

1 **NERO: A Biomedical Named-entity (Recognition) Ontology with a Large,**
2 **Annotated Corpus Reveals Meaningful Associations Through Text Embedding**
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4 ^{1,2}Kanix Wang

5 ³Robert Stevens

6 ⁴Halima Alachram

7 ⁵Yu Li

8 ⁶Larisa Soldatova

9 ⁷Ross King

10 ^{3,8}Sophia Ananiadou

11 ^{3,8}Maolin Li

12 ^{3,8}Fenia Christopoulou

13 ⁹Jose Luis Ambite

14 ⁹Sahil Garg

15 ⁹Ulf Hermjakob

16 ⁹Daniel Marcu

17 ⁹Emily Sheng

18 ⁴Tim Beißbarth

19 ¹⁰Edgar Wingender

20 ⁹Aram Galstyan

21 ⁵Xin Gao

22 ¹¹Brendan Chambers

23 ^{2,12}Bohdan B. Khomtchouk

24 ¹¹James A. Evans

25 ^{1,2,12,13*}Andrey Rzhetsky

26

27 ¹The Committee on Genetics, Genomics, and Systems Biology, University of Chicago,
28 Chicago, IL 60637, US;

29 ²The Institute of Genomics and Systems Biology, University of Chicago, Chicago, IL
30 60637, US;

31 ³Department of Computer Science, University of Manchester, M13 9PL, UK;

32 ⁴Institute of Medical Bioinformatics, University of Göttingen, Goldschmidtstrasse 1,
33 37077 Göttingen, Germany.

34 ⁵Computational Bioscience Research Center;
35 Computer, Electrical and Mathematical Sciences and Engineering Division;
36 King Abdullah University of Science and Technology (KAUST)
37 Thuwal, 23955, Saudi Arabia;

38 ⁶Goldsmiths, University of London, 8 Lewisham Way, New Cross, London SE14 6NW,
39 UK;

40 ⁷Department of Chemical Engineering and Biotechnology, University of Cambridge,
41 Philippa Fawcett Dr, Cambridge CB3 0AS, United Kingdom

42 Alan Turing Institute, 96 Euston Rd, Somers Town, London NW1 2DB, United Kingdom
43 Department of Biology and Biological Engineering, Chalmers University of Technology,
44 SE-412 96 Göteborg, Sweden.

45 ⁸National Centre for Text Mining, University of Manchester, M1 7DN, UK;

46 ⁹The Information Sciences Institute, University of Southern California, Marina del Rey,
47 CA 90089, US;

48 ¹⁰geneXplain GmbH, Am Exer19b, 38302 Wolfenbüttel, Germany;

49 ¹¹Knowledge Lab, Department of Sociology, University of Chicago, IL 60637, US;

50 ¹²Department of Medicine, University of Chicago, Chicago, IL 60637, US;

51 ¹³Department of Human Genetics, University of Chicago, Chicago, IL 60637, US;

52
53 *Corresponding author, andrey.rzhetsky@uchicago.edu.

54
55 **Machine reading is essential for unlocking valuable knowledge contained in the**
56 **millions of existing biomedical documents. Over the last two decades ^{1,2}, the most**
57 **dramatic advances in machine-reading have followed in the wake of critical**
58 **corpus development³. Large, well-annotated corpora have been associated with**
59 **punctuated advances in machine reading methodology and automated**
60 **knowledge extraction systems in the same way that ImageNet ⁴ was fundamental**
61 **for developing machine vision techniques. This study contributes six**
62 **components to an advanced, named-entity analysis tool for biomedicine: (a) a**
63 **new, Named-Entity Recognition Ontology (NERO) developed specifically for**
64 **describing entities in biomedical texts, which accounts for diverse levels of**
65 **ambiguity, bridging the scientific sublanguages of molecular biology, genetics,**
66 **biochemistry, and medicine; (b) detailed guidelines for human experts annotating**
67 **hundreds of named-entity classes; (c) pictographs for all named entities, to**
68 **simplify the burden of annotation for curators; (d) an original, annotated corpus**
69 **comprising 35,865 sentences, which encapsulate 190,679 named entities and**
70 **43,438 events connecting two or more entities; (e) validated, off-the-shelf, named-**
71 **entity recognition automated extraction, and; (f) embedding models that**
72 **demonstrate the promise of biomedical associations embedded within this**
73 **corpus.**

74
75 Even the relatively specialized subfields of present-day biology and medicine are facing
76 a deluge of accumulating research articles, patents, and white papers. It is increasingly
77 difficult to stay up-to-date with contemporary biomedicine without the use of
78 sophisticated machine reading (MR) tools. MR tool development, in turn, has been
79 limited by the availability of biomedical corpora carefully annotated by experts. This is
80 especially true with respect to information extraction, such as named entity recognition
81 and relation or event extraction. Although several corpora have been developed for
82 specialized biomedical subdomains, the need for a corpus that can bridge biological,
83 general scientific, environmental, and clinical scientific sub-languages is greater than
84 ever before.

