Information based clustering: Supplementary material

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This technical report provides the supplementary material for a paper entitled “Information based clustering” to appear shortly in Proceedings of the National Academy of Sciences (USA). In Section I we present in detail the iterative clustering algorithm used in our experiments and in Section II we describe the validation scheme used to determine the statistical significance of our results. Then in subsequent sections we provide all the experimental results for three very different applications: the response of gene expression in yeast to different forms of environmental stress, the dynamics of stock prices in the Standard and Poor’s 500, and viewer ratings of popular movies. In particular, we highlight some of the results that seem to deserve special attention. All the experimental results and relevant code, including a freely available web application, can be found at [http://www.genomics.princeton.edu/biophysics-theory](http://www.genomics.princeton.edu/biophysics-theory).

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I. THE ICLUST ALGORITHM

Although clustering is a widely used method of data analysis and exploration, there is at present no unique or universal mathematical formulation of the clustering problem. In practice, clustering a given data set involves many choices at different levels of the analysis. In recent work we suggest that some generality can be achieved through the use of information theory \(I\). Here we review this formulation briefly and then proceed to the technical details of its implementation that were left out of Ref \(I\).

We formulate clustering as a tradeoff between maximizing the mean similarity of elements within a cluster and minimizing the complexity of the description provided by cluster membership. Thus if we have some similarity measure \(s(i,j)\) between elements \(i\) and \(j\), optimal clustering is a probabilistic assignment to clusters \(C\) according to \(P(C|i)\) such that we maximize

\[
\mathcal{F} = \langle s \rangle - TI(C; i),
\]

where \(\langle s \rangle\) is the mean similarity of elements chosen at random out of each cluster,

\[
\langle s \rangle = \sum_i \frac{1}{C} \sum_j P(C|i)P(j|C)s(i,j),
\]

and \(I(C; i)\) is the information that clusters provide about the identity of their elements,

\[
I(C; i) = \sum_i \sum_j P(C|i)P(i) \log \left( \frac{P(C|i)}{P(C)} \right);
\]

as usual we have

\[
P(i|C) = P(C|i)P(i) \cdot \frac{1}{P(C)},
\]

\[
P(C) = \sum_i P(C|i)P(i),
\]

and since in many cases all examples \(i\) occur with equal probability \([P(i) = 1/N]\) we consider this case for simplicity, although it is not essential. This formulation can be generalized to handle similarity measures defined on groups of more than two elements \(I\), but here we concentrate on the conventional case where only pairwise
interactions are considered. Importantly, as opposed to using a problem specific similarity measure \( s \), we use the generality of information theory once more, and take \( s(i, j) \) to be the pairwise mutual information \( I_{ij} \) between the observed patterns that correspond to data items \( i \) and \( j \).\(^1\)

It is shown in Ref \(^1\) that any stationary point of our target functional, \( F \), must obey

\[
P(C| i) = \frac{P(C)}{Z(i; T)} \exp \left\{ \frac{1}{T} [2s(C; i) - s(C)] \right\}, \tag{6}
\]

where \( Z(i; T) \) is a normalization function, \( s(C; i) \) is the expected similarity between \( i \) and a member of cluster \( C \),

\[
s(C; i) = \sum_{i_1 = 1}^{N} P(i_1|C)s(i_1, i), \tag{7}
\]

and \( s(C) \) is the average similarity among pairs chosen independently out of the cluster \( C \),

\[
s(C) = \sum_{i_1 = 1}^{N} \sum_{i_2 = 1}^{N} P(i_1|C)P(i_2|C)s(i_1, i_2). \tag{8}
\]

Eq. \(^6\) defines an implicit set of equations since the right hand side depends on \( P(i|C) \) and \( P(C) \). This is a common situation in variational methods, also present, for example, in conventional rate-distortion clustering \(^3\), in maximum likelihood estimation with hidden variables \(^4\) and in the Information Bottleneck framework \(^5\). The standard strategy is to turn the self-consistency condition into an iterative algorithm. Specifically, let us denote the intermediate solution of the algorithm at the \( m \)th iteration by \( P^{(m)}(C| i) \). Then, at the \( m + 1 \)st iteration, the algorithm applies the following update rule:

\[
P^{(m+1)}(C| i) \leftarrow P^{(m)}(C) \exp \left\{ \frac{1}{T} [2s^{(m)}(C; i) - s^{(m)}(C)] \right\}, \tag{9}
\]

followed by a normalization step. Notice that the terms \( \{ P^{(m)}(C), \ s^{(m)}(C; i), \ s^{(m)}(C) \} \) all are calculated using \( P^{(m)}(C| i) \). Pseudo-code for this algorithm is given in Figure \( \textit{1} \). It is easy to verify that with a straightforward implementation, the complexity of this algorithm is \( O(N^3 \cdot N_c) \) for a single pass over the entire data set, where \( N_c \) is the number of clusters. We will refer to this algorithm as the \textit{Iclust} algorithm.

To gain some intuition let us consider a typical situation where \( i \) is relatively similar to elements in \( C \), but very different from elements in \( C' \). Thus, the exponent in Eq \(^6\) will be positive for \( i \) and \( C \), but might be negative for \( i \) and \( C' \). Consequently, while applying the update step the weight of assignment of \( i \) to \( C \) \[ P(C| i) \] will be boosted while its assignment to \( C' \) will be decreased. This is clearly a desirable outcome, which in particular should increase \( F \). Thus, since \( F \) is upper bounded (as a sum of information terms), after a finite number of such updates the algorithm is expected to converge to a fixed point which corresponds to a (possibly local) maximum of \( F \).

This example also illustrates one of the differences between our algorithm and previous approaches. While in the Blahut–Arimoto algorithm in rate–distortion theory \(^6\), in the iterative Information Bottleneck algorithm \(^5\), and typically also in EM for maximum likelihood \(^4\), the sign of the exponent is constant (for a given \( i \)), this is not true in our case. In principle, such a non–constant exponent sign should imply faster convergence to a local stationary point, but might also imply higher sensitivity to the random initialization of \( P(C| i) \). Thus, as in other work, we typically perform several runs with different random initializations of \( P(C| i) \) from which we choose the best solution, \( i.e. \), the one that maximizes \( F \).

The \textit{Iclust} algorithm presented here uses a sequential, or incremental iterative procedure in which the updates for some \( i \) incorporate the implications of the updates for preceding elements, \( i' \neq i \). As a simple example, consider the case where we have three elements \( (N = 3) \) and two clusters \( (N_c = 2) \). We start from some random conditional distribution matrix, \( P(0)(C| i) \), which in particular defines \( s(0)(C), \forall C = 1:2 \). At the first iteration we find a new distribution for the first element \( (i = 1) \) over the two clusters. Thus, we now have a new conditional distribution matrix, \( P(1)(C| i) \) which differs from the previous \( P(0)(C| i) \) only by its first row. This distribution is used to define \( s(1)(C), \forall C = 1:2 \). Now, in the next iteration, we find a new distribution for the second element \( (i = 2) \) over the two clusters. This yields another new conditional distribution matrix, \( P(2)(C| i) \) which differs from the previous \( P(1)(C| i) \) only by its middle row, and so on. This process is somewhat in the spirit of the incremental EM \(^4\) and the sequential Information Bottleneck algorithm \(^5\). An alternative optimization routine, which seems less natural in our case, would be parallel optimization, used \( e.g. \), in standard EM \(^4\). In this case, if we continue our example, at the first iteration we will update \( all \) the rows in the conditional distribution matrix, \( P(0)(C| i) \) using \( s(0)(C) \), to find the new \( P(1)(C| i) \).

