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Dipartimento di Ingegneria e Scienza dell'Informazione

– KnowDive Group –

The human microbiome and person-to-person interactions

Document Data:	Reference Persons:
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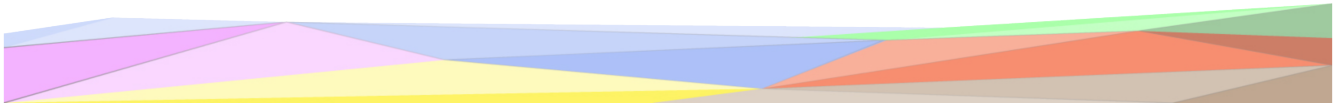

Index:

Revision History:

Revision	Date	Author	Description of Changes
0.1	27.10.2024	Roan	Document created
0.2	29.10.2024	All	Purpose Definition, Informal, DoI, Scenarios, Personas, CQ
0.3	02.11.2024	Andrea, Roan	Concepts Identification, ER model definition
0.4	14.11.2024	All	Dataset cleaning, filtering
0.5	16.11.2024	Roan, Vlad	Information gathering
0.6	24.11.2024	All	Language Definition

1 Introduction

In the age of big data, the ability to organize, manage, and interpret biological information has transformed how we understand complex systems like the human microbiome. This project aims to systematically organize and interlink data on the transmission of human microbiome species, social relationships, and environmental factors within a Knowledge Graph (KG). By capturing these intricate relationships, this KG will facilitate detailed queries on how microbes are shared across different populations, family structures, and social interactions, offering insights into population-specific microbiome dynamics and their potential health implications.

The project will utilize the iTelos methodology [1], a structured framework that streamlines the Knowledge Graph Engineering (KGE) process by emphasizing reusability and documentation. This approach enables the reuse of project resources for future applications, minimizing the effort required to develop new KGs for similar purposes. Following iTelos principles, the project will focus on creating reusable, well-documented resources that capture valuable data on microbiome transmission across various social and environmental contexts.

This project aims to serve as a valuable resource for researchers interested in microbiome transmission, potentially supporting further applications in public health, clinical research, and specialized education.

2 Purpose Definition

2.1 Informal Purpose

The purpose of this project is the create a system that enables users to explore the transmission dynamics of the human microbiome together with various social interactions and environmental elements that can affect it. It is done by also supporting comparative analysis (ex. different bacterial populations present in different samples) and exhibiting key transmission patterns, highlighting the influence of factors such as cohabitation and geographic location on microbial diversity and bacterial phenotypes. The resulting Knowledge Graph will be used to embed both the information about microbiome species shared between individuals, the phenotypic information of the transmitted microbial species, and the information about the social relationships between the considered individuals.

2.2 Domain of Interest

The Domain of Interest encompasses the composition of gut bacterial metagenomes in individuals and their transmission rates within different populations worldwide.

2.2.1 Space

The study spans a global geography, including diverse regions across Africa (e.g., Ghana, Tanzania, Ethiopia), the Americas (e.g., USA, Argentina, Colombia), Europe (e.g., Germany, Italy, Spain, United Kingdom, Sweden, Finland, Luxembourg), and Asia-Pacific (e.g., China, Fiji). This broad sampling from Western and non-Western countries comprehensively represents varied genetic and environmental backgrounds.

2.2.2 Time

The raw metagenomics datasets, which were used as the basis of this project, were constructed from **2014** to **2021**.

2.3 Scenarios

We identify the following possible usage scenarios for our project:

1. A microbiologist wants to study the differences in the human microbiome between different geographical ethnic groups to assess population-specific dynamics. To do so, they are looking for a way to retrieve population-specific metagenomic data that specifies, for each ethnicity, the main bacterial strains found.
2. A clinician, given an instance of a bacterial infection, is taking care of a patient presenting severe gastric problems, the patient is known to have a twin living abroad. The clinician wants to see if the reason for the health problems is associated more with the microbial environment or geographical context.
3. A university student attending a microbiology course has to make a presentation about what are the main ways in which bacteria are transmitted between individuals but is unsure of where to access the information they need straightforwardly.
4. A Dental Hygienist professor wants to teach their students the differences in transmission rates between different bacterial strains in the oral cavity. To do so, they need a one-to-one link between bacterial strains and how often they are transmitted.
5. A researcher studies social interactions and wants to measure the level of interactions by microbial transmission between individuals. He needs access to existing knowledge in a structured form about microbial transmission.

Although we identified scenarios that space as much variability as we deemed necessary, our starting focus is directed especially towards the first two scenarios (microbiologist and clinician), with the possibility of expanding in a later phase our Knowledge Graph by letting it tackle more information.