85 Unfortunately, the annotation of natural science texts is more challenging than in
86 other domains. Biomedical language is replete with ambiguity distinct from that
87 observed in news articles or informal text online. When a word or phrase's semantic
88 meaning is clearly separated (*the east bank of the Danube* versus *Deutsche Bank*), we
89 can implement automated sense disambiguation using machine learning tools. In
90 biomedical texts, however, alternative meanings are not always clearly separated. The
91 problem is not that a phrase can refer to several distinct, real-world entities in different

92 contexts, but that the scientists writing articles typically do not separate competing,
93 close meanings. For example, in some biomedical contexts, a named entity may refer to
94 a *gene* or a *protein* with nearly equal probability; for example, “a mutant hemoglobin α_2 ”
95 can refer to either a gene or a protein. If the author meant *gene-or-protein A*, and we
96 force an annotator to choose either interpretation *gene A* or *protein A*, the resulting
97 annotation is of limited utility because the choice between *gene* and *protein* is random if
98 the meanings are equally likely based on context. Ideally, a specialized ontology of text
99 entities would allow an annotator to choose the proper level of annotation granularity
100 (*gene-or-protein*, in this example), minimizing the need for forced, random decisions. To
101 the best of our knowledge, there is no biomedical ontology that meets the requirements
102 for capturing semantic ambiguity. We aimed to fill this gap by developing a specialized,
103 variable-level meaning resolution ontology, a carefully curated corpus, along with
104 corpus annotation tools, and a collection of text embedding analyses to evaluate our
105 annotated corpus.

106 Our new ontology, called NERO, short for Named-entity Recognition Ontology,
107 attempts to minimize unwarranted, arbitrary annotative semantic label assignments in
108 text entities, see Figure 1. NERO captures named entities, starting with most broad and
109 vague concepts close to the taxonomy’s root, finishing with the most narrow and
110 concrete concepts at the taxonomy’s leaves. Hence, *DomainEntity*—and all ambiguous
111 semantic classes—correspond to NERO’s taxonomy root. The basic division thereafter is
112 between *TextEntity* and *AbstractEntity*, where *TextEntity* further splits into *NamedEntity*,
113 *NamedEntityGroup*, *Relationship*, and *Pronoun*. After *NamedEntity*, the hierarchy
114 reflects that which is written in biological entity descriptions, rather than in those entities’
115 lexical representation. NERO defines ambiguous concepts, such as *GeneOrProtein*,
116 which subsumes both *Gene* and *Protein* using the following axiom: *EquivalentTo*:
117 ‘*Gene*’ or ‘*Protein*.’ There are no biological entities that are either a gene or a protein,
118 but there are lexical entities that can belong to either named entity class. NERO uses
119 this pattern to express appropriate ambiguity regarding text entities, preserving
120 uncertainty from the text. In this way, NERO classes represent textual instances and not
121 the actual biological entities to which these instances refer. It is, therefore, straight-
122 forward to link between the lexical and biological entity through a relationship such as ‘*is*
123 *about*’. So, the NERO class *Protein* ‘*is about*’ some specific concept ‘*protein*’ in an
124 ontology pointing to real biological entities, such as the Protein Ontology⁵.

125 Striving to make the ontology practically useful, we designed guidelines for
126 annotators making decisions in annotating text entities, available in the *Supplementary*
127 *Data*. Furthermore, by recruiting a team of postdoctoral-level experts, we annotated a
128 large biomedical corpus to enable a broad range of natural language processing and
129 biomedical machine learning tasks. Our annotations span 35,865 unique sentences,
130 8,650 of which were annotated by multiple annotators with remarkably high inter-
131 annotator agreement (see Table 1). In our annotated corpus, we aimed to encompass
132 all entity types that might occur in biomedical literature. In addition to named entities,
133 our ontology captures *events* which represent relationships between biomedical
134 concepts. The frequencies of all diverse entity types in our corpus are shown in Figure
135 2A; Figure 2B shows the frequencies of relations represented in the taxonomy. The
136 most frequent entity type is *GeneOrProtein*, which accounts for 14.7 percent of all
137 named entities in the corpus (see Figure 2A). The second most populous category is

138 *Process*, with nine percent tagged. *Process* has six sub-concepts and almost half of
139 *Process* instances (49.7 percent) are annotated as more specific sub-concepts; the
140 *BiologicalProcess* and the *MolecularProcess* are the fifth and seventh most frequent
141 entity types (see Figure 2). Entity type frequencies follow a heavy-tail distribution, with
142 the least frequent types being *Journal*, *Unit*, and *Citation* (see Figure 2). In addition to
143 190,679 named entities, we annotated 43,438 action terms, events connecting two or
144 more entities. The most annotated action term is *bind*, accounting for 28.4% of all
145 actions, see *Supplementary Figure 1*. When we normalize the action terms and
146 combine actions such as *bind*, *binds*, and *binding*, the normalized action *bind* accounts
147 for 31.8% of all actions, as shown in *Supplementary Figure 1*. We deployed a package
148 called NERO-nlp for researchers interested in diving deeper into our annotated corpus;
149 the installation guides and scripts are available online at <https://pypi.org/project/NERO-nlp>
150 and <https://github.com/Bohdan-Khomtchouk/NERO-nlp> respectively.