In some extreme cases the above algorithm might produce a non–monotonic behavior in \( F \). That is, some of the updates might reduce \( F \), suggesting that obtaining a general proof of convergence is a challenging goal. Nonetheless, even in these extreme cases, and more generally in all our experiments (which included more than 1000 runs over real world problems with different \( T \) values and different numbers of clusters), the algorithm always converged to a stationary point. Moreover, for the regime \( T \geq \max_{i,j} s(i_1, i_2) \) it is possible to prove this

\(^1\) This report does not deal with the technical details of estimating mutual (and multi) information from empirical data. The reader is referred to \(^3\) for a complete description of the estimation procedure used in our experiments.
convergence analytically (the details will be presented elsewhere).

II. EVALUATING CLUSTERS’ COHERENCE

The central question in clustering is whether an essentially unsupervised analysis of a data set can recover categories that have “meaning.” In practice we assess this by comparison with some set of labels for the data that were generated by human intervention. To get started, then, we need a set of annotations (or labels) provided for every data item we clustered. Importantly, these annotations are not used during the clustering process but rather are exposed only for the post–clustering validation. Every data item might be assigned more than one annotation via different sources of information. The assumption is that these annotations reflect to some extent the “real” structure of the data that one wishes to reveal through the clustering process.

To be more concrete, let us assume that we clustered \( N \) elements, where each one of these elements is assigned some set of annotations. Formally, this could be represented through an annotation matrix, denoted as \( A \), with \( N \) rows and \( R \) columns, where \( R \) is the number of distinct annotations in our data. Thus, \( A(i,j) = 1 \) if and only if the \( i \)-th element is assigned annotation \( a_j \), and zero otherwise. A simple example is given in Table I.

When we examine a single cluster, consisting of \( n < N \) elements, the first question we might ask is whether some annotations occur in this cluster with a “suspiciously” high frequency. Let us consider a specific annotation \( a_j \) that is assigned to \( K \leq N \) elements in the entire population and to \( x \leq n \) elements in the cluster. The probability of this event, under the null hypothesis that elements are assigned to clusters at random, is given by the hypergeometric distribution:

\[
P_{\text{hyper}}(x \mid n, K, N) = \binom{K}{x} \binom{N-K}{n-x} / \binom{N}{n}.
\]

The corresponding \( P \)-value is defined as the tail of this distribution:

\[
P_{\text{val}}(x \mid n, K, N) = \sum_{x' = x}^{\min(K,n)} P_{\text{hyper}}(x' \mid n, K, N).
\]

In words, it is the probability of observing \( x \) or more elements in the cluster with annotation \( a_j \) where the members of the cluster are chosen independently of this annotation. Alternatively, it is the probability of wrongly rejecting the hypothesis that the cluster has nothing to do with the annotation \( a_j \). The smaller the \( P \)-value the more unlikely this null hypothesis becomes. To gain some intuition, several examples are presented in Table I.

Having defined the statistical significance of a single event we need to bear in mind that in a single cluster one typically observes several (perhaps many) different annotations. Naturally, the more hypotheses one tests the less surprising it is to find one with a small \( P \)-value, even in a randomly chosen cluster. The simplest and most conservative approach to correct for this multiple hypotheses testing effect is to apply the Bonferroni correction (see, e.g., (3)). Specifically, if the statistical significance level is \( q \) (e.g., \( q = 0.05 \)), an event is considered significant if and only if its \( P \)-value satisfies:

\[
P_{\text{val}} < \frac{q}{H},
\]

where \( H \) is the number of hypotheses being tested. We will say that a cluster is enriched with the annotation if the corresponding \( P \)-value satisfies Eq. (12).

Finally, while the above procedure determines the significance of every annotation that occurs in the cluster, it also is useful to have a single score that roughly summarizes how homogeneous the cluster is with respect to all annotations. Different alternatives have been proposed to this end and here we use the coherence score, suggested by Segal et al. (4),

\[
\text{coh}(C) \equiv 100 \cdot \frac{n_{\text{enriched}}}{n},
\]

where \( n \) is the number of items in the cluster \( C \), and \( n_{\text{enriched}} \) is the number of items in \( C \) with an annotation that was found to be significantly enriched in \( C \). In other words, the coherence of a cluster is simply the percentage of the cluster’s elements covered by some annotation that was found to be enriched in that cluster. In particular, a coherence value above zero means that at least one annotation is enriched in the cluster, namely that there is at least a single hint regarding the reason for forming this cluster.

III. FIRST APPLICATION: THE YEAST ESR DATA

A. Description of the data

We considered experiments on the response of gene expression levels in yeast to various forms of environmental stress (10). Previous analysis of expression patterns from all \( \sim 6000 \) genes identified a group of 283 stress–induced and 585 stress–repressed genes that had apparently “nearly identical but opposite” expression profiles (10). This collection of 868 genes was thus termed the yeast environmental stress response (ESR) module. As seen in Figure 2, differences in expression profiles within the ESR module indeed are relatively subtle. More recent manual analysis with attention to background biological data suggests that some of these differences are biologically significant (11). Thus, it seems a good challenge for our approach to ask if we can discover automatically any meaningful substructure in these data.

Each of the 868 ESR genes was represented by its log–ratio expression profile in the 173 microarray experiments (10), available at
From these data we estimated all the $\sim 376,000$ pairwise mutual information relations $I_{ij}$, as described in \(^2\), ending up with a $868 \times 868$ matrix which defined the input to our clustering procedure. For convenience, we provide here some statistics of the estimated mutual information values. For a complete description, including different verification schemes that support the reliability of our estimates, the reader is referred to (2).

Across all pairs of genes, the average estimated mutual information was 0.48 bits with a variance of 0.0425 bits\(^2\). This relatively high average value corresponds to the strong positive/negative linear correlations known to be present in these data. Almost 7,000 pairs had a mutual information greater than 1 bit, and the maximal estimated mutual information was 1.58 bits. All the pairwise mutual information relations are presented in Figure 3, where the genes are sorted according to the clustering partition into $N_c = 20$ clusters that we analyze in detail (see below). The diagonal elements of this matrix, or self-information, were set to $I_{ii} = \log_2(5)$, the maximal possible information under a quantization into five bins \(^2\).

### B. Quality–complexity trade–off curves

Given the pairwise mutual information matrix we applied the Iclust algorithm described in Section 1. Recall that our target functional, $\mathcal{F}$, is given by:

$$\mathcal{F} = \langle s \rangle - T I(C;i), \quad (14)$$

where $T$ is a (temperature) trade–off parameter,

$$\langle s \rangle = \sum_{C=1}^{N_c} P(C) \sum_{ij} P(i|C)P(j|C)I_{ij} \quad (15)$$

measures the quality of the clusters, and $I(C;i)$ measures the cost of coding cluster identity.