2.4 Personas

Based on our usage scenarios, we can distinguish between two groups of Personas:

- **Researchers & Students**:
    1. Francesca - 28 - (Scenario 1) - A microbiologist doing PhD at the University of Toronto. Her scientific interest is the research of clinical significance of microbiome population in the human gut. Currently, she is researching the relationship between microbial composition in the gut and phenotypic features, therefore she wants to explore the available data on microbial transmission to identify the crucial part of the microbiome that is strongly related to phenotype and transmitted.
    2. Herald - 67 - (Scenario 5) - He is a Professor of Social sciences at the University of Oxford. He is interested in research that captures social interaction with microbiome assays. He wants to revise the existing data on relationships between transition and social interactions.
    3. Franco - 20 - (Scenario 3) - He is a university student following the course of Microbial Genomics, taught by Nicola Segata at the University of Trento, in the CIBIO department. After completing the theoretical section of the course, he was assigned to a group work to present a topic of interest; the workgroup settled on the topic of microbial transmission.
- **Healthcare professionals**:
    4. Karmen - 32 - (Scenario 2) - an infectiologist at Maribor clinic. He is working on microbial infections and for better treatment prescription he needs to know the possible origin of a pathogen that caused the disease.
    5. Juana - 46 - (Scenario 4) - She is a Dental Hygienist working in collaboration with the Sociedad Española de Microbiologìa. She was asked to give some lessons regarding the link between the microbial environment and dental healthcare. She wanted to highlight the effect of the transmission of different strains in the oral environment.

2.5 Competency Questions

Given the scenarios and personas, we created a list of CQs that would align to the previously described heterogeneity, while also avoiding unnecessary intricacy or complexification of the following ER model. Competency Questions span different scenarios and sometimes share some similarities when involved in different fields, but are heterogeneous in same-scenario situations.

1. **Francesca, Microbiologist, PhD student**
    1.1. I'm studying the gut microbiome. Can I get a list of the most commonly transmitted bacterial species within family households?
    1.2. What are the transmission rates of *S. parasanguinis* between Westernized and non-Westernized populations?
    1.3. Which bacterial strains show a significant correlation with Gram staining?

1.4. Does cohabitation affect the presence of *Prevotella intermedia* in the gut microbiome?

2. **Herald, Social Sciences Professor**

   2.1. How do the transmission rates differ between siblings and parents of gut bacteria?

   2.2. Which transmission types are most associated with Westernized society?

   2.3. Which is the most frequent microbial transmission within a family?

   2.4. How does the cohabitants number influence the diversity of the gut microbiome?

3. **Franco, university student of Microbial Genomics**

   3.1. I need to learn about microbial transmission. What are the primary mechanisms of bacterial transmission between individuals?

   3.2. Which bacteria are more likely to be found in saliva compared to stool samples?

   3.3. Which parental relationships mostly influence bacterial transmission in families?

   3.4. Can I find examples of anaerobic bacterial strains commonly transmitted in Italian families?

4. **Karmen, Infectiologist**

   4.1. My patient has a twin living abroad in Germany. Which of the bacterial infections is related to the environmental difference between Slovenia and Germany?

   4.2. How does the gut microbiome diversity differ between patients with *S. aureus* in Slovenia?

   4.3. If the patient comes to Italy which spore-forming strains should I look preferably?

5. **Juana, Dental Hygienist**

   5.1. I want to teach about bacterial transmission. Which bacterial strains exhibit the highest transmission rates in the oral mouth in Westernized and non-Westernized populations?

   5.2. Can I get data on how bacterial transmission rates differ between infants and older children?

   5.3. How does the transmission mode between individuals affect the abundance of *Treponema Denticola* in the oral cavity?

   5.4. Does the presence of other people in the household significantly affect the Dental microbiome?

2.6 Concepts Identification

CQ	Common entities	Core entities	Contextual entities
1.1	Family	Sample, SGB, Taxonomy	Transmission
1.2	Country	Dataset, Sample, SGB, Taxonomy	Transmission
1.3		Sample, SGB, Taxonomy	Phenotype
1.4	Country, Person	Dataset, Sample, SGB, Taxonomy	Transmission
2.1	Person, Sibling	SGB, Taxonomy	Transmission
2.2	Country	Dataset	Transmission
2.3	Person		Transmission
2.4	Person	Dataset, SGB	Transmission
3.1			Transmission
3.2		Sample, SGB, Taxonomy	Transmission
3.3	Person, Sibling	Sample, SGB	Transmission
3.4	Country	Dataset, Sampe, SGB, Taxonomy	Phenotype
4.1	Country, Sibling	Dataset, Taxonomy	Twin
4.2	Country	Dataset, Sample, SGB, Taxonomy	
4.3	Country	SGB, Taxonomy	Phenotype
5.1	Country	Dataset, Sample, SGB, Taxonomy	Transmission
5.2	Person	Dataset, Sample, SGB	Transmission
5.3		Dataset, Sample, SGB, Taxonomy	Transmission
5.4	Person	Dataset, Sample, SGB, Taxonomy	Transmission

2.7 ER model definition

Based on the defined Competency Questions, we created the following Entity-Relationship diagram. We took into consideration all scenarios and personas, prioritizing the microbiology and clinical areas of interest. In order to do so, we extracted from Valles-Colomer, et. al (2023) [2] the files containing the necessary data for the ER-diagram development, found in the Supplementary Tables of the article. We carefully inspected each file, while also noting down information, variables, and features that could be of interest. During the ER-diagram creation, we kept in mind the possible ways to diversify and group those features/ETypes/properties aligning them with the formalized purpose.