151 Below, we present two practical applications of our ontology and text annotations:
152 1) Machine learning experiments, which automatically identify named entities, and; (2)
153 Word embedding experiments, which leverage the automated discovery of semantic
154 relationships among real-world concepts referenced by a text's named entities.

155 *Machine learning experiments*: Using NERsuite⁶, we conducted a ten-fold cross-
156 validation, dividing the corpus into training and test subsets. The classification results
157 are presented in *Supplemental Table 1*. The overall automated named entity recognition
158 performance is moderate, with 54.9% precision, 37.3% recall and a 43.4% F_1 score.
159 The best performance class, *GeneOrProtein*, had baseline results of 67.0% precision,
160 65.3% recall, and a 66.2% F_1 score. In addition to the default baseline implementation
161 of NERsuite, we added additional features in the training process to improve its
162 performance⁷. These are dictionary features derived from lookups in technical term
163 dictionaries. The classifier with dictionary features manifests 54.7% precision, 37.9%
164 recall and a 43.8% F_1 score. We observed a scant 0.35% increase in F_1 score from
165 adding dictionary features. We then implemented an ensemble method called stacking,
166 where we trained a higher-level model to learn how to best combine contributions from
167 each base model. The base model in this case is the baseline model from NERsuite.
168 Stacking yielded a 0.27% increase in F_1 score compared to baseline results. While
169 ensemble methods are commonly used to boost model accuracy by combining the
170 predictions of multiple machine learning models, choices of second-level and base
171 models can influence the amount of improvement in model accuracy. The overall
172 performance statistics are shown in *Supplementary Table 2*. As our corpus is made
173 public with this study's publication, we hope that other researchers will use this training
174 data to achieve core MR task performance that surpasses our initial experiments.

175 To examine how NERsuite performs in comparison to other popular open-source
176 Named-Entity recognition tools, we trained a custom NER model on our annotated
177 corpus using spaCy⁸. We evaluated the trained model on the test subset, which
178 consists of a random 10% sample from the corpus. Classification results are presented
179 in *Table 3*. Overall automated named entity recognition performance is low, with 30.9%
180 precision, 8.6% recall and a 13.4% F_1 score. The best performance class,
181 *GeneOrProtein*, had results of 45.1% precision, 36.4% recall, and a 40.3% F_1 score.
182 These statistics indicate a much poorer performance of spaCy compared to that of
183 NERsuite.

184 To help explain the huge difference in performance between NERsuite and
185 spaCy, we considered the set of input features used by each tool for insight. NERsuite's
186 baseline implementation uses an extra set of input features including the lemma, POS-
187 feature and chunk-feature, whereas our custom spaCy NER model only relies on
188 character offsets and entity labels. There is potential for further customizing spaCy's
189 processing pipelines by adding more components such as tagger and parser⁸, but no
190 established approaches in this regard have been made available partly because
191 spaCy's model architecture is different from those of other popular NER tools. We also
192 observed that some entities classes, such as Gene and Protein, have zero values for
193 precisions, recalls and F_1 scores, which likely translate to no correct classifications
194 made for those entities. The zero values occur partly due to the relatively smaller
195 number of tokens for those entity classes in the training set, and as a result, the trained
196 NER model generalized poorly on the minority class entities in the test subset.

197 Due to spaCy's computational demands, we did not conduct 10-fold cross-
198 validation. NERsuite provides a well-integrated pipelined system where training a new
199 model consists of a few lines of code. In addition, NERsuite has a demonstrated record
200⁵ on two biomedical tasks, the BioCreative2 gene mention recognition task and the
201 NLPBA 2004 named entity recognition task. Therefore, one could argue that it offers an
202 advantage over spaCy for NLP tasks in specialized domains such as biomedicine.

203 We've also identified another package called scispacy⁹ that contains spaCy
204 models for processing biomedical, scientific or clinical text. SciSpaCy acts as an
205 extension to spaCy and provides a set of practical tools for text processing in the
206 biomedical domain⁹. In particular, scispacy includes a set of spaCy NER models
207 trained on popular biomedical corpora, which covers entity types such as chemicals,
208 diseases, cell types, proteins and genes. As an extension to spaCy, it also has the
209 flexibility for users to train a custom NER model from scratch or update the existing
210 NER models with users' own training data. Since our NER ontology adopts a more
211 diverse and detailed annotation methodology for named entity types, it will be
212 challenging to update scispacy's pretrained named entity recognizer with our annotated
213 corpora.

