Universität Rostock Traditio et Innovatio

Elaine electrically active implants SFB 1270

Towards in-situ knowledge acquisition for research data provenance from electronic lab notebooks

November 2nd, 2020

Max Schröder[1,2], Susanne Staehlke[3], Barbara Nebe[3,4], and Frank Krüger[1]

[1] Institute of Communications Engineering, University of Rostock

[2] University Library, University of Rostock

[3] Department of Cell Biology, University Medical Center Rostock

[4] Department Life, Light & Matter, University of Rostock

Motivation I

Elaine
electrically active implants
SFB 1270

How are these research objects created and how are they used?

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
1	Ref PPAAm, n3, 1. Zeitserie von 240 Zyklen, beim 90. Zyklus ATP Zugabe (10 µl 100mM)														
2															
3	Mean Intensity von definierten Bereichen														
4	Sekunden	Cell1	Cell2	Cell3	Cell4	Cell5	Cell6	Cell7	Cell8	Cell9	Cell10	MW	SD	SEM	
5	0	49,02849	66,292086	93,65812	69,991279	104,41667	151,89511	63,987252	78,186047	39,308131	44,534226	76,129741	33,702127	10,657548	
6	2	48,478632	66,130935	89,517094	68,122093	101,24569	147,91092	63,453258	74,790698	39,413695	43,090774	74,215379	32,415243	10,2506	
7	4	47,39886	64,332374	87,571225	66,563953	100,3204	143,43103	62,002833	73,440407	38,697575	42,258929	72,601759	31,503862	9,9623959	
8	6	46,619658	63,309353	85,22792	66,321221	98,093391	140,56322	61,240793	71,731105	38,43224	42,316964	71,385586	30,602524	9,6773679	

A data.frame: 6 × 32

Time	R1_1	R2_1	R3_1	R4_1	R5_1	R6_1	R7_1
<dbl>	<dbl>	<dbl>	<dbl>	<dbl>	<dbl>	<dbl>	<dbl>
0.00000000	46.72451	41.20412	61.08680	49.62056	46.63363	56.50184	53.88043
0.03333333	47.42576	41.16292	59.47378	49.35888	46.36106	55.51838	52.87681
0.06668333	47.51699	40.81461	58.82821	48.74019	47.51150	55.99632	51.09420
0.10005000	46.64937	41.20599	57.90958	48.95701	47.66018	55.79963	50.66304
0.13336667	46.97317	41.40075	56.84448	48.80000	46.85133	54.34559	50.37862
0.16673333	46.06977	40.94944	56.06510	49.34579	46.72389	55.16360	49.93297

	Ti	Ti+PPAAm	Ti+Col	IBIDI
CaSignal				
Basal Level	38.8±0.3	52.0±0.5	44.5±0.4	17.2±0.2
After ATP	49.9±0.6	89.1±1.0	55.2±0.6	23.6±0.3

Source: M. Schröder, S. Staehlke, J. B. Nebe, and F. Krüger. Sfb-elaine/biomedical-jupyter-examples: v1.0, 2019. DOI: 10.5281/zenodo.3548652