We define the following Entity Types and distinguish them between Common (very general ETypes that could be possibly used in other Domains of Interest and that are not necessarily bound to the purpose), Core (specific ETypes that are very relevant to the purpose and constitute

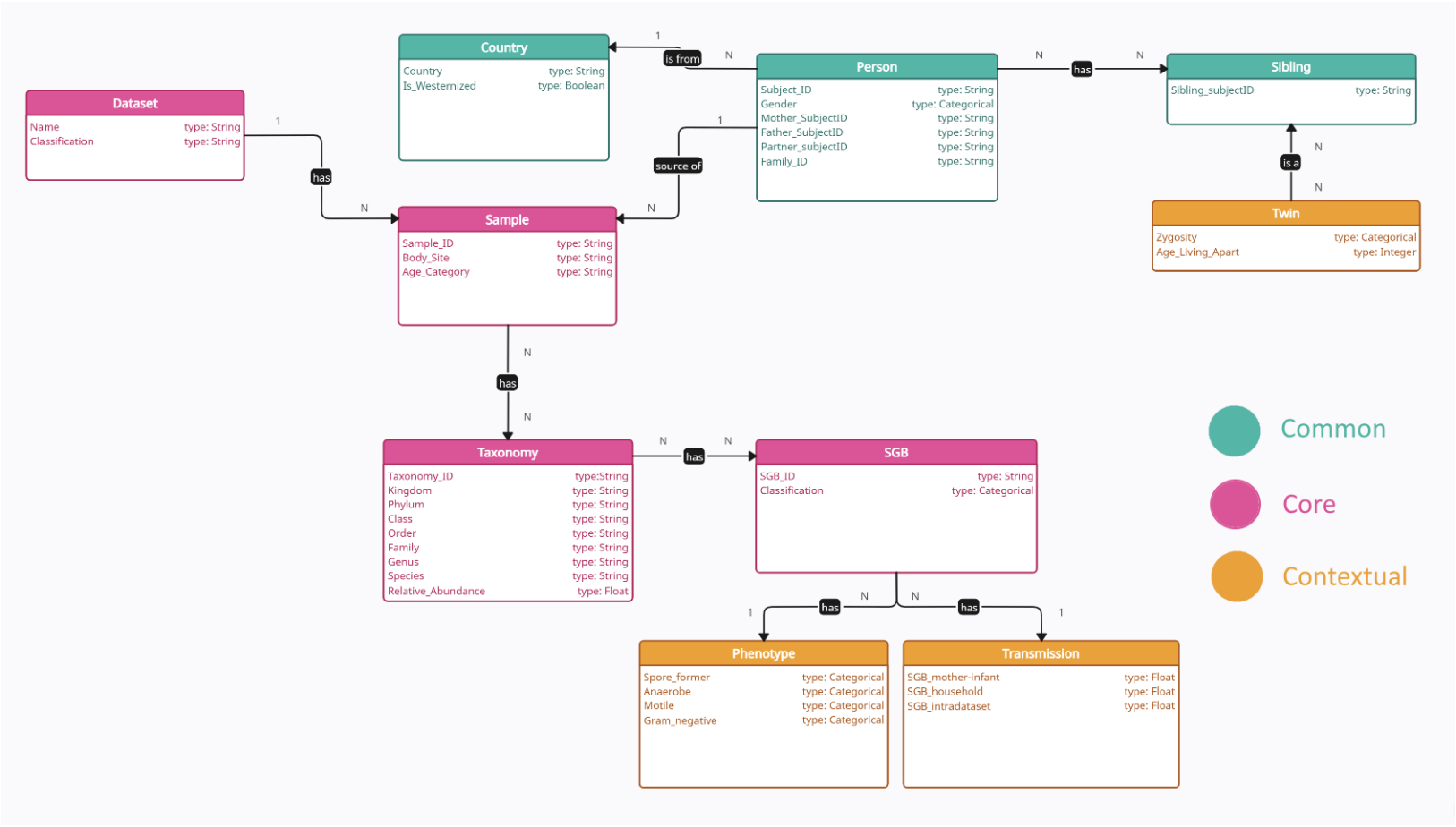

Figure 1: ER Diagram; in green the common ETypes, in red the core ones and in yellow the contextual ones.

its skeleton) and Contextual (even more specific ETypes, extremely related to the purpose that add value to it and generally would not be found in other applications used this way):