	p	r	f
Cell	16.88	5.10	7.83
CellComponent	35.71	4.44	7.91
GeneOrProtein	45.11	36.44	40.31
Organism	16.99	5.53	8.34
Disease	11.79	8.12	9.61
Drug	11.11	1.20	2.17
SmallMolecule	0.00	0.00	0.00
BiologicalProcess	8.02	1.88	3.05
MolecularProcess	12.67	2.45	4.10
Gene	0.00	0.00	0.00
Protein	0.00	0.00	0.00
BodyPart	15.17	5.54	8.12
AminoAcid	12.50	0.88	1.64

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215

216 Table 3: Experimental results using spaCy for NER evaluated on 10% of the corpus

217

218 *Word embedding experiments:* Semantic associations, automatically extracted
219 from text using neural network embedding operations, can function as a kind of “digital
220 double” of real-world phenomena embedded in text, facilitating inferences that were
221 previously imagined only possible from the original experimental data. For example,
222 word embeddings built from chemical and material science texts predict much of the
223 subsequent decades’ material discoveries⁸, just as the corpus of molecules can recover
224 the periodic table⁹, and texts are able to recover the subtle, psychological and
225 sociological biases of cultures that produced them^{10,11}. We used word embedding
226 models to evaluate the biomedical veracity of NERO and its text annotation. Embedding
227 models like Google’s *word2vec*^{12,13} initially received substantial attention based on
228 their capacity to solve analogy problems and automatically capture deep semantic
229 relationships among concepts. Building on these capacities^{10,14,15}, we proposed a
230 general method for constructing meaningful dimensions by taking the arithmetic mean
231 of word vectors representing antonyms along a dimension and using them to diagnose
232 their meanings. This approach has been widely validated¹⁵⁻¹⁹, and we employed it here
233 to construct and compare the meanings embedded in NERO and our annotated corpus
234 with ground truth data about drugs and diseases. In order to evaluate word embeddings
235 based on NERO, we identified two disease properties —(1) severity and (2) gender
236 specificity—and likewise two therapeutic drug properties —(1) toxicity and (2)
237 expense—not directly present in text, but highly relevant to diagnosis and treatment,
238 and on which text-independent ground truth data exists.

239 We embedded named entities associated with diseases and drugs into a high-
240 dimensional space in which every NERO term was assigned a 300-dimensional vector,
241 (see Figure 3 for a three-dimensional projection of this embedding), along with a
242 selection of diseases and medications used to treat them. We then compared drug and
243 disease projections into the embedding dimensions for severity, gender, toxicity, and
244 expense with ground truth about these qualities. We constructed the severe-mild axis
245 with the following contrasting term pairs: (harmful, beneficial), (serious, benign), (life-
246 altering, common), (disruptive, undisruptive), (dying, recovering), (dangerous, safe),
247 (threatening, low-priority), (high mortality, harmless), (costly, cheap), (hospitalized, self-
248 administered), (hospital, work), (debt, savings), (low quality of life, undisruptive), and
249 (hazard, routine). Then we compared disease projection in this dimension with World
250 Health Organization data on the burden of living with each of those diseases (DALYs²⁰)
251 and found a correlation of 0.329 ($p=0.0614$, $n=33$). We then constructed a gender
252 dimension with similarly contrasting pairs: (male, female), (prostate, ovary), (penile,
253 uterine), (penis, uterus), (man, woman), (men, women), (masculine, feminine), (he,
254 she), (him, her), (his, hers), (boy, girl), and (boys, girls). We compared the disease
255 projection in this gender dimension with the prevalence of those diseases for men and
256 women from a substantial sample of doctor-patient insurance records capturing
257 approximately 47% of all of U.S. doctor-patient visits between 2003 and 2011 and found
258 a correlation of 0.436 ($p=1.46 \times 10^{-13}$, $n=261$).

259 Together, these patterns suggest that not only does NERO facilitate efficient and
260 accurate concept-by-concept annotation, but that the distribution of biomedical
261 properties underlying NERO-annotated texts have emergent validity and predict data
262 patterns not explicitly present in biomedical articles. Following the same pattern, we
263 projected medications onto a toxicity axis composed from: (harmful, beneficial), (toxic,
264 nontoxic), and (noxious, benign) and an expense dimension anchored by: (expensive,
265 inexpensive), (costly, cheap), (brand, generic), and (patented, off-patent). The
266 correlation of drug projections onto the toxicity dimension correlates at 0.32 ($p=1.1 \times 10^{-4}$)
267 with the median lethal dose, or dose required to kill 50% of subjects as documented
268 in the LD50 database²¹. Finally, the correlation of drug projections into an expense
269 dimension and the price of each drug as listed in the IBM MarketScan database²² was
270 0.42 ($p=1.5 \times 10^{-15}$) (see Figure 4). When a disease projects low in the *male – female*
271 dimension, it is much more likely to afflict women than men, such as ornithosis and
272 related infectious diseases. When a disease projects high in the *serious – benign*
273 dimension like leprosy, it is likely to incur substantial suffering. When a medication
274 projects high in the *toxic – nontoxic* dimension, such as Riluzole, a treatment for
275 amyotrophic lateral sclerosis with potential severe side effects ranging from unusual
276 bleeding to nausea and vomiting. Drug projections high in the *expensive – inexpensive*
277 dimension suggest a stiff medical bill, as in the case of Simvastatin, which is used to
278 reduce the risk of heart attack and stroke, and which, before it went off-patent, cost
279 hundreds of dollars per bottle. The robust accuracy of these associations suggest that
280 for qualities on which we do not have relevant or inexpensive data outside text,
281 associations from text represent a significant signal for biomedical research and can be
282 considered robust hypotheses meriting empirical study.

