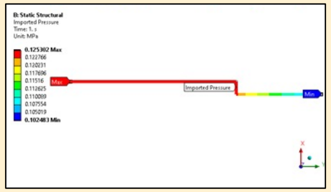
Step 6
System Exploration and Reliability Analyses

Cost Analysis

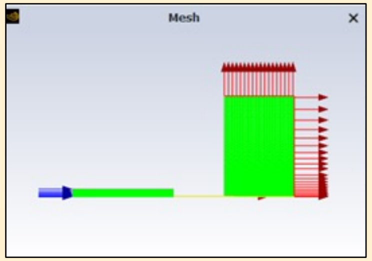
	A	B	C
1	Barrel Design Properties		
2	Barrel Inner Diameter	1	mm
3	Barrel Wall Thickness	0.5	mm
4	Barrel Length	0.05	m
5	Glass Volume	1.19381E-07	m^3
6			
7	Glass Cost		
8	Glass Volumic Cost	97.05	$/m^3
9	Barrel Glass Cost	1.16E-05	$

Step 2
Simulation Models Automation

1-way FSI Workflow

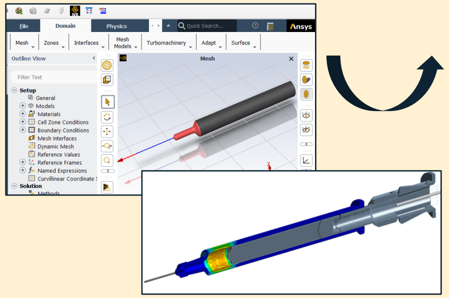


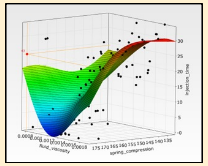