- **Common ETypes**:
  - Country: a very general way to represent the ”space” location of someone or something: in our case the origin of our samples/datasets. This will be useful combined with other ETypes to assess differences (for example, bacterial transmission rates) based on the origin of our dataset.
  - Person: a general EType to represent someone, together with its gender and parental relationships. This is needed as the same individual can produce multiple Samples; furthermore, it is useful in order to link individuals to one another, specifying possible transmission rate differences when comparing parents and children.
  - Sibling: a more specific, but still general, EType to represent brother-sister relationships. This has been specified into another EType rather than an ”Individual” property to assign to it the Contextual ”Twin” EType.
- **Core ETypes**:

- Dataset: a collection of Samples, under a name and a classification regarding its collection.
- Sample: our hub EType where much of the knowledge flows through: it is a collection of genetic sequences and other metadata. It is needed to tackle the most relevant competency questions and to obtain much of the data that follows.
- SGB: Species Level Genome Bins are groupings of genome data corresponding to the closest (known or unknown) microbial species (or taxonomic classification). They are derived from grouping DNA sequences obtained from metagenomic samples into bins that representing closely related genomes. Another important hub EType that will lead to other entities closer to the purpose.
- Taxonomy: a way to represent the bacterial taxonomic classification of known or unknown SGBs. It is needed to output the scientific name of the SGBs found in a sample.

- **Contextual ETypes**:
  - Transmission: contains specific values associated with the transmission types and rates in different contexts for each SGB. Very relevant to our purpose in distinguishing the most/least transmitted bacterial strains.
  - Phenotype: contains categorical variables that give insights into the phenotype of each SGB that are useful to answer competency questions strictly related to the phenotype itself.
  - Twin: a more specific type of sibling; to our purpose it represents a way to distinguish differences in transmissibility between twins of different zygosity or years of living apart.

Regarding the relationships between ETypes, we identify straight-forward ones such as ”Twin is a Sibling” or ”Individual is part of Family” that tackle the family relationships and others like ”SGB has Transmission/Phenotype/Taxonomy” to subdivide our purpose based on the Competency Questions we want to answer. For example, if we need to compare different phenotypes for a group of SGBs we rely on the related ETypes ”SGB” and ”Phenotype” (CQ 1.3, 3.4, 4.4). We can apply a similar reasoning to other ”has” relationships.

3 Information Gathering

This section describes the second primary input for the project: the data source list. This phase will document and describe every resource (language, schema and data values) needed and used in the next steps in order to produce standardized datasets that satisfy the formalized purpose.

3.1 Data value datasets

All the data necessary to our purpose is derived from two sources:

- The person-to-person transmission landscape of the gut and oral microbiomes[2]: a paper regarding the human microbiome and its transmission within and across populations. It contains 35 Supplementary Tables comprising data regarding datasets of the study, samples, taxonomies, SGBs, transmission rates, phenotypes, correlation statistics and other data values.
  - **Sample Metadata and Overview (Tables S1–S2):** Contains metadata for 9,700 samples, including demographic data, body sites, and age categories. These tables also link samples to individuals and families, enabling relational analyses.
  - **Microbiome Profiling and Taxonomic Data (Tables S4–S9):** Provides microbial taxonomy data such as phylum, genus, and species classifications. It includes microbial group identifiers (SGBs), diversity indices, and profiles for specific environments like stool and saliva.
  - **Statistical Analyses and Diversity Patterns (Tables S3, S10–S19):** These tables focus on statistical tests (e.g., PERMANOVA) and diversity metrics to examine variability within and between groups. They also analyze microbial sharing rates and group-level comparisons.
  - **Transmissibility Data (Tables S9, S16, S20, S30–S32):** Includes detailed metrics on microbial transmissibility, such as mother-infant, household, and intradataset sharing. **Table S16** and **S20** evaluate transmissibility through the **Intra_inter_ratio** metric, showing how microbial sharing differs within and between groups. **Table S30** provides age-specific transmission rates, particularly for mother-offspring pairs.
  - **Functional Traits and Phenotypes (Tables S34–S35):** Describes microbial traits such as spore formation, motility, and anaerobic status. These features offer insights into microbial adaptability and ecological roles.
  - **Supplementary and Specialized Data (Tables S21–S29, S33):** Includes comparisons of microbial sharing across populations, environments, and relationships, such as twin studies and inter-household sharing rates.
- curatedMetagenomicData[3]: an R package containing datasets that include the relative abundance of a microbial organism (expressed with a taxonomic assignment) for each sample.

3.2 Knowledge datasets

- Schema.org: describing hierarchies between Entity types together with their properties.
- Schema.org LOV: schema of the schema.org vocabulary.
- Bioschemas.org: uses Schema.org markup specifically designed for Life Sciences. It includes structures named Profiles over Types together with properties that are either designed by Bioschemas or deriving from Schema.org.