283 This study's main limitation is that, even though our NERO ontology aimed to
284 cover all entities contained in the biomedical research literature, we did not cover all

285 levels of granularity in classifying entities. Moreover, while the major concepts are well-
286 annotated, several concept types were not well-represented because of the heavy-tail
287 distribution of ontological class frequencies. In addition, we note that satisfactory results
288 of Named-entity Recognition (NER) rely heavily on a large quantity of hand-annotated
289 data, which is often costly in terms of time and resources spent. Therefore, adoption of
290 semi-supervised learning methods, which incorporates unlabeled data to improve
291 learning accuracy, could reduce the need for manual annotation²³.

292 While there is popular belief that pretraining on general-domain text can be
293 helpful for developing domain-specific language models, a recent study has shown that
294 for specialized domains, such as biomedicine, pretraining on in-domain text from
295 scratch offers noticeable improvements in model accuracy compared to continual
296 pretraining of general-domain language models²⁴. Therefore, we trained on our
297 annotated corpus from scratch using in our machine learning experiments²⁵.

298 The resources offered in our study can be applied to a wide range of scientific
299 problems. First, the proposed NERO ontology can facilitate more robust and accurate
300 large-scale text mining of biomedical literature. As discussed above, NERO is the first
301 knowledge graph in this field, accounting for context-relevant levels of ambiguity. Graph
302 neural networks²⁶ can leverage such prior knowledge from human experts for learning
303 embedding of biomedical entities, which is likely to preserve both semantic meaning in
304 the original literature and domain knowledge from human experts. Second, researchers
305 can combine the curated corpus from this study with self-supervised learning²⁷. Such a
306 learning scenario can utilize the unlabeled data in a supervised way by predicting part of
307 the sentence using the rest of the sentence. The annotated corpus from this study can
308 be used to fine-tune language models, orienting them for critical biomedical tasks.

309

310 Competing interests

311 The authors declare that they have no competing financial interests.

312

313 Acknowledgments

314 We are grateful to E. Gannon and M. Rzhetsky, for comments on earlier versions of this
315 manuscript. This work was funded by the DARPA Big Mechanism program under ARO
316 contract W911NF1410333, by National Institutes of Health grants R01HL122712,
317 1P50MH094267, and U01HL108634-01, and by a gift from Liz and Kent Dauten.
318 Additional support came from King Abdullah University of Science and Technology
319 (KAUST), awards number FCS/1/4102-02-01, FCC/1/1976-26-01, REI/1/0018-01-01,
320 and REI/1/4473-01-01.

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396

397 Figure Legends

398

399 **Figure 1.** Named Entity Recognition Ontology (NERO). The Ontology is shown here as
400 a multifurcating tree, with taxonomy nodes corresponding to ontology classes. Class
401 name and class mentions count in the corpus are shown in parentheses next to each
402 named entity class. Each taxonomy class is provided with a unique pictogram (black
403 and red shapes on yellow background) intended to simplify expert manual annotation of
404 the corpora. In total, we annotated 35,865 sentences. These sentences encapsulated
405 190,679 named entities and 43,438 events connecting two or more entities. In addition
406 to the almost two dozen, more sparsely-used branches (such as *ExperimentalFactor*
407 and *GeographicalLocation*) under the *NamedEntity* cluster, there are three heavily-
408 represented branches in our corpus: *AnatomicalPart*, *Chemical*, and *Process*. Slightly
409 more than half (51.6 percent) of all entities are from these three classes, with 26.6
410 percent of all entities originating from *Process* alone. We designed our ontology and its
411 annotations to capture the named entities associated with research activities and
412 facilities; these types of entities can be important for encoding methods used in

413 scientific experiments or patient treatment. The semantic classes *ResearchActivity* and
414 *MedicalProcedures* turn out to be the ninth and the tenth most frequent, respectively.
415 Other top concepts related to research include *Measurement*, *IntellectualProducts*,
416 *PublishedSourceOfInformation*, *Facility*, and *MentalProcess*.
417