For a fixed number of clusters, $N_c$, the term $\langle s \rangle$ gradually saturates as the temperature $T$ is lowered, while $I(C;i)$ increases accordingly. We explored this trade–off for different numbers of clusters: $N_c = 5, 10, 15, 20$. For each of these values we tried several values of $T$; we found that $1/T = \{5, 10, 15, 20, 25\}$ typically suffices to obtain a relatively clear saturation of $\langle s \rangle$, hence we present the results for these $T$ values.

For each $\{N_c, T\}$ pair we performed 10 different random initializations, ending up with 10 (possibly) different local maxima of $\mathcal{F}$, from which we chose the best one. The resulting trade–off curves are presented in the left panel of Figure 4. For a given $N_c$, as $T$ is lowered, $\langle s \rangle$ increases but so does $I(C;i)$. In addition, the solutions become more deterministic. For example, for $N_c = 20$ and $1/T = 15$, only $\sim 44\%$ of the genes have nearly deterministic assignment $[i.e., \ P(C|i) > 0.9$ for a particular $C]$. For $1/T = 25$ this percentage grows to $\sim 85\%$.

The entire continuum of solutions, represented by the trade–off curves, may encompass a lot of insights about the data. Nonetheless, for brevity, we focus our analysis on solutions for which the saturation of $\langle s \rangle$ is relatively clear, i.e., on the four solutions with $N_c = \{5, 10, 15, 20\}$ and $1/T = 25$. In all these partitions most of the genes (between 75% to 85%) had a nearly deterministic assignment $[P(C|i) > 0.9$ for a particular $C]$. In the rest of the analysis we treat these solutions as hard (i.e., deterministic) partitions where every gene is assigned solely to its most probable cluster. In the next section we explore the possible hierarchical relations between these four solutions. In later sections we analyze in detail the specific solution with $\{N_c = 20, 1/T = 25\}$ that obtained the highest value of $\langle s \rangle$.

### C. Comparing solutions at different numbers of clusters

A common dichotomy in the cluster analysis literature is between hierarchical and non–hierarchical, or partitioning clustering algorithms [see, e.g., Ref (13)]. What is often missed, though, is the fact that applying a hierarchical clustering algorithm typically enforces the output to be of a hierarchical nature, regardless of whether the data indeed call for this view. For example, applying an agglomerative clustering algorithm to the ESR data will produce, by definition, a nested tree–like hierarchy of partitions, although \textit{a priori} it is not obvious whether the functional classification of these genes should be of a hierarchical nature.

Because our approach is not constrained to hierarchical structures, the emergence of even an approximate hierarchy would be a genuine result. To test for this, we start with several solutions that were found independently at different numbers of clusters and ask to what extent these solutions form a hierarchy. This is done in two steps. First, for every cluster we identify its best parent in the next (less detailed) level. Specifically, if $C$ is some cluster at a partition with $N_c$ clusters, then its best parent in a less detailed partition with $N_c' < N_c$ clusters will be the one that includes the maximal number of $C$ members. Second, we measure how well this parent includes its child and represent the result through the type of the edge that we draw between the two clusters.

The hierarchical graph produced by this scheme is different from the standard output of hierarchical clustering algorithms in several aspects. To start, a cluster might have more than one parent if its members are equally distributed among several clusters in the less detailed partition. Next, a cluster might have no children if it is not the best parent of any cluster at the more detailed partition. Last, the characteristics of the edges convey further in-
formation regarding how well the independent solutions form a hierarchy. In particular, a graph with many high quality inclusion edges is a good indication that the data are hierarchical in nature. In contrast, a graph in which many of the inclusions from one level to the other are only partial suggests that a hierarchical view of the data is somewhat misleading.

We applied this scheme to the four solutions we obtained independently for $N_c = \{5, 10, 15, 20\}$ with $1/T = 25$. The results are presented in Figure 5. As can be seen in the figure, the independent solutions form an approximately hierarchical structure. Interestingly, some functional modules are better preserved than others across the different levels. For example, the ribosome cluster, c18, clearly is identified at all the independent solutions.

D. Coherence results

1. Constructing the annotation matrices

As already mentioned, clusters’ coherence is estimated with respect to a given annotation matrix. For yeast genes, different sources of information may provide these data. One important resource is the Gene Ontology (GO) database (13), which is the one that we use in this work; specifically, we used the December 2003 version.

The GO database consists of three structured ontologies (controlled vocabularies) that describe gene products in terms of their associated Biological Processes (GOBP), Molecular Functions (GOMF), and Cellular Components (GOCC). For each of these three ontologies we constructed a corresponding annotation matrix. Thus, for example, if $A_{BP}$ is the matrix constructed for the GOBP ontology then $A_{BP}(i,j) = 1$ if and only if the i-th gene in our data is assigned to the j-th biological process. A small subset of this annotation matrix is presented in Table 11.

Each of the GO ontologies is organized in a hierarchical manner where more specific annotations correspond to nodes which are more distant from the ontology root. This might yield evaluation difficulties if one considers only the particular GO terms with which a gene is annotated (14). An example is given in Table 11. Here, several genes that were all assigned to the same cluster are annotated with different specific GOBP terms, and their functional relationship becomes evident only if one notices that all these annotations have a common (more general) ancestor in the ontology. We applied a standard routine to overcome this difficulty, in which every gene was assigned not only its direct GO annotations but also all the ancestors of these annotations in the GO hierarchy. This is consistent with the GO organization, in which if a GO term describes some gene product then all its parent terms in the ontology also apply to that gene product.

Last, while estimating clusters’ coherence we removed annotations that were assigned to less than two genes in our data, since these annotations obviously can not be enriched in any cluster. We also removed from the analysis genes that were not assigned any annotations, or assigned the unknown annotation. The details of the resulting annotation matrices are given in Table 11.

2. Coherence results and comparisons

We estimated the statistical coherence of the clusters obtained at the low–temperature end of the trade–off curves where $1/T = 25$. This coherence was estimated with respect to each of the three Gene Ontologies. To gain some perspective, we applied similar analysis with a recent release of the Cluster software, called Cluster 3.0 (15). This software is considered to be a state–of–the–art (and quite popular) tool for cluster analysis of gene expression data. We experimented extensively with all the basic algorithms available in this package. These include two different variants of iterative K–means clustering (K–means and K–medians) and four different variants of hierarchical clustering (Complete linkage, Average linkage, Centroid linkage, and Single linkage). With each of these algorithms we tried three standard similarity measures: the Pearson correlation (“centered correlation”) 30, the absolute value of the Pearson correlation, and the Euclidean distance. Thus, altogether we compared our performance to 18 different configurations of this software which are probably the most commonly used configurations. For the six K–means variants we tried 100 different random initializations in every run, from which the best solution (the one with the smallest sum of within–cluster distances) was chosen. The comparison was undertaken at all the different numbers of clusters, $N_c = 5, 10, 15, 20$. The results are summarized in Table VI to Table IX. The average results are given Figure 6.

In all cases the Iclust algorithm was clearly superior to all of the 12 hierarchical algorithms we tried. It should be stressed that these algorithms are considered a powerful tool for analyzing genomic datasets, and many published applications are based on this type of hierarchical analysis. Nonetheless, standard hierarchical clustering typically failed to see a significant substructure in the ESR module. In most cases Iclust was also superior to the average performance of the six K–means variants, and in some cases (e.g., $N_c = 5$) it was in fact superior to all the K–means variants. Averaging over all three Gene Ontologies and over all four $N_c$ values, Iclust obtains a coherence of $\sim 56\%$ while the average K–means coherence is $\sim 42\%$ and the average Hierarchical coherence is $\sim 12\%$.