3.3 Data cleaning, filtering, standardization

Out of these 35 tables, we decided to keep 11 (Figure **2**, cleaned and modified each one in the following way:

- Table S1: containing information about the datasets and their classification; we kept only the datasets that had a corresponding one in the *curatedMetagenomicData* R package. Some studies of the paper (like the Italian and Chinese datasets) were brand new and were not imported yet to the R package due to them being unpublished. We removed the datasets having *NA* values in "PMID", then kept only the columns "Dataset", and "Dataset_classification" (Figure **3**). Some datasets (like Ghana, Tanzania) have different names in the R package but are present: this is fixed by exporting the R datasets with the same names as the ones present in the Supplementary Table 1.

Table	Description
Table S1	Summary of the 9715 samples included in the study by dataset.
Table S2	Metadata of the 9715 samples included in the study.
Table S4	List of profiled SGBs in stool samples, taxonomic classification, and strain identity thresholds.
Table S5	List of profiled SGBs in saliva samples, taxonomic classification, and strain identity thresholds.
Table S9	Gut SGB mother-infant, household, and intrapopulation transmissibility.
Table S16	Gut SGB mother-infant transmissibility (Chi2 tests, two-sided).
Table S20	Gut SGB household transmissibility and twin transmissibility (Chi2 tests, two-sided).
Table S30	Oral SGB mother-infant, household, and intrapopulation transmissibility.
Table S31	Oral SGB mother-infant transmissibility (Chi2 tests, two-sided).
Table S32	Oral SGB household transmissibility (Chi2 tests, two-sided).
Table S34	SGB predicted phenotypical traits.

Figure 2: Legend table containing information regarding the Supplementary Tables we kept.

Dataset	Dataset_classification
PasolliE_2019_Madagascar	Households
PehrssonE_2016_PER	Households
PehrssonE_2016_SLV	Households
CosteaPI_2017_KAZ	Longitudinal_set
LouisS_2016	Longitudinal_set
MehtaRS_2018	Longitudinal_set
NielsenHB_2014_ESP	Longitudinal_set
AsnicarF_2017	Mother_offspring
BackhedF_2015	Mother_offspring
ChuDM_2017	Mother_offspring
FerrettiP_2018	Mother_offspring
ShaoY_2019	Mother_offspring
TettAJ_2019_Ethiopia	Mother_offspring
WampachL_2018	Mother_offspring
YassourM_2018	Mother_offspring
BritoIL_2016	Mother_offspring and Households
Ghana	Mother_offspring and Households
Tanzania	Mother_offspring and Households
CosteaPI_2017_DEU	Mother_offspring and Households
AsnicarF_2021	Twins
XieH_2016	Twins
HMP_2019_ibdmdb	NA

Figure 3: Table S1 containing the datasets we kept together with their classification.

- Table S2: containing information about the samples and individuals of the study. We filtered out all samples (rows) that belonged to datasets we would not be using and kept the columns you can see in Figure **4**.

sampleID	subjectID	body_site	age_category	gender	familyID	mother_subjectID	father_subjectID	partner_subjectID	sibling_subjectID	zygosity	age_twins	country	non_Westernized	Dataset
MV_FEI1_t1Q14	MV_FEI1	stool	<=1y	female	AsnicarF_2017_MV_1	MV_FEM1	NA	NA	NA	NA	NA	ITA	no	AsnicarF_2017

Figure 4: A row of table S2 containing the information we decided to keep for each sample. It includes sampleID and subjectID, information about the person, its parental relations, provenance and related dataset.

- Tables S4 and S5: containing information regarding SGBs and taxonomic classification of each one (respectively of stool and saliva samples). We reworked this tables in order to keep the entire taxonomy as a needed ID to link it with the tables of the R package, but also by creating new columns to represent each taxonomic level independently to tackle specific queries (ex. Kingdom, Phylum, Class etc.).

- Tables S9 and S30: containing useful information about the transmissibility of each SGB in different contexts (including mother-to-offspring, in households and intra-datasets). These tables were not changed.
- Table S34: containing information about the phenotype of each SGB (Spore_former, Anaerobe, Motile, Gram_negative). This table was not changed.
- Tables S16, S20, S31, S32: extra tables containing Chi-Square statistics about relatedness between SGBs and the Person's age, transmission mode vs environment, SGBs and datasets (households vs twins).

The reworked tables were all exported as *.tsv* files for standardization. Furthermore, we extracted data about the relative abundance of each bacterial species (meaning the percentage representing how much the species is present within a sample with respect to all others) for each sample using the R library *curatedMetagenomicData*. The following procedure can be repeated for each of the datasets listed in Figure **3** to get the relative abundance of a specific bacterial species, represented by a taxonomic classification (rows), for all samples (columns) of a dataset.

```
# load the R library
library(curatedMetagenomicData)
# load a dataset; curatedMetagenomicData("dataset_name.relative_abundance")
current_dataset <- curatedMetagenomicData("2021-03-31.XieH_2016.relative_abundance", dryrun = FALSE)
# load the relative abundance table
rl <- current_dataset$`2021-03-31.XieH_2016.relative_abundance`@assays@data@listData$relative_abundance
# export .tsv of the relative abundance table
write.table(rl, file = "XieH_2016.tsv", sep = "\t")
```