CFD Analysis



Structural Analysis

2-way FSI Workflow





Metamodel Generation

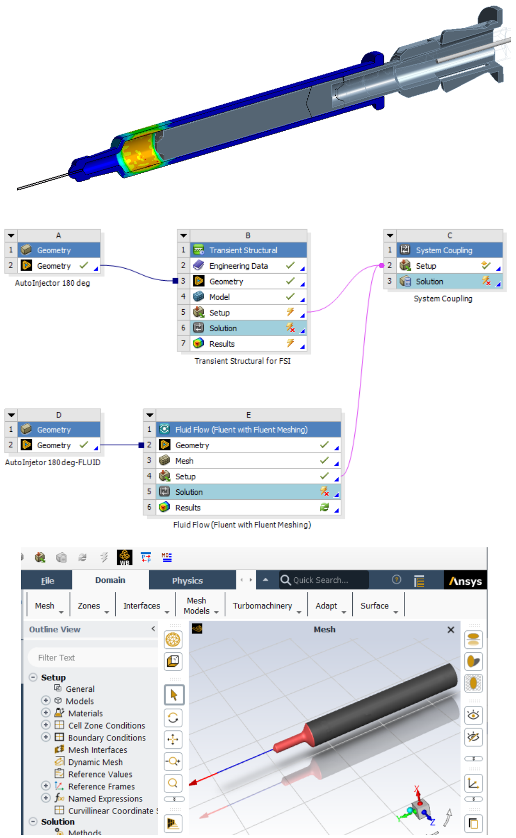
Component Catalogs

Additional detailed analyses

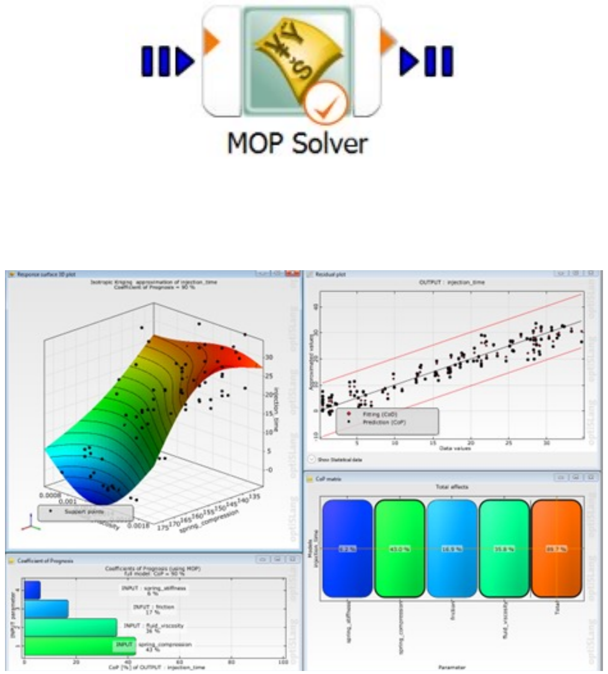
Simulation Models

Surrogate Model Generation

2-way FSI Model

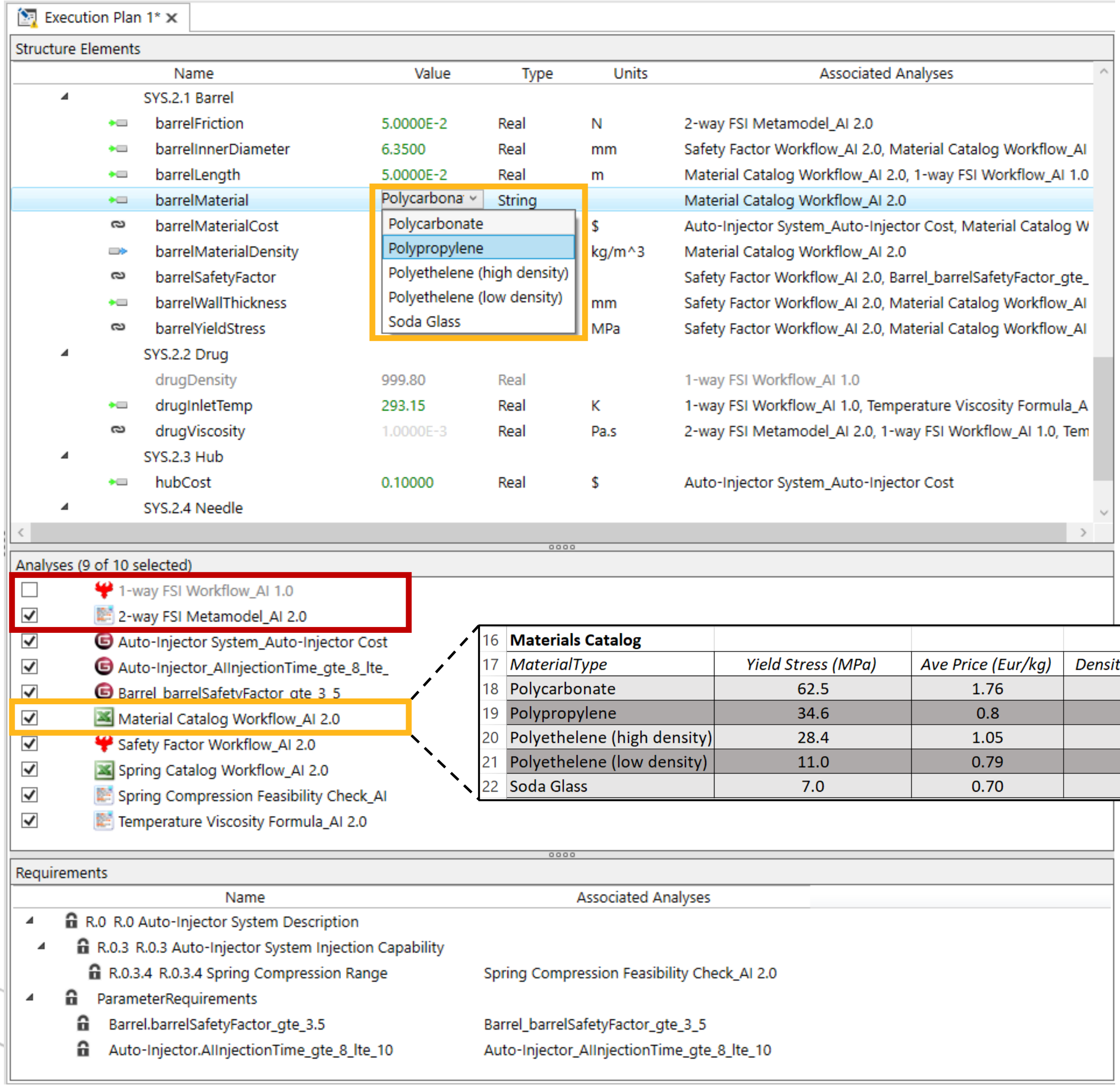


Surrogate Model



Detailed Analyses Integration in the SAM

- Low-Fidelity Analyses replaced by higher fidelity models
- Additional Simulation Models connected to the SAM
- Further Design Exploration Studies