We further repeated this comparison with all the competing algorithms while considering the log2 ratios of expression profiles as input, instead of the raw ratios. Even with this preprocessing (to which our approach is invariant), the Iclust average performance is superior to almost all the 18 alternatives, typically by a significant
margin. Specifically, when averaging over all three Gene Ontologies and over all four $N_c$ values, the average $K$–means coherence is $\sim 52\%$ and the average Hierarchical coherence is $\sim 19\%$. While there exists some intuitive motivation for the log$_3$ preprocessing, there is no formal justification. Clearly, from a principled point of view, an approach which is invariant to such transformations is preferable, even if it were to generate only comparably good results.

E. Detailed results for $N_c = 20$ clusters

In Table X we present all enriched annotations for the Iclust partition with $N_c = 20$ clusters and $1/T = 25$. Further examination of these clusters yields several observations that allow us to see in more detail what makes these clusters meaningful solutions to our problem.

First, in several cases the extracted clusters consist of genes from both the nominal induced and repressed groups. For example, $c_5$ consists of 26 induced genes (enriched with oxidoreductase activity) and 6 repressed ones. In Figure 7A we see that the genes in this cluster have a relatively augmented response under Menadione exposure and a relatively reduced response in a stationary phase, as opposed to genes not in this cluster.

In Figure 7B we display the average behavior of the 22 induced genes in $c_8$ versus the 49 induced genes in $c_9$ in two opposing temperature shifts. Although all are induced by heat, the genes in $c_9$ are more sensitive to this treatment which is consistent with the enrichment of heat shock protein activity in this cluster.

Cluster $c_{18}$ consists of 122 repressed genes which were mainly ribosomal proteins. In Figure 7C we see that the genes in this cluster exhibit a distinguished transient expression pattern under, e.g., Diamide treatment, a fact that was already mentioned in 11. On the other hand, cluster $c_{16}$ consists of 87 repressed genes and is enriched for ribosome biogenesis and other related annotations. In the same figure we see that this cluster exhibits another distinctive behavior with respect to the rest of the repressed genes.

In Figure 7D we consider again two clusters, $c_2$ and $c_7$, which seem to involve ribosomal proteins and ribosome biogenesis, respectively. As seen in the figure, when the cells converge to a quiescent state under Nitrogen depletion, these two clusters exhibit quite different behaviors.

In Figure 7E we see another intriguing behavior of two clusters, $c_{15}$ and $c_{17}$, under steady–state growth at different temperatures. From the GO annotations we find that $c_{15}$, which includes 12 repressed genes, is enriched for tRNA aminoacylation, while $c_{17}$ which includes 7 repressed genes is enriched with cell cycle related annotations. Figure 7F demonstrates that the distinction between these two clusters is not spurious, as they display different behaviors, e.g., in response to hyper-osmotic shock.

As two complementary validation schemes we used the regulator–promoter region interactions reported in 17, and the DNA–binding sequence motifs provided in 18. In most of our clusters we found enrichment of regulatory interactions and/or known sequence motif in the corresponding upstream sequences ($Pval < 0.05$, Bonferroni corrected). For example, $c_5$, $c_{19}$, and $c_{17}$ were enriched for YAP1, HSF1, and MBP1, respectively. As YAP1 is known to be involved with response to oxidative stress, HSF1 with response to heat, and MBP1 with cell cycle regulation, these enrichments are clearly in consistent with the GO enrichments for the same clusters. $c_{18}$ and $c_2$ (Figs. 4C,D) were enriched with FHL1 which is required for rRNA processing, and $c_{18}$ was further enriched with RAP1 – known to be involved in regulating ribosomal proteins, and with four other regulators (GAT3, YAP5, PDR1, and RGM1), suggesting similar, yet not identical regulatory programs for these two functionally related clusters. $c_{16}$ was enriched for ABF1 and both $c_7$ and $c_{16}$ were enriched with several motifs which are known to be related to rRNA processing and synthesis, consistently with the GO annotations enriched for these clusters.

F. A cluster enriched with uncharacterized genes

In the statistical validation of our clusters (Section III), we removed from the analysis uncharacterized genes. Nonetheless, the distribution of the uncharacterized genes among our clusters yields an intriguing result. One might have suspected that almost every process in the cell has a few components that have not been identified, and hence that as these processes are regulated there would be a handful of unknown genes that are regulated in concert with many genes of known function. For at least one of our clusters, our results reveal a different picture.

Given the fraction of uncharacterized genes in a cluster and the corresponding fraction at the entire population, one can use the hypergeometric distribution to calculate a $P$-value for this event (see Section III). Applying this to our partition into $N_c = 20$ clusters we find that $c_7$ is significantly enriched with genes that are uncharacterized in the GO$_{BP}$ and GO$_{MF}$ ontologies.

Specifically, out of the 123 genes in $c_7$, 72 have an

3 In these data, every gene is “annotated” with 106 “$P$-value” scores that determine the probability of this gene being regulated by each of 106 yeast transcriptional regulators. By considering only interactions with a $P$-value lower than 0.005 we constructed out of these data an annotation matrix with 868 (gene) rows, 106 (regulator) columns and a total 1307 predicted interactions.

4 Here, again, one can construct an annotation matrix where $A(i,j) = 1$ if and only if the 1,000 base–pair promoter sequence of the i-th gene includes the j-th motif. After considering only the 100 most frequent motifs we ended up with an annotation matrix, with 868 (gene) rows, 100 (motif) columns and 19,517 predicted interactions.
unknown molecular function. This level of concentration has a \( P \)-value probability of \( \sim 10^{-8} \) to have arisen by chance. Moreover, if we consider only the repressed genes in the ESR module (since \( c7 \) consists mainly of such genes), we see that 69 out of the 114 repressed genes in \( c7 \) are uncharacterized in the GO\(_{MF}\) ontology, which has a \( P \)-value of \( \sim 10^{-15} \).

Closer examination of the GO\(_{BP}\) characterized genes in the same cluster reveals several enriched annotations (see Table \( \text{X} \)) related to ribosome biogenesis and ribosomal RNA processing, suggesting that most of the previously unannotated genes in this cluster are involved in these processes as well. Nonetheless, the extremely high concentration of uncharacterized genes in this cluster suggests that these genes are involved with biological processes which are harder to detect and characterize with the current technologies.

Finally, it is also worthwhile to point out that the cluster \( c7 \) is extremely conserved when one tries to find partitions with a smaller number of clusters, as demonstrated in Figure \( \text{B} \). In fact, all the parent clusters of this \( c7 \) cluster (for \( N_c = 5, 10, 15 \)) were similarly enriched for GO\(_{BP}\) and GO\(_{MF}\) uncharacterized genes.

IV. SECOND APPLICATION: THE SP500 DATA

A. Description of the data

In our second application we consider a very different data set, the companies in the Standard and Poor’s 500 list. We used the May 2004 listing of the 500 companies, available at [http://www.standardandpoors.com](http://www.standardandpoors.com). For these companies we examine the day-to-day fractional changes in stock price during the trading days between December 2, 2002, and December 31, 2003, (a total of 273 trading days), as seen in Figure \( \text{B} \).