418 **Figure 2. The relative abundance of annotated named entity classes in our**
419 **corpus.** As is typically the case with human languages, semantic classes are
420 represented unevenly in free texts, following a heavy-tail (Zipf's) distribution. (A) In
421 biomedical corpora, unsurprisingly, named entities associated with *genes* and *proteins*
422 are the most prevalent (15 percent), followed by *processes* (9 percent), *medical findings*
423 (8.8 percent), and *chemicals* (6.7 percent). At the low-frequency end of the named entity
424 spectrum, we find *journal names*, *units*, *citations*, and *languages*. (B) Events connecting
425 two or more entities are also approximately Zipf-law distributed. Event frequencies are
426 closely tracking corresponding named entity classes. For example, the most frequent
427 event, *bind*, is associated with the most frequently named entity, *GeneOrProtein*. We
428 tried fitting the rank-ordered frequency distribution of annotated named entities with a
429 Discrete Generalized Beta Distribution (DGBD). The result showed a significant
430 deviation from Zipf's law²⁸. The observed distribution's tail was not heavy enough to
431 match Zipf's distribution, most likely due to the relatively small number of classes in our
432 ontology.²⁹ In other words, we expect that frequencies of semantic classes in a very
433 large corpus, annotated with classes from a hypothetical perfect named entity ontology,
434 would follow a Zipfian (discrete Pareto) distribution of named entity classes. Our action
435 annotations have moved beyond interactions between proteins and genes (e.g., *bind*,
436 *inhibit*, *phosphorylate*, *encode*), into interactions involving genetic variants and
437 environmental factors (e.g., *associated with*, *occur in presence of*, *trigger*, *lack*).
438 Ambiguity levels varied broadly across the named entities captured in our corpus. For
439 example, in the class *AnatomicalPart*, almost all (99.3 percent) are annotated at the
440 most specific levels, with the majority of entities belonging to *BodyPart*,
441 *CellularComponent*, and *Cell*. In contrast, the general (most vague) concept, *Chemical*,
442 turns out to be the most annotated within its cluster, although more specific subclasses,
443 such as *Protein*, *NucleicAcid*, and *Drug* are also well represented in the corpus. In the
444 *Process* concept cluster, about a third of all concept instances are annotated at a more
445 general *Process* level, and the rest of them are specific concepts, such as
446 *MedicalProcedure*, *MolecularProcess*, *ResearchActivity*, and *BiologicalProcess*. In
447 addition to these major clusters of concepts, several individual concepts are well
448 represented in the corpus. For example, *MedicalFinding* represents 7.3 percent of all
449 entities. Other well-represented concepts include *Duration*, *IntellectualProduct*,
450 *Measurement*, *Organism*, *PersonGroup*, *PublishedSourceOfInformation*, and *Quantity*.
451 In total, about 70.4 percent of all entities are annotated at the most specific ontology
452 level. There are five concepts in the NERO ontology that allow the semantic flexibility
453 needed to avoid arbitrary concept assignment. Entities annotated as
454 *AminoAcidOrPeptide*, *QuantityOrMeasurement*, *PublicationOrCitation*
455 *MedicalProcedureOrDevice*, and *GeneOrProtein* account for 17.8 percent of all entities,
456 while less than a quarter (23 percent) of entities representing either genes or proteins
457 are cleanly annotated with class *Gene* or class *Protein*. The remainder are annotated
458 with class *GeneOrProtein*. In addition to the action *bind*, actions indicating entities'