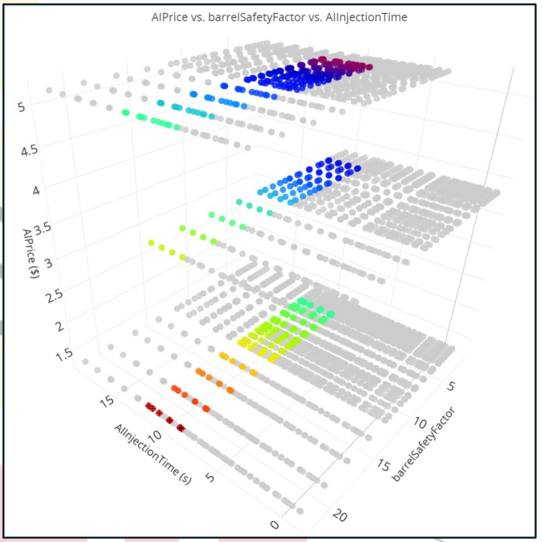


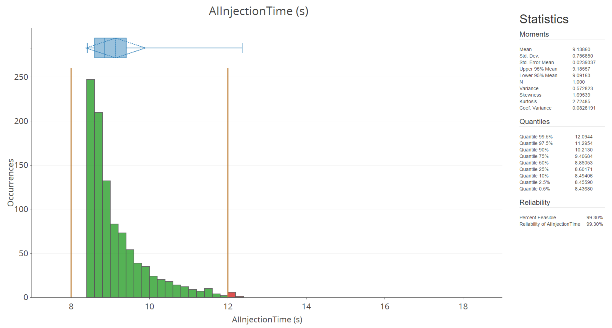
16	**Materials Catalog**			
17	*MaterialType*	*Yield Stress (MPa)*	*Ave Price (Eur/kg)*	*Density (kg/m^3)*
18	Polycarbonate	62.5	1.76	1200
19	Polypropylene	34.6	0.8	931
20	Polyethelene (high density)	28.4	1.05	954
21	Polyethelene (low density)	11.0	0.79	921
22	Soda Glass	7.0	0.70	2520

Step 6: Trade Study Results and Reliability Check

Spring Type	Spring Compression (mm)	Barrel Wall Thickness (mm)	Barrel Material Type	Barrel Friction (N)	Barrel Safety Factor	AI Price ($)	AI Injection Time (s)
PC965-12065	132	0.8	Polycarbonate	0.0362	21.78	1.29	11.96
PC1143-25400	132	0.8	Polycarbonate	0.029	21.78	1.29	11.55
PC965-12065	132	0.8	Polycarbonate	0.0344	21.78	1.29	10.92
PC965-12065	132	0.8	Polycarbonate	0.0326	21.78	1.29	9.89
PC965-12065	137.6	0.8	Polycarbonate	0.038	21.78	1.29	9.87
PC965-12065	132	0.8	Polycarbonate	0.0308	21.78	1.29	8.91
PC965-12065	137.6	0.8	Polycarbonate	0.0362	21.78	1.29	8.77

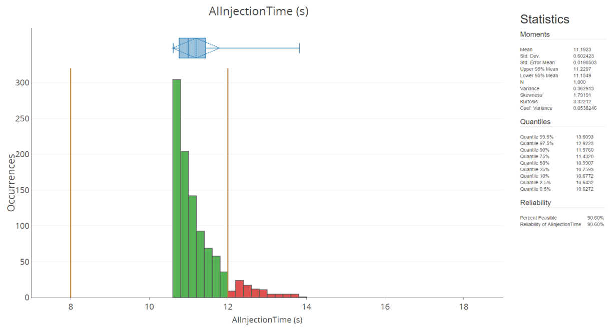
- Trade studies identified a set of potential optimal design configurations
- Monte Carlo analysis was then used to check the reliability of select design configurations against drug temperature variation





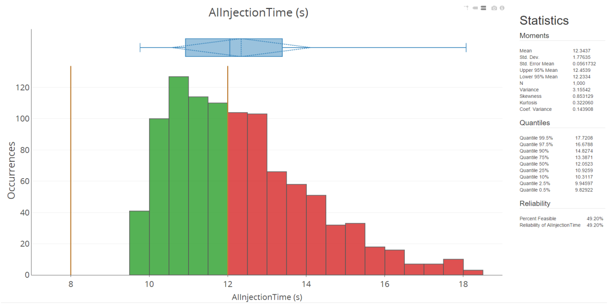
Optimal Design Candidate 1

Reliab: 99.30%



Optimal Design Candidate 2

Reliab: 90.60%



Optimal Design Candidate 3

Reliab: 49.20%

Benefits & Challenges

Keys Benefits

- Tooling and methodology to **support collaboration** between Systems Engineers and SMEs
- **Gain** in productivity & **Reduce risks**
- **More time** spent on Trades from early Conceptual Stage
- Drive **innovation**

Challenges

- **Accessibility** to analytical models from experts
- **Complexity** going into detailed design: need to reduce models.
  - Where to stop the integration?
- **Process change** required for companies having SMEs and Systems Engineers working in silos.
- Architectural Trade-Off: Implies having a 150% model.
  - How to handle **variation points** in simulations?
  - Requires creation of customized workflows for now.
- In this study, integration with Physical Architecture only, not with the **Functional Architecture**.
  - Potential topic to address next.

Take-aways

Keys - Parameterization and Constraint Definition

The key to successful integration of Systems Models and Multi-Fidelity Analytical Models is proper parameterization and constraint definition.

Unlocking the promise of MBSE

Bridge the gap between Systems Engineering and Domain / Disciplinary Engineering by connecting System Models to Simulation and Analytical Models.

Verifying Requirements and Trading off Cost, Performance & Risk

Leverage Simulation to perform Requirements Verification, and to trade between several architectures / design configurations, from the early stages of the Development Process.

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