Motivation II

Elaine
electrically active implants
SFB 1270

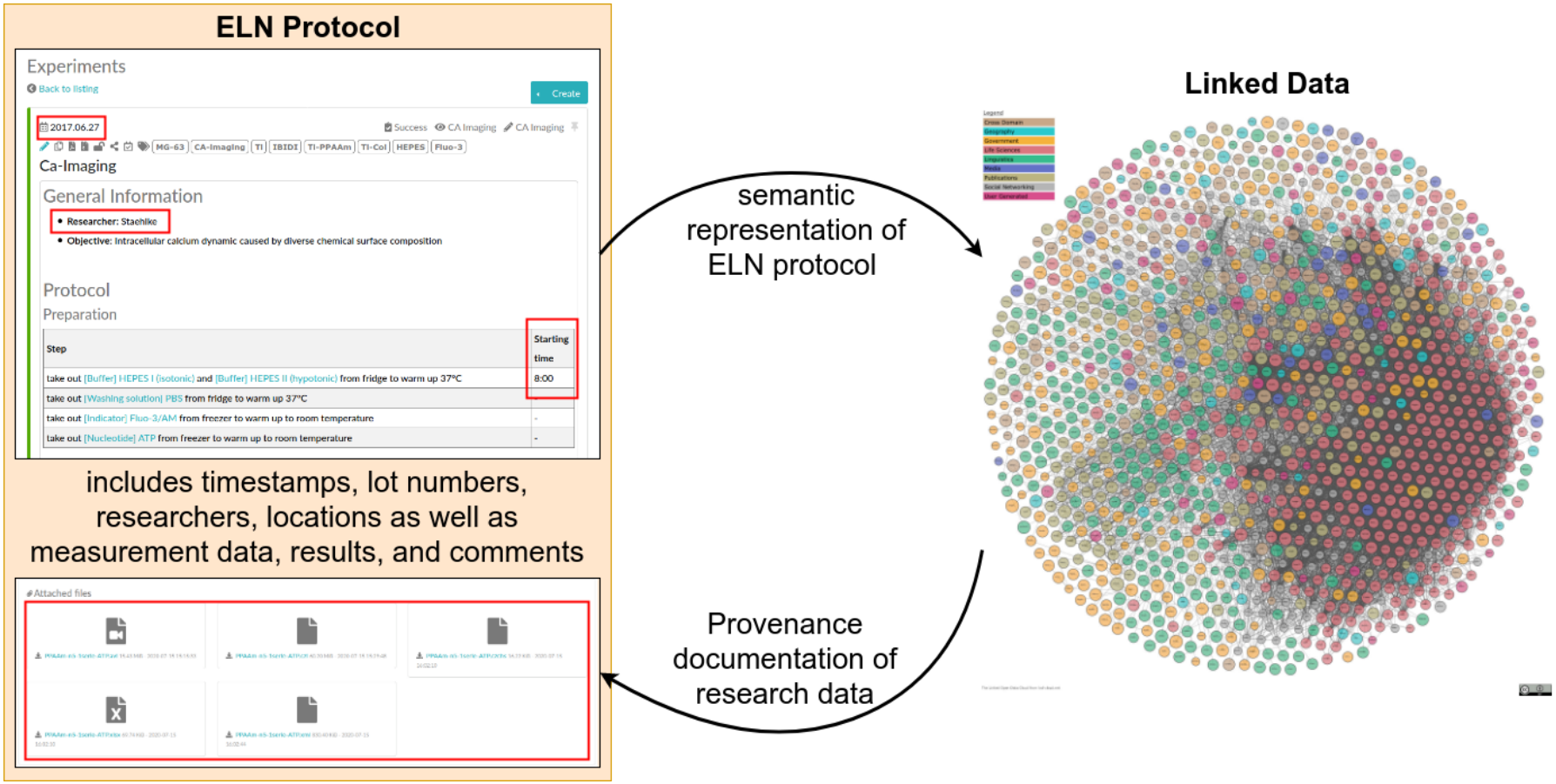
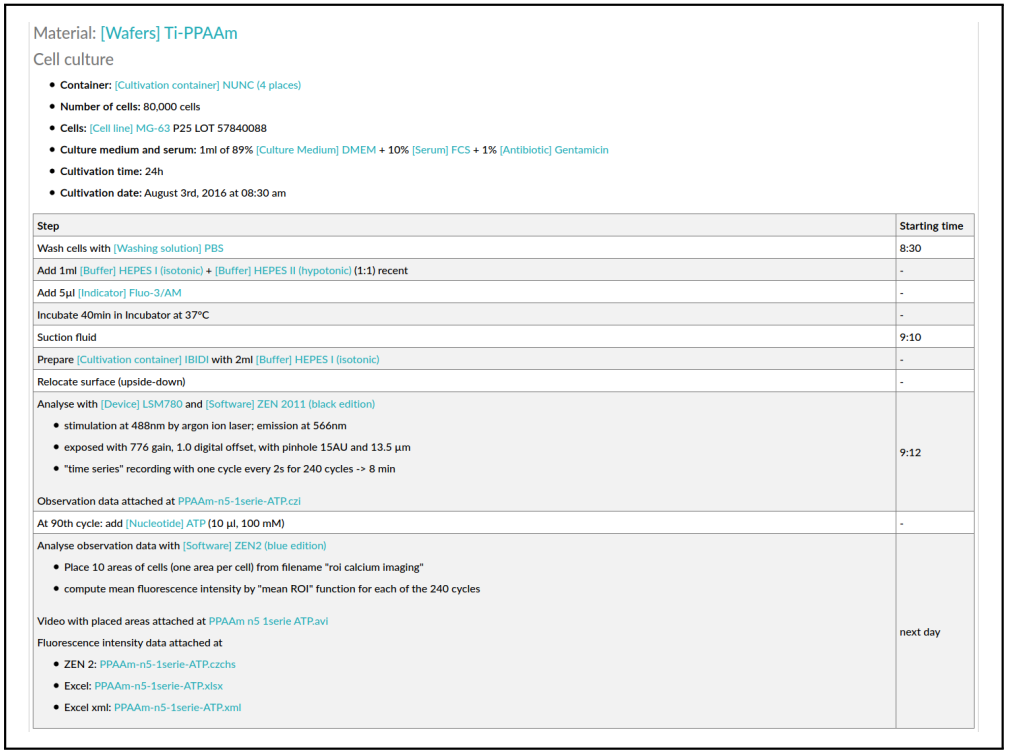