	YSZC12003_35365	YSZC12003_35366	YSZC12003_35387	YSZC120
k__Bacteria|p__Firmicutes|c__Clostridia|o__Clostridiales|f__Eu...	19.61446	14.37897	0.00131	
k__Bacteria|p__Firmicutes|c__Clostridia|o__Clostridiales|f__Lac...	8.39258	0.00000	0.01835	
k__Bacteria|p__Firmicutes|c__Clostridia|o__Clostridiales|f__Ru...	7.89178	6.47709	0.00100	
k__Bacteria|p__Bacteroidetes|c__Bacteroidia|o__Bacteroidales...	7.37049	2.23896	0.00578	
k__Bacteria|p__Bacteroidetes|c__Bacteroidia|o__Bacteroidales...	5.18316	12.39338	5.65945	
k__Bacteria|p__Bacteroidetes|c__Bacteroidia|o__Bacteroidales...	5.05453	12.89000	4.92746	
k__Bacteria|p__Bacteroidetes|c__Bacteroidia|o__Bacteroidales...	4.93714	3.87848	3.49791	
k__Bacteria|p__Firmicutes|c__Clostridia|o__Clostridiales|f__Ru...	4.36169	1.89050	1.72699	
k__Bacteria|p__Firmicutes|c__Clostridia|o__Clostridiales|f__Lac...	3.02199	0.19740	0.05757	

Figure 5: A snapshot of the datasets deriving from the R library *curatedMetagenomicData*. The rows represent taxonomical classifications, the columns the sample IDs that are dataset-specific.

3.4 Finalized datasets

After cleaning, exporting and standardizing all of our data, we end up with the following datasets:

File	Source	Content	Related ETypes
datasets.tsv	Table S1	Dataset and classification	Dataset
samples.tsv	Table S2	Sample Metadata	Sample, Person, Country, Sibling, Twin
taxonomy_SGB_stool.tsv	Table S4	Stool SGBs	Taxonomy, SGB
taxonomy_SGB_saliva.tsv	Table S5	Saliva SGBs	Taxonomy, SGB
transmission_rates_1.tsv	Table S9	Transmission rates	Transmission
transmission_rates_2.tsv	Table S30	Age-specific transmission rates	Transmission
phenotypes.tsv	Table S34	Phenotype of each SGB	Phenotype
SGB_age.tsv	Table S16	Relatedness SGB-age	SGB
SGB_transmission.tsv	Table S20	Relatedness SGB-transmission	SGB
transmission_env.tsv	Table S33	Relatedness transmission-environment	Transmission

Moreover, there is a *.tsv* file for each dataset listed in *datasets.tsv*. For example, *"XieH_2016.tsv"* will contain data about the dataset named XieH_2016, specifically the relative abundance of each species for each sample of the dataset. In total, we have 22 datasets that are also present in the *curatedMetagenomicData* R library. These datasets were added in a second moment with respect to the ones present in the previous table as we noticed we were missing a very important link present in our ER model: the one between the Sample and the Taxonomy. Specifically, we needed a straight-forward way to have, for each sample, all the species that were found inside it: this is given by the relative abundance, a numeric value that measures the percentage of a bacterial species inside a sample. Of course, this gives us the possibility to also say whether a species is present in a sample or not just by looking at the percentages (0% meaning that that specific species is not present in the sample).

3.5 Knowledge Layer, Schemas, Ontologies

The cleaned dataset contains various entities and properties essential for analyzing microbial transmission and diversity. For most entity types, no existing schema from Schema.org or Bioschemas.org is available, so we use the schema derived directly from the dataset. However, for some types, we align with existing standards where applicable.

3.5.1 Dataset (from Schema.org)

- **name** (Text, from Schema.org): Name of the dataset.
- **classification** (Text, from the original data): Classification of the dataset.

3.5.2 Country (from Schema.org)

- **name** (Text, from Schema.org): Country associated with samples or individuals.
- **isWesternized** (Boolean, from the original data): Whether the country is considered Westernized.

3.5.3 Person (from Schema.org)

- **identifier** (Text, from Schema.org): Identifier for an individual.
- **gender** (Text, from Schema.org): Gender of the individual.
- **mother_subjectID**, **father_subjectID** (Text, from the original data): Identifiers for parents.
- **sibling_subjectID** (Text, from the original data): Identifier for siblings.
- **familyID** (Text, from the original data): Identifier linking the individual to a family.

3.5.4 BioSample (from bioschema.org)

- **identifier** (Text, from Bioschemas.org): Unique identifier (sampleID) for a sample.
- **samplingAge** (Text, from bioschema.org): The age of the object when the Sample was created.
- **bodySite** (Text, from the original data): Anatomical site where the sample was collected.