From these data we estimated all the \( \sim 125,000 \) mutual information relations, as described in \( \text{B} \), ending up with a 500 \( \times \) 500 matrix \( f_{ij} \) which, as before, defines the input to our clustering procedure. For convenience, we provide here some statistics of the estimated mutual information values. For a complete description, including different verification schemes that support the reliability of our estimates, the reader is referred to \( \text{B} \).

Across all pairs of companies, the average estimated mutual information was 0.10 bits with a variance of 0.0054 bits\(^2\), and the maximal estimated mutual information was 0.97 bits. All the pairwise mutual information relations are presented in Figure \( \text{B} \) where the companies are sorted according to the clustering partition into \( N_c = 20 \) clusters that we analyze in detail (see below). The self-information relations were set to \( I_0 = \log_2(5) \) which corresponds to the maximal possible information under a quantization into five bins \( \text{B} \).

B. Quality–complexity trade–off curves

Given the pairwise mutual information matrix we applied the Iclust algorithm described in Section \( \text{B} \). As in the first application, we explored the trade–off between \( \langle s \rangle \) and \( I(C;i) \) for different numbers of clusters: \( N_c = 5, 10, 15, 20 \) and for different values of the trade–off parameter, \( T \). Specifically, we found that \( 1/T = \{15, 20, 25, 30, 35\} \) were typically sufficient to obtain a relatively clear saturation of \( \langle s \rangle \), hence we present the results for these \( T \) values. For each \( \{N_c, T\} \) pair we performed 10 different random initializations ending up with 10 (possibly) different local maxima of \( F \), from which we chose the best one. The resulting trade–off curves are presented in the middle panel of Figure \( \text{B} \).

As before, as \( T \) is lowered, \( \langle s \rangle \) increases but so does \( I(C;i) \). In addition, the solutions become more deterministic. For example, for \( N_c = 20 \) and \( 1/T = 25 \), only \( \sim 36\% \) of the companies have nearly deterministic assignment \(|P(C;i)| > 0.9\) for a particular \( C \). On the other hand, for \( 1/T = 35 \), all the assignments are nearly deterministic \( |P(C;i)| > 0.9\).

For brevity, we focus our analysis on solutions for which the saturation of \( \langle s \rangle \) is relatively clear, i.e., on the four solutions with \( N_c = \{5, 10, 15, 20\} \) and \( 1/T = 35 \). In all these partitions almost all of the companies had a nearly deterministic assignment \(|P(C;i)| > 0.9\) for a particular \( C \), so we treat these solutions as hard partitions where every company is assigned solely to its most probable cluster.

C. Comparing solutions at different numbers of clusters

We examine directly how well our independent solutions form a hierarchical structure. Accordingly, we apply exactly the same scheme as described in Section \( \text{B} \) to the four solutions we obtained independently for \( N_c = \{5, 10, 15, 20\} \) with \( 1/T = 35 \). The results are presented in Figure \( \text{B} \). Again, the independent solutions form only an approximate hierarchy. Nonetheless, this approximation seems more suitable in this case, as demonstrated, e.g., by the larger percentage of nearly perfect inclusion relations (solid bold edges in the figure). It should be noted that indeed the standard classification of these companies is hierarchical in nature (see Section \( \text{IV.B} \)).

Again, it is worthwhile to point out that some of the clusters are better preserved than others across the different levels. For example, the Semiconductor Equipment
cluster, c11, is clearly identified in all the independent solutions.

D. Coherence results

1. Constructing the annotation matrices

We used the Global Industry Classification Standard (GICS), which classifies companies at four different levels: sector, industry group, industry, and sub-industry (see [http://www.standardandpoors.com](http://www.standardandpoors.com)). These four levels are arranged in a well-defined, tree-like hierarchy. The bottom (sector) level consists of 10 different annotations: Consumer Discretionary, Consumer Staples, Energy, Financials, Health Care, Industrials, Information Technology, Materials, Telecommunication Services, and Utilities. The next (industry group) level consists of 24 distinct annotations. The next (industry) level consists of 59 distinct annotations. The last (sub-industry) level consists of 114 distinct annotations. Thus, altogether there are 207 different annotations where every company is assigned exactly four annotations, one at every level of the hierarchy.

As in the first application, while estimating clusters’ coherence we removed annotations that were assigned to less than two companies in our data, ending up with a total of 178 distinct annotations.

2. Coherence results and comparisons

We estimated the coherence of the clusters obtained at the low-temperature end of the trade-off curves where \(1/T = 35\). To gain some perspective, we applied a similar analysis to the results obtained with the Cluster 3.0 software. We experimented with the same 18 basic configurations as in the previous application (K-means variants, again with 100 different initializations), and applied the comparison to all the different numbers of clusters we examined, \(N_c = 5, 10, 15, 20\). The results are summarized in Table X to Table XIV and in Figure 11.

In all cases, Iclust was superior to the average performance of the K–means and the hierarchical Cluster 3.0 variants. In fact, except for the K–medians configurations, none of the other algorithms came even close to the Iclust performance. Averaging over all four \(N_c\) values, Iclust obtains an average coherence of \(\sim 90\%\) while the average K–means coherence is \(\sim 79\%\) and the average Hierarchical coherence is only \(\sim 19\%\).

It is interesting to point out that although the annotations for these data are arranged in a relatively simple and clear hierarchical structure, the performance of the hierarchical algorithms are still relatively poor, perhaps due to the greedy nature of these optimization routines, which typically yield suboptimal solutions.

E. Detailed results for \(N_c = 20\) clusters

In Table XV we present all enriched annotations for the Iclust partition with \(N_c = 20\) clusters and \(1/T = 35\). Several specific results are noted in the following.

First, 8 out of the 20 clusters are perfectly (100%) coherent. For example, c11 consists of 18 companies which are all Information Technology companies, mainly sub-classified as Semiconductors & Semiconductor Equipment companies such as Intel and Texas Instruments. In contrast, c17 consists mainly of different types of retail stores: Department Stores like Sears, General Merchandise Stores like Target, Speciality Stores like Staples, and so on.

Perhaps more interesting is the relatively subtle distinction between c7 and c1, both of which are perfectly coherent. The former includes mainly companies which are classified as Investment Banking & Brokerage (e.g., Merrill Lynch) or Asset Management & Custody Banks, while the latter corresponds to Commercial (Regional) Banks like PNC. Indeed, in Figure 10 we see that these two clusters nicely merge with each other at the independent solution found for \(N_c = 15\) clusters. A similar relatively subtle distinction also is captured between c6 and c20 (again, both are perfectly coherent), where both clusters correspond to different sub-classifications of the Oil & Gas category. As for the previous pair, these two clusters also merge for \(N_c = 15\).

Even in clusters with non–perfect coherence we typically see a clear reasoning behind the automatically recovered structure. For example, c16 is enriched only for three Hotels Resorts & Cruise Lines’ companies, with a coherence level of only 30%. Nonetheless, it further contains two banks (MBNA and Capital One Financial) which specialise in credit card issuing and therefore consumer spending, a company (CINTAS) which is a builder of corporate identity, and another company (Paychex) which handles payroll and human resource services for employees. In addition, the Walt Disney Co. is also in this cluster, presumably due to its parks and resorts division.