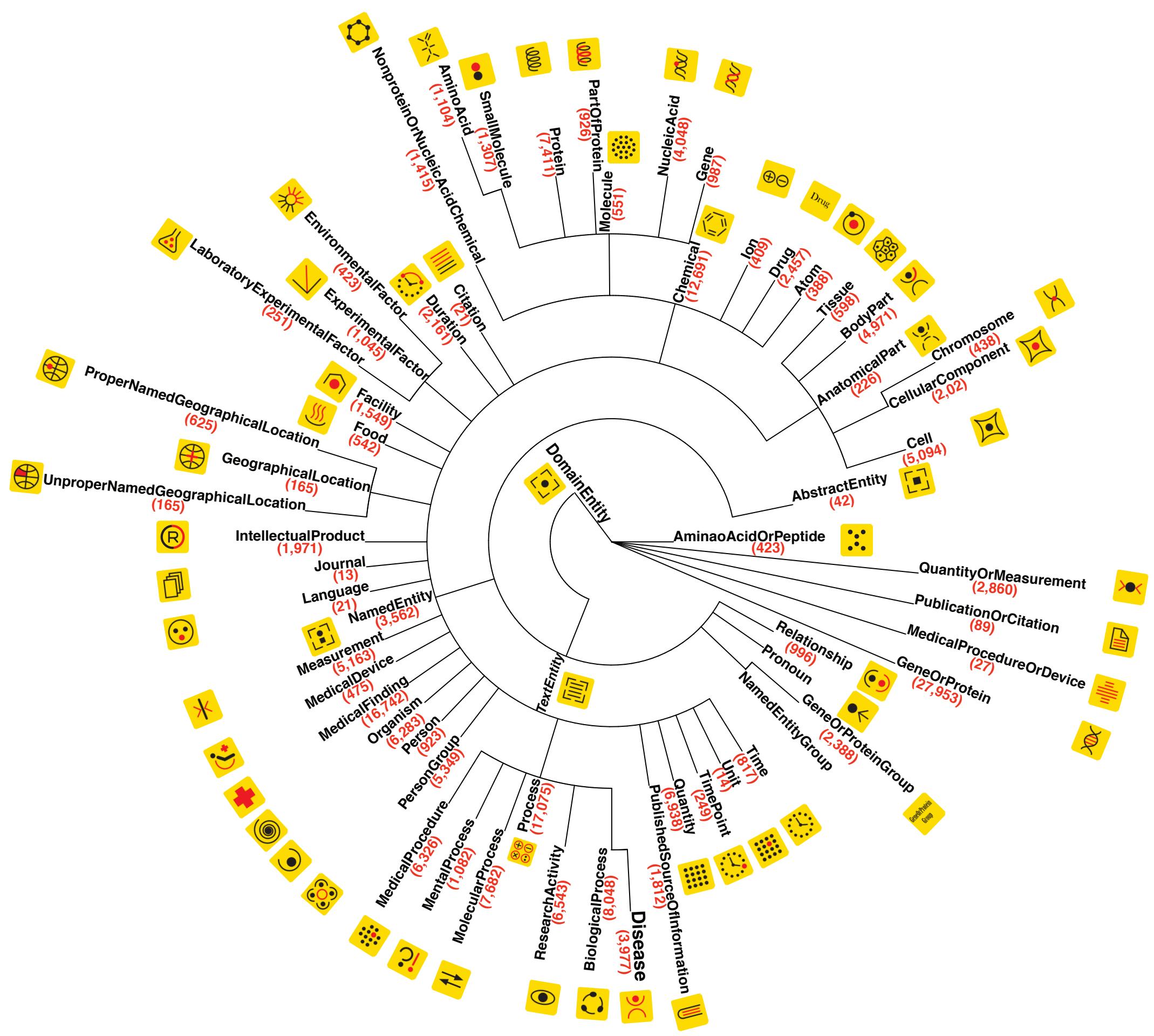
459 attributes are the next most frequent. Other biological relationships are also well-
460 represented in this annotation, such as *inhibit*, *activate*, *mediate*, *interact*, *contain*, and
461 *regulate*. The top 30 action categories account for 64.4 percent of all actions annotated
462 with the top ten action categories accounting for 52.2 percent. Interestingly, negations of
463 actions were also quite abundant in our annotated corpus. For example, *do not bind*
464 was the sixth most frequent normalized action. Other well-represented negations of
465 actions include *do not affect* and *do not inhibit* (see *Supplementary Figure 1*).
466