3.5.5 Taxon (from bioschema.org)

- **identifier** (Text, from Bioschemas.org): Unique identifier for the taxonomic entity.
- **scientificName** (Text, from Bioschemas.org): The currently valid scientific name of the taxon.
- **alternateScientificName** (Text, from Bioschemas.org): Synonym or alternate scientific name for the taxon, if available.
- **parentTaxon** (Text, from Bioschemas.org): Closest parent taxon of the taxon in question.
- **childTaxon** (Text, from Bioschemas.org): Closest child taxa of the taxon in question.
- **taxonRank** (Text, from Bioschemas.org): The taxonomic rank of this taxon.
- **relativeAbundance** (Float, from the original data): Relative abundance of the taxon in the sample.

3.5.6 SGB (Species-level Genome Bin) (from the original data)

- **SGB_ID** (Text): Identifier for the species group bin.
- **classification** (Text): Type of SGB classification (e.g., kSGB, uSGB).

3.5.7 Phenotype (from the original data)

- **sporeFormer** (Boolean): Indicates if the microbial species forms spores.
- **anaerobe** (Boolean): Indicates if the microbial species is anaerobic.
- **motile** (Boolean): Indicates if the microbial species is motile.
- **gramNegative** (Boolean): Indicates if the microbial species is Gram-negative.

3.5.8 Transmission (from the original data)

- **motherInfantTransmissibility** (Number): Rate of transmission from mother to infant.
- **householdTransmissibility** (Number): Rate of transmission within a household.
- **intraInterRatio** (Number): Ratio comparing intra-group and inter-group transmissibility.

This schema reflects the dataset's structure while incorporating standards from Schema.org and Bioschemas.org where applicable, providing a robust framework for representing microbiome-related entities and relationships.

4 Language Definition

The language definition phase has, as main objective, to formally define the concepts and information that will be present and used in the final Knowledge Graph to satisfy the project purposes. In order to do so, we have to consider and identify all the concept structures such as ETypes, relations and the object properties to be formally defined. This operation was done with the help of the Universal Knowledge Core (UKC) [4], aligning each identified concept to the integrated search engine to examine if the concept was already present or not. The results coming from this section can be seen in Table 1. If a concept was not found in UKC, it was either looked into using a different ontology or, if still not found, it was identified and defined by us. Due to the context of the project, some of the elements taken into account are very purpose specific (for example the EType Transmission and its properties) and therefore had to be fully defined and specified. Since our study presents many words and concepts that are specific for the biological field, we had to search for other ontologies to retrieve the needed information with which we completed our Language Resource table. We identified 3 ontologies, all coming from NCBO BioPortal [5], depending on the concepts that still needed identification and definition:

- **D3O**: the DSMZ Digital Diversity Ontology, used to retrieve details related to microbial specific phenotypes.
- **GENO**: the Genotype Ontology, used to represent the genetic variations described in genotypes, linking them to phenotypes; in our case the twin's zygosity.
- **OHMI**: the Ontology of Host-Microbe Interactions, a biomedical ontology used to represent relationships between host-microbe interactions; in our case the bacteria's relative abundance.

4.1 Concept Identification

In the end we were able to produce the Language Resource Table in which each identified concept was listed and represented in a table having 3 columns:

- Column 1: ConceptID; it has three different ”formats” based on whether the word was found in UKC (ID: UKC-number), found in other ontologies (ID: link) or defined it ourselves (ID: KGE24-QCB2-number).
- Column 2: containing the labels or words associated to the concept
- Column 3: containing the glossary/definition for each word

Furthermore, we decided to color-code our table for better visualization in the following way:

- In black the concepts aligned and found in UKC;
- In blue those aligned and not found in UKC but in different ontologies;
- In red those concepts not found in any other resource and that we defined ourselves;
- In **bold** we can see the E-Types, in *italics* the relationships and as plain simple text the Properties.

ConceptID	Word-en	Gloss-en
https://purl.dsmz.de/schema/Dataset	**Dataset**	A structured collection of data, often presented in tabular or other formats, that is used for analysis, research, or reference purposes. Datasets can consist of numerical, textual, or categorical information
UKC-2	Name	a language unit by which a person or thing is known
UKC-42540	Classification, Group	a group of people or things arranged by class or category
UKC-46463	**Sample**	all or part of a natural object that is collected and preserved as an example of its class
UKC-26728	Age_Category, Age	how long something has existed
KGE24-QCB2-1	Body Site	extraction point of a sample from a person
UKC-36	**Person**	a human being
UKC-27174	Gender	the properties that distinguish organisms on the basis of their reproductive roles
UKC-51131	Mother	a woman who has given birth to a child (also used as a term of address to your mother)
UKC-49598	Father	a male parent (also used as a term of address to your father)
UKC-52872	Partner	a person’s partner in marriage
UKC-43042	Family	a social unit living together
UKC-45187	**Country**	the territory occupied by a nation
KGE24-QCB2-2	Westernized	a population that has adopted Western cultural norms, values, and lifestyles.
UKC-52619	**Sibling**	a person’s brother or sister