V. THIRD APPLICATION: THE EACHMOVIE DATA

A. Description of the data

In our third test case we consider the EachMovie dataset, movie ratings provided by more than 70,000 viewers. These data are inherently quantized as only six discrete possible ratings were used. Indeed, many real life clustering problems involve such categorical data. In these cases the issue of what similarity measure to use seems even more obscure, especially if the descriptive at-
tributes are not naturally ordered, and our general information theoretic approach seems especially promising.

We represented each movie by its ratings from different viewers and focused on the 500 movies that got the maximal number of votes. These data are presented in Figure 12. We estimated all the ~125,000 mutual information relations as in the previous applications; again see Ref [2] for details. Notice that in estimating the mutual information for a pair of movies, only viewers who voted for both movies can be considered.

Across all pairs of movies, the average estimated mutual information was 0.052 bits, with a variance of 0.0026 bits$^2$, and the maximal estimated mutual information was 0.89 bits. All the pairwise mutual information relations are presented in Figure 13 where the movies are sorted according to the clustering partition into $N_c = 20$ clusters that we analyze in detail (see below). The self-information relations were set to $I_{ii} = \log_2(6)$ which corresponds to the maximal possible information under a quantization into six bins.

B. Quality–complexity trade–off curves

Given the pairwise mutual information matrix we applied the Iclust algorithm described in Section II. As in the previous applications, we explored the trade–off between $\langle s \rangle$ and $I(C;i)$ for different numbers of clusters: $N_c = 5, 10, 15, 20$ and for different values of the trade–off parameter, $T$. Specifically, we found that $1/T = \{20, 25, 30, 35, 40\}$ were typically sufficient to obtain a relatively clear saturation of $\langle s \rangle$, hence we present the results for these $T$ values. For each $\{N_c , T\}$ pair we performed 10 different random initializations ending up with 10 (possibly) different local maxima of $F$, from which we chose the best one. The resulting trade–off curves are presented in the right panel of Figure 11.

As before, as $T$ is lowered, $\langle s \rangle$ and $I(C;i)$ increase and the solutions become more deterministic. For example, for $N_c = 20$ and $1/T = 30$, only ~32% of the movies have nearly deterministic assignment, while for $1/T = 40$ almost all the movie assignments are nearly deterministic [$P(C|j) > 0.9$ for a particular $C$].

For brevity, we focus our analysis on solutions for which the saturation of $\langle s \rangle$ is relatively clear, i.e., on the four solutions with $N_c = \{5, 10, 15, 20\}$ and $1/T = 40$, and we treat these solutions as hard partitions where every movie is assigned solely to its most probable cluster.

C. Comparing solutions at different numbers of clusters

We examine directly how well our independent solutions form a hierarchical structure by applying the same scheme as in Section III.C. The results are presented in Figure 14. Clearly, the relations between solutions at different numbers of clusters are relatively weak, suggesting that the data really do not support a robust hierarchical structure. Only a few clusters are somewhat preserved as we vary $N_c$, like the Family–Animation–Classic cluster, c12, or the Action cluster, c9.

D. Coherence results

1. Constructing the annotation matrices

We used the genre labels provided for these data to construct the annotation matrix. Specifically, these labels are: Action (110 movies), Animation (25 movies), Art-Foreign (45 movies), Classic (44 movies), Comedy (149 movies), Drama (160 movies), Family (67 movies), Horror (33 movies), Romance (61 movies), and Thriller (90 movies). Almost half of the movies were annotated with more than one genre and the average number of genre annotations per movie was 1.6, with a maximal number of 4 different genres for a single movie.

It is important to notice that these annotations are broad, providing a somewhat simplistic view of the structure in these data. For example, it is quite reasonable that more subtle distinctions like the movie director and/or main actors are reflected in the viewer preferences that were used to cluster the movies. Nonetheless, for practical reasons we used these broad labels as a first–order approximation for our evaluation.

2. Coherence results and comparisons

We estimated the statistical coherence of the clusters obtained at the low–temperature end of the trade–off curves where $1/T = 40$. As before, to gain some perspective, we also used the Cluster 3.0 software [15]. We experimented with the same 18 basic configurations as in the previous applications ($K$–means variants, again with 100 different initializations), and applied the comparison to all the different numbers of clusters we examined, $N_c = 5, 10, 15, 20$. The results are summarized in Table XVI to Table XIX and in Figure 15.

In all cases, Iclust was clearly superior to the average performance of the $K$–means and the Hierarchical Cluster 3.0 variants. In fact, except for the hierarchical complete-linkage configuration with the Pearson correlation as the similarity measure, none of the other algorithms came even close to the Iclust performance. Averaging over all four $N_c$ values, Iclust obtains an average coherence of ~53% while the average $K$–means coherence is only ~12% and the average Hierarchical coherence is ~24%.

Notice that, in contrast to the previous applications, here the $K$–means algorithms are inferior to some of the hierarchical algorithms (and both are inferior to Iclust). These results demonstrate that while standard clustering algorithms might work well in certain circumstances and fail completely in others, our principled and model–independent approach maintains a high and robust performance across a wide variety of applications.
E. Detailed results for \( N_c = 20 \) clusters

In Table XX we present all enriched annotations for the Iclust partition with \( N_c = 20 \) clusters and \( 1/T = 40 \). Several results should be noted specifically.

For example, c12 consisted solely of 14 classic family movies such as The Wizard of Oz and Snow White. c8 consisted mainly of Art–Foreign movies, including all the Three Colors trilogy by Kieslowski. c15 included all seven Star Trek movies. Moreover, some of the obtained clusters reflect more subtle distinctions than the broad genre definitions. For example, both c4 and c6 were enriched for Comedy, but while c4 was further enriched for Romance c6 consisted mainly of Jim Carrey and Adam Sandler movies. Both c7 and c17 were enriched for Action, but c7 was further enriched for Classic with some emphasis on Science Fiction movies such as the Star Wars trilogy, the Terminator movies, Alien, and Back to the Future. In contrast c17 consisted mainly of movies starring Sylvester Stallone, Jean-Claude Van Damme etc.

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VI. FIGURES AND TABLES
Input:
Pairwise similarity matrix, $s(i_1, i_2)$, $\forall i_1 = 1, ..., N$, $i_2 = 1, ..., N$.
trade-off parameter, $T$.
Requested number of clusters, $N_c$.
Convergence parameter, $\epsilon$.

Output:
A (typically “soft”) partition of the $N$ elements into $N_c$ clusters.

Initialization:
$m = 0$.
$P^{(m)}(C|i) \leftarrow$ A random (normalized) distribution $\forall i = 1, ..., N$.

While True
For every $i = 1, ..., N$:
• $P^{(m+1)}(C|i) \leftarrow P^{(m)}(C) \exp \left\{ \frac{1}{T} [s^{(m)}(C; i) - s^{(m)}(C)] \right\}, ~\forall C = 1, ..., N_c$.
• $P^{(m+1)}(C|i) \leftarrow \frac{P^{(m+1)}(C|i)}{\sum_{C' = 1}^{N_c} P^{(m+1)}(C'|i)}, ~\forall C = 1, ..., N_c$.
• $m \leftarrow m + 1$.

If $\forall i = 1, ..., N, \forall C = 1, ..., N_c$ we have $|P^{(m+1)}(C|i) - P^{(m)}(C|i)| \leq \epsilon$, Break.