Image source: https://lod-cloud.net (right)

Electronic Lab Notebooks (ELNs)

Elaine
electrically active implants
SFB 1270

- ELNs are software tools for textual documentation of wet-lab experiments
- In contrast to analog lab notebooks: sharing and searching
- Inventory database allows re-use of defined research objects
- File attachments for data

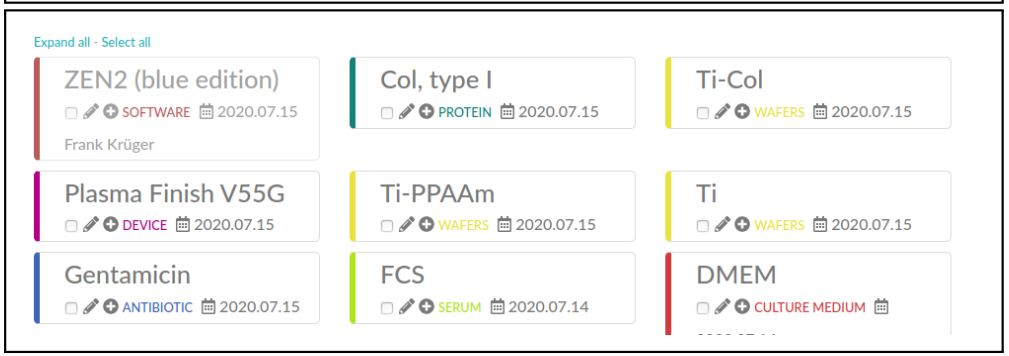


Material: [Wafers] Ti-PPAAm

Cell culture

- **Container:** [Cultivation container] NUNC (4 places)
- **Number of cells:** 80,000 cells
- **Cells:** [Cell line] MG-63 P25 LOT 57840088
- **Culture medium and serum:** 1ml of 89% [Culture Medium] DMEM + 10% [Serum] FCS + 1% [Antibiotic] Gentamicin
- **Cultivation time:** 24h
- **Cultivation date:** August 3rd, 2016 at 08:30 am