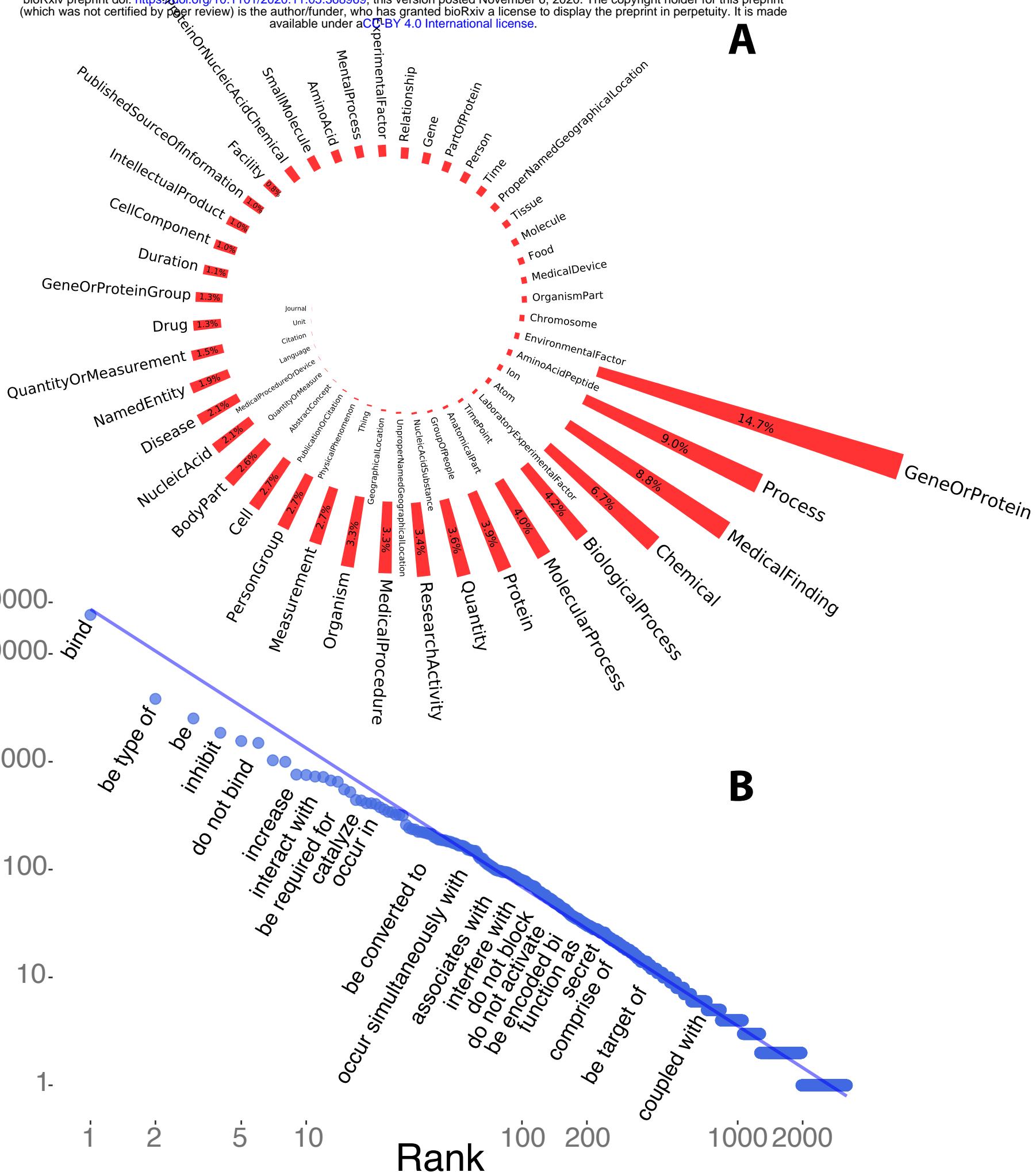
467 **Figure 3.** Properties of diseases and drugs visible in the first three principal
468 components of our multi-dimensional text embedding. The figure shows a projection of
469 text embedding into three-dimensional space, with named entities corresponding to
470 diseases and drugs shown with prisms and spheres, respectively. The figure represents
471 several projections of the same embedding, preserving spatial layout and projection,
472 with distinct elements of the embedding indicated by shape color. The central image
473 shows all disease systems and their corresponding medications together. More
474 specifically, the additional projections show: (A) Zollinger-Ellison syndrome and
475 associated medications; (B) cancers and associated therapies; (C) central nervous
476 system diseases and corresponding medications, and; (D) and (E) Viral and bacterial
477 infectious diseases, respectively, together with corresponding antiviral and antibiotic
478 agents. Another view of the same dataset is presented in Figure 4.
479


480 **Figure 4. Two-dimensional projections of diseases and medications. (A) We**
481 **projected diseases into two dimensions: female-male (X-axis) and severe-mild (Y-**
482 **axis).** We defined the “male-female” axis using the following pairs of terms: (‘male,’
483 ‘female’), (‘prostate,’ ‘ovary’), (‘penile,’ ‘uterine’), (‘penis,’ ‘uterus’), (‘man,’ ‘woman’),
484 (‘men,’ ‘women’), (‘masculine,’ ‘feminine’), (‘he,’ ‘she’), (‘him,’ ‘her’), (‘his,’ ‘hers’), (‘boy,’
485 ‘girl’), and (‘boys,’ ‘girls’). We defined the severe-mild axis with the following term pairs:
486 (‘harmful,’ ‘beneficial’), (‘serious,’ ‘benign’), (‘life-altering,’ ‘common’), (‘disruptive,’
487 ‘undisruptive’), (‘dying,’ ‘recovering’), (‘dangerous,’ ‘safe’), (‘threatening,’ ‘low-priority’),
488 (‘high mortality,’ ‘harmless’), (‘costly,’ ‘cheap’), (‘hospitalized,’ ‘self-administered’),
489 (‘hospital,’ ‘work’), (‘debt,’ ‘savings’), (‘low quality of life,’ ‘undisruptive’), and (‘hazard,’
490 ‘routine’). **(B)** We projected medications into “benign-toxic” (X-axis) and “cheap-costly”
491 (Y-axis). For the “benign-toxic” axis, we used the following pairs of antonym words:
492 (‘harmful,’ ‘beneficial’), (‘toxic,’ ‘nontoxic’), and (‘noxious,’ ‘benign’). We defined the
493 “expensive–inexpensive” dimension using the following pairs of terms: (‘expensive,’
494 ‘inexpensive’), (‘costly,’ ‘cheap’), (‘brand,’ ‘generic’), and (‘patented,’ ‘off-patent’).
495

496 **Table 1. Inter-annotator Agreement Statistics.**
497

Agreement Type	IAA (%)
Exact Match	86.49
Relaxed Match	93.66
Exact Match	86.56
Parent Match	87.66
Superclass Match	86.72
Ambiguity Match	97.58







Diseases

Drugs