FIG. 1 Pseudo-code of the Iclust algorithm. Extending the algorithm for the general case (of more than pairwise relations) is straightforward. In principle we repeat this procedure for different initializations and choose the solution which maximizes $\mathcal{F} = \langle s \rangle - TI(C; i)$.
FIG. 2 Expression profiles of the 868 genes in the ESR data across 173 microarray experiments. Data taken from Gasch *et. al* (10). Missing values are set to zero. The genes are sorted according to the clustering partition into 20 clusters that we analyze in detail later on. Inside each cluster, genes are sorted according to the average mutual information relation with other cluster members.
FIG. 3 Pairwise mutual information relations for the 868 genes in the ESR data. The genes are sorted according to the clustering partition into 20 clusters that we analyze in detail later on. Inside each cluster, genes are sorted according to the average mutual information relation with other cluster members.
FIG. 4 (Left) Tradeoff curves obtained for the ESR data. Each curve describes the solutions obtained for a particular $N_c$ value, i.e., for a fixed number of clusters. Different points along each curve correspond to different local maxima of $F$ at different $T$ values. The results are presented for $\frac{1}{T} = \{5, 10, 15, 20, 25\}$ which suffices to obtain a relatively clear saturation of the average mutual information per cluster, $\langle s \rangle$. In Section III.C we explore the possible hierarchical relations between the four saturated solutions at $\frac{1}{T} = 25$ and $N_c = \{5, 10, 15, 20\}$. Further detailed analysis refers to the solution with $N_c = 20$ and $\frac{1}{T} = 25$ that obtained the highest $\langle s \rangle$ value. (Middle) Similar tradeoff curves that were obtained for the SP500 data. The results are presented for $\frac{1}{T} = \{15, 20, 25, 30, 35\}$ which suffices to obtain a relatively clear saturation of $\langle s \rangle$. Notice, that due to the lower average mutual information relations in these data (with respect to the ESR example), one must apply lower $T$ values to obtain a clear saturation. In Section IV.C we explore the possible hierarchical relations between the four saturated solutions at $\frac{1}{T} = 35$ and $N_c = \{5, 10, 15, 20\}$. Further detailed analysis refers to the solution with $N_c = 20$ and $\frac{1}{T} = 35$. (Right) Similar tradeoff curves that were obtained for the EachMovie data. The results are presented for $\frac{1}{T} = \{20, 25, 30, 35, 40\}$ which suffices to obtain a relatively clear saturation of $\langle s \rangle$. In Section V.C we explore the possible hierarchical relations between the four saturated solutions at $\frac{1}{T} = 40$ and $N_c = \{5, 10, 15, 20\}$. Further detailed analysis refers to the solution with $N_c = 20$ and $\frac{1}{T} = 40$. 
FIG. 5 Relations between the optimal solutions with $N_c = \{5, 10, 15, 20\}$ at $T = 25$ for the ESR data. At the upper level, $N_c = 20$ clusters, and the clusters are sorted as in Figure 2 and Figure 3. The numbers above every cluster indicate the number of genes in this cluster. The title of each cluster correspond to the most enriched GO_BP (biological process) annotation in the cluster, i.e., to the GO_BP annotation with the smallest $P$-value in the cluster (see Section III.D.1). The only exceptions are $c_6$, not enriched in GO_BP, and $c_{19}$, enriched with a non-informative annotation (response to stress). For these two clusters we use their most enriched GO_MF (molecular function) annotation as a title. The titles of the five clusters at the lower level ($N_c = 5$) are by their most enriched GO_CC (cellular component) annotation. Notice, that most clusters were enriched with more than one annotation, hence the short titles might be too concise in some cases (see Section for a detailed description of every cluster at the top level). Red and green clusters represent clusters with a clear majority of stress–induced or stress–repressed genes, respectively. In the cytoplasm cluster we had a relatively balanced mixture of stress-repressed (58%) and stress-induced (42%) genes.
FIG. 6 ESR data: Comparison of average coherence results of the Iclust algorithm (yellow) with conventional clustering algorithms: $K$–means (green); $K$–medians (blue); Hierarchical (red). For the hierarchical algorithms, four different variants are tried: complete, average, centroid, and single linkage, respectively from left to right. For every algorithm, three different similarity measures are applied: Pearson correlation (left); absolute value of Pearson correlation (middle); Euclidean distance (right). The white bars correspond to applying the algorithm to the logarithmically transformed expression ratios. In all cases, the results are averaged over all the different numbers of clusters that we tried: $N_c = 5, 10, 15, 20$, and over the three Gene Ontologies.
FIG. 7 Examples of the average behavior of some of the clusters obtained with $N_c = 20$. Error-bars indicate standard deviation. The vertical axis measures the log$_2$ of expression ratio. The dashed (“Other genes”) curve displays the average behavior of the repressed genes, excluding those in the clusters that are mentioned in the figure. In panel A the upper dashed curve corresponds to the average behavior of the induced genes, excluding those in $c_5$. (A) $c_5$ in Menadione exposure and stationary phase. (B) $c_8$ and $c_9$ in different temperatures shifts. (C) $c_6$ and $c_8$ in Diamide treatment. (D) $c_7$ and $c_2$ in Nitrogen depletion. (E) $c_7$ and $c_5$ in steady-state growth. (F) $c_7$ and $c_5$ in hyper-osmotic shock.
FIG. 8 Fractional changes in stock price of the Standard and Poor's companies we considered during the 273 trading days of December 2002 – December 2003. The companies are sorted according to the clustering partition into 20 clusters that we analyze in detail later on. Inside each cluster, companies are sorted according to the average mutual information relation with other cluster members.
FIG. 9 Pairwise mutual information relations for the SP500 data. The companies are sorted according to the clustering partition into 20 clusters that we analyze in detail later on. Inside each cluster, companies are sorted according to the average mutual information relation with other cluster members.
FIG. 10 Relations between the optimal solutions with $N_c = \{5, 10, 15, 20\}$ at $\tau = 35$ for the SP500 data. At the upper level, $N_c = 20$ clusters, and the clusters are sorted as in Figure 8 and Figure 9. The numbers above every cluster indicate the number of companies in this cluster. The title of each cluster corresponds to the most enriched annotation in the cluster, i.e., to the annotation with the smallest $P$-value in the cluster. Similar color of text boxes indicate that the corresponding annotations belong to the same major sector of economy (see Section IV.D.1). Notice, that most clusters were enriched with more than one annotation, hence the short titles might be too concise in some cases (see Section IV.E for a detailed description of every cluster).
FIG. 11 **SP500 data**: Comparison of average coherence results of the *Iclust* algorithm (yellow) with conventional clustering algorithms (15): $K$–means (green); $K$–medians (blue); Hierarchical (red). For the hierarchical algorithms, four different variants are tried: complete, average, centroid, and single linkage, respectively from left to right. For every algorithm, three different similarity measures are applied: Pearson correlation (left); absolute value of Pearson correlation (middle); Euclidean distance (right). In all cases, the results are averaged over all the different numbers of clusters that we tried: $N_c = 5, 10, 15, 20$. 
FIG. 12 Discrete movie ratings for the 500 movies with the maximal number of votes in the EachMovie data. The ratings are presented only for the 1000 viewers who rated the maximal number of movies. Zeros represent missing values (i.e., no vote). The movies are sorted according to the clustering partition into 20 clusters that we analyze in detail later on. Inside each cluster, movies are sorted according to the average mutual information relation with other cluster members.
FIG. 13 Pairwise mutual information relations for the EachMovie data. The movies are sorted according to the clustering partition into 20 clusters that we analyze in detail later on. Inside each cluster, movies are sorted according to the average mutual information relation with other cluster members.
FIG. 14 Relations between the optimal solutions with $N_c = \{5, 10, 15, 20\}$ at $\frac{1}{T} = 40$ for the EachMovie data. At the upper level, $N_c = 20$ clusters, and the clusters are sorted as in Figure 12 and Figure 13. The numbers above every cluster indicate the number of movies in this cluster. The title of each cluster corresponds to (all) enriched genre annotations in the cluster, i.e., to all annotations with a (Bonferroni corrected) $P$-value below 0.05. See Section V.E for a detailed description of every cluster.
FIG. 15 EachMovie data: Comparison of average coherence results of the Iclust algorithm (yellow) with conventional clustering algorithms (15): \(K\)-means (green); \(K\)-medians (blue); Hierarchical (red). For the hierarchical algorithms, four different variants are tried: complete, average, centroid, and single linkage, respectively from left to right. For every algorithm, three different similarity measures are applied: Pearson correlation (left); absolute value of Pearson correlation (middle); Euclidean distance (right). In all cases, the results are averaged over all the different numbers of clusters that we tried: \(N_c = 5, 10, 15, 20\).
TABLE I A simple example for an annotation matrix. Here, the total number of elements is $N = 5$ and the total number of distinct annotations is $R = 4$. The first element is assigned the second and third annotations, and so on.