Step	Starting time
Wash cells with [Washing solution] PBS	8:30
Add 1ml [Buffer] HEPES I (isotonic) + [Buffer] HEPES II (hypotonic) (1:1) recent	-
Add 5µl [Indicator] Fluo-3/AM	-
Incubate 40min in Incubator at 37°C	-
Suction fluid	9:10
Prepare [Cultivation container] IBIDI with 2ml [Buffer] HEPES I (isotonic)	-
Relocate surface (upside-down)	-
Analyse with [Device] LSM780 and [Software] ZEN 2011 (black edition) • stimulation at 488nm by argon ion laser; emission at 566nm • exposed with 776 gain, 1.0 digital offset, with pinhole 15AU and 13.5 µm • "time series" recording with one cycle every 2s for 240 cycles -> 8 min Observation data attached at PPAAm-n5-1serie-ATP.czi	9:12
At 90th cycle: add [Nucleotide] ATP (10 µl, 100 mM)	-
Analyse observation data with [Software] ZEN2 (blue edition) • Place 10 areas of cells (one area per cell) from filename "roi calcium imaging" • compute mean fluorescence intensity by "mean ROI" function for each of the 240 cycles Video with placed areas attached at PPAAm n5 1serie ATP.avi Fluorescence intensity data attached at • ZEN 2: PPAAm-n5-1serie-ATP.czchs • Excel: PPAAm-n5-1serie-ATP.xlsx • Excel xml: PPAAm-n5-1serie-ATP.xml	next day



Expand all - Select all

ZEN2 (blue edition) SOFTWARE 2020.07.15 Frank Krüger

Col, type I PROTEIN 2020.07.15

Ti-Col WAFERS 2020.07.15

Plasma Finish V55G DEVICE 2020.07.15

Ti-PPAAm WAFERS 2020.07.15

Ti WAFERS 2020.07.15

Gentamicin ANTIBIOTIC 2020.07.15

FCS SERUM 2020.07.14

DMEM CULTURE MEDIUM

ELN Protocols vs. Experimental Protocols

Elaine
electrically active implants
SFB 1270

Experimental Protocols: (published) instructions to conduct experimental investigations, e. g. Standard Operating Procedures

Reagents	• *n*-octylglucoside (Merck Millipore, Billerica, MA, #494459) • Cardiolipin (Sigma-Aldrich, St. Louis, MO, #C0563) • Diethylenetriaminepentaacetic acid (DETAPAC) (Sigma-Aldrich, #D1133) • Chloroform ($CHCl_3$) • Methanol (MeOH) • $CHCl_3$-MeOH mixture (C/M, volume/volume) • Distilled water (DW) • TLC plate (Silicagel 60, 20 × 20 cm, Merck Millipore)
Instruments	• Speed Vac concentrator (Thermo Fisher Scientific Inc., Waltham, MA) • Imaging analyzer (FLA 5000, Fujifilm, Tokyo, Japan) • Dounce homogenizer
	1. Preparation of the Recombinant Ceramide Kinase 1) Transfect the HEK293 cells with a human CerK expression vector. Comment 0 2) Wash the transfected cells with cold phosphate-buffered saline (PBS) after 1 day. Comment 0

Protocol source: https://jcggdb.jp/GlycoPOD/protocolShow.action?nodeId=t27

ELN Protocols: instances of experimental protocols with timestamps, lot numbers, measurement data, and others

Use case: Ca-imaging

Elaine
electrically active implants
SFB 1270

Detection of intracellular calcium ions (Ca^{2+}) dynamics by Ca-imaging

Original study published by Staehlke et al.[1] in their article "*Enhanced calcium ion mobilization in osteoblasts on amino group containing plasma polymer nanolayer*"

- Intracellular Ca^{2+} are responsible as a second messenger system for signal transmission, which ultimately control cell functions
- The role of intracellular Ca^{2+} dynamic on different chemical surface conditions is investigated:
  1. bare titanium (Ti),
  2. Ti with plasma polymerized allylamine (Ti+PPAAm) which was provided by Leibniz Institute for Plasma Science and Technology (INP) Greifswald
  3. Ti with a collagen type-I-layer (Ti+COL)
  4. tissue culture plastic (IBIDI)

[1] Staehlke, S., Rebl, H., Finke, B., Mueller, P., Gruening, M., Nebe, J.B.: Enhanced calcium ion mobilization in osteoblasts on amino group containing plasma polymer nanolayer. Cell & Bioscience 8(1) (Mar 2018). https://doi.org/10.1186/s13578-018-0220-8

Semantic Modelling: Modelling Process

Elaine
electrically active implants
SFB 1270

Modelling Process:

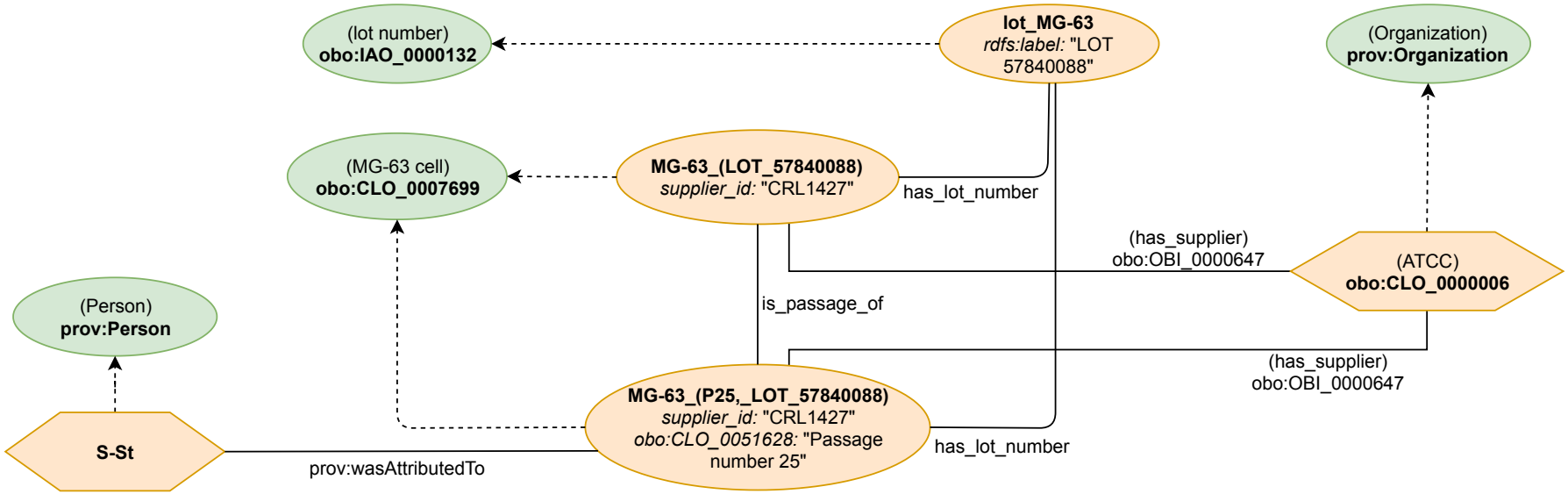
1. Search BioPortal and Ontobee for relevant ontologies
2. Select set of ontologies (prefer BFO compatible ones)
3. Add identifier of ontology classes into ELN protocol/database
4. Create semantic model: instances of classes represent particular entities and activities
5. Add references to other knowledge graphs (e. g. Wikidata, DBpedia)

Semantic Model available at Github:
https://github.com/m6121/Semantic-Modelling-CA-Imaging