UKC-53445	**Twin**	either of two offspring born at the same time from the same pregnancy
http://purl.obolibrary.org/obo/GENO_0000133	Zygosity	An allelic state that describes the degree of similarity between features in a 'single locus complement', within the genome of a cell or organism (i.e., whether the alleles or haplotypes that reside at the same location on paired chromosomes are the same or different)
KGE24-QCB2-3	Age Living Apart	the age twins started to live apart
UKC-44477	**Taxonomy**	a classification of organisms into groups based on similarities of structure or origin etc
UKC-42545	Kingdom	the highest taxonomic group into which organisms are grouped; one of five biological categories: Monera or Protoctista or Plantae or Fungi or Animalia
UKC-43156	Phylum	(biology) the major taxonomic group of animals and plants; contains classes
UKC-43160	Class	(biology) a taxonomic group containing one or more orders
UKC-43163	Order	(biology) taxonomic group containing one or more families
UKC-43166	Family	(biology) a taxonomic group containing one or more genera
UKC-43171	Genus	(biology) taxonomic group containing one or more species
UKC-43176	Species	(biology) taxonomic group whose members can interbreed
http://purl.obolibrary.org/obo/OHMI_0000468	Relative Abundance	A quality of ecological community that refers to how common or rare a species is relative to other species in a defined location or community
KGE24-QCB2-4	**SGB**	Species-level Genome Bins - microbial genomes from metagenomic data, representing species-level groupings
UKC-26778	**Phenotype**	what an organism looks like as a consequence of the interaction of its genotype and the environment
https://purl.dsmz.de/schema/SporeFormation	Spore former	The ability of certain microorganisms to form spores, a resistant structure that allows survival in adverse conditions. Spore formation is a significant trait for microbial classification and survival strategies
UKC-6534	Anaerobe	an organism (especially a bacterium) that does not require air or free oxygen to live
UKC-82548	Motile	(of spores or microorganisms) capable of movement
https://purl.dsmz.de/schema/GramNegativeBacteria	Gram negative	Bacteria that do not retain the crystal violet stain used in Gram staining. Gram-negative bacteria have an outer membrane and are often resistant to certain antibiotics

KGE24-QCB2-5	**Transmission**	the transfer of microorganisms (bacteria, viruses, fungi, etc.) between individuals, environments, or species, influencing their microbiome composition
KGE24-QCB2-6	mother-infant transmission	the microbial transmission between mother and her infant (i.e. transmissibility)
KGE24-QCB2-7	household transmission	the microbial transmission within people living in the same dwelling (i.e. transmissibility)
KGE24-QCB2-8	intradataset transmission	the microbial transmission within metagenomics samples of same dataset (i.e. transmissibility)
UKC-103527	*has*	have or possess, either in a concrete or an abstract sense
KGE24-QCB2-9	*is from*	has origin, association, or ownership related to a source, place, or entity.
UKC-95876	*source of*	specify the origin of

Table 1: This table represents the purpose-specific concepts, formalized and defined. The terms in **bold** represent the ETypes, the ones in *italics* the relations and all the others are the properties of the corresponding ETypes. Furthermore, the words in black are the ones also present in UKC (and have the UKC-ID), the ones in blue are present in other ontologies (with the ID being the link to that concept) and the ones in red are defined by us (and have ID: KGE-QCB2-number).

4.2 Dataset filtering

Dataset filtering aims at aligning all the concept previously identified with the data layer resources (3.1). This also means filtering out all resources or elements that are not formally defined. In our case this step is trivial as we aimed to identify (and put in our language resource table) all concepts that are found in our data layer. To be more precise, we go through each table presented in 3.4:

- *dataset.tsv*: fully defined with ”Dataset”, ”Name” and ”Classification”.
- *samples.tsv*: fully defined (”Sample”, ”Age”, ”Body Site”, ”Person”, ”Gender”, ”Mother”, ”Father”, ”Partner”, ”Family”, ”Country”, ”Westernized”, ”Sibling”, ”Twin”, ”Zygosity”, ”Age Living Apart”).
- *taxonomy_SGB_stool.tsv* and *taxonomy_SGB_saliva.tsv*: fully defined (”Taxonomy”, ”Kingdom”, ”Phylum”, ”Class”, ”Order”, ”Family”, ”Genus”, ”Species”, ”SGB”, ”Classification”).
- *transmission_rates_1.tsv* and *transmission_rates_2.tsv*: fully defined (”Transmission”, ”Age”, ”mother-infant transmission”, ”household transmission”, ”intradataset transmission”).
- *phenotypes.tsv*: fully defined (”Phenotype”, ”Spore former”, ”Anaerobe”, ”Motile”, ”Gram negative”).
- *SGB_age.tsv*, *SGB_transmission.tsv*: fully defined (”Age”, ”SGB”, ”Classification”).

- *transmission_env.tsv*: not defined as this dataset was dropped; it did not provide relevant information to properly answer the Competency Questions.
- (*dataset_name*).*tsv*: each is fully defined (”Taxonomy”, ”Name”, ”Sample”, ”Relative abundance”).

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