Semantic Modelling: Inventory Items

Elaine
electrically active implants
SFB 1270

Modelling of MG-63 cells with LOT number 57840088 supplied from ATCC

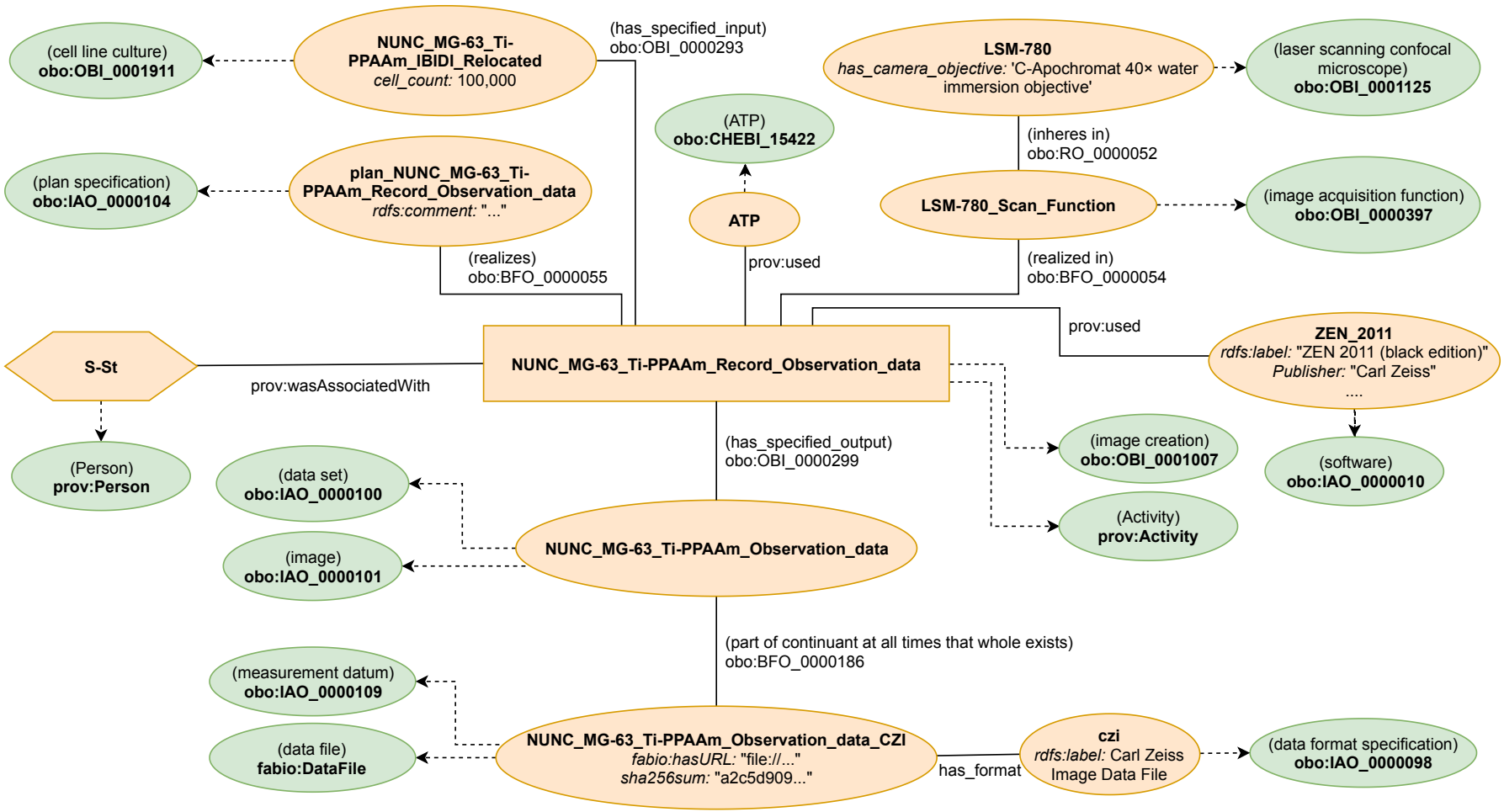


- Biological and chemical resources such as FCS, DMEM, or PBS are modelled employing this schema
- Similarly, devices and software are modeled by creating instances of existing classes

Semantic Modelling: Activities

Elaine
electrically active implants
SFB 1270

Modelling of the data recording employing the LSM 780 microscope



Summary

Elaine
electrically active implants
SFB 1270

- **ELN protocols** are more than **descriptions of experimental procedures**. In contrast to published experimental protocols, they also **include timestamps, measurement data, results and more**.
- **ELN protocols** can be used for the **provenance** documentation of **research data**.
- **Semantic models** can be created employing **well-engineered ontologies** referenced in **databases**.

Thanks for your attention.
Questions?

OpenScience.ELAINE@uni-rostock.de

www.elaine.uni-rostock.de

github.com/SFB-ELAINE

twitter.com/SFB_ELAINE

Funded by the Deutsche Forschungsgemeinschaft
(DFG, German Research Foundation):
SFB 1270/1 - 299150580.

Gefördert durch
DFG Deutsche Forschungsgemeinschaft