| Element index | $a_1$ | $a_2$ | $a_3$ | $a_4$ |
|---------------|-------|-------|-------|-------|
| $element_1$   | 0     | 1     | 1     | 0     |
| $element_2$   | 1     | 0     | 1     | 1     |
| $element_3$   | 1     | 0     | 0     | 0     |
| $element_4$   | 0     | 1     | 1     | 1     |
| $element_5$   | 1     | 0     | 1     | 1     |

TABLE II Examples of $P$-values. When the annotation is over-abundant in the cluster (with respect to its frequency in the entire population) the $P$-value is reduced accordingly.

| $N$ (Population size) | $K$ (Annot. freq.) | $n$ (Cluster size) | $x$ (Annot. freq. in cluster) | $Pval$ |
|-----------------------|--------------------|--------------------|-------------------------------|--------|
| 1000                  | 100                | 50                 | 5                             | 0.57   |
| 1000                  | 100                | 50                 | 20                            | $10^{-8}$ |
| 1000                  | 20                 | 100                | 2                             | 0.61   |
| 1000                  | 20                 | 100                | 20                            | $10^{-21}$ |

TABLE III A small subset of the $A_{BP}$ annotation matrix, constructed for the ESR data out of the $GO_{BP}$ ontology.

| ORF     | Metabolism | Transcription | RNA processing | Ribosome biogenesis | ... |
|---------|------------|---------------|----------------|---------------------|-----|
| YKL144C | 1          | 1             | 0              | 0                   | ... |
| YML060W | 1          | 0             | 0              | 0                   | ... |
| YGR251W | 1          | 1             | 1              | 1                   | ... |
| YLL036C | 1          | 0             | 1              | 0                   | ... |
| YNL163C | 0          | 0             | 0              | 1                   | ... |
| ...     | ...        | ...           | ...            | ...                 | ... |
TABLE IV An example for a subset of genes from a single cluster that are assigned different specific \textit{GO\textsubscript{BP}} terms. The functional relationship between these genes becomes statistically significant only if one considers the fact that all these annotations have a common ancestor in the \textit{GO\textsubscript{BP}} database, the \textit{tRNA aminoacylation for protein translation} term.

| ORF      | Direct \textit{GO\textsubscript{BP}} annotation                     |
|----------|-------------------------------------------------------------------|
| YDR037W  | lysyl-tRNA aminoacylation                                         |
| YGR09jW  | valyl-tRNA aminoacylation                                         |
| YLR060W  | phenylalanyl-tRNA aminoacylation                                  |
| YNE\textit{Euclidean}47W | cysteinyl-tRNA aminoacylation                                  |
| YPL160W  | leucyl-tRNA aminoacylation                                         |

TABLE V Details of the different annotation matrices used for evaluating the statistical significance of the obtained clusters for the yeast ESR genes. \textsuperscript{a}Data source for constructing the annotation matrix. \textsuperscript{b}Number of distinct annotations in the annotation matrix, assigned at least two genes and thus participate in the analysis. \textsuperscript{c}Number of genes assigned at least one annotation and thus participate in the analysis. Notice that this number determines the population size \((N)\) for the \(P\)-value estimation. \textsuperscript{d}Average number of distinct annotations per gene. \textsuperscript{e}Maximal number of distinct annotations for a single gene.

| Data source\textsuperscript{a} | # Annotations\textsuperscript{b} | # Genes | Avg. # Annot. per gene\textsuperscript{c} | Maximal # Annot. per gene\textsuperscript{d} |
|-------------------------------|-------------------------------|---------|----------------------------------------|----------------------------------------|
| \textit{GO\textsubscript{BP}} (13) | 472                           | 614     | 11.4                                   | 63                                     |
| \textit{GO\textsubscript{MF}} (13) | 215                           | 561     | 4.6                                    | 18                                     |
| \textit{GO\textsubscript{CC}} (13) | 94                            | 747     | 5.4                                    | 14                                     |
TABLE VI Coherence results for the ESR data with respect to the three Gene Ontologies with $N_c = 20$ clusters. $a$Clustering algorithm. In the $\langle K$–means $\rangle$ row we present the average results of all the six $K$–means variants. For each of these variants we performed 100 runs from which the best solution is chosen. In the $\langle$ Hier. $\rangle$ row we present the average results of all the 12 Hierarchical clustering variants. In parenthesis we present the results where the input are the log$_2$ of the expression ratio profiles. $b$Correlation measure used by the algorithm. PC stands for the (centered) Pearson Correlation. $|PC|$ is the absolute value of this correlation. Euclidean stands for the Euclidean distance. $c$Number of clusters with a positive coherence with respect to the GO$_{BP}$ ontology. $d$Average coherence of all 20 clusters with respect to the GO$_{BP}$ ontology. $e$Number of clusters with a positive coherence with respect to the GO$_{MF}$ ontology. $f$Average coherence of all 20 clusters with respect to the GO$_{MF}$ ontology. $g$Number of clusters with a positive coherence with respect to the GO$_{CC}$ ontology. $h$Average coherence of all 20 clusters with respect to the GO$_{CC}$ ontology.

| $N_c = 20$ | BP | BP | MF | MF | CC | CC |
|------------|----|----|----|----|----|----|
| Algorithm $a$ | Similarity $b$ | $N_{c}^{\text{pos}}$ $c$ | $\langle\text{Coh}\rangle$ $d$ | $N_{c}^{\text{pos}}$ $e$ | $\langle\text{Coh}\rangle$ $f$ | $N_{c}^{\text{pos}}$ $g$ | $\langle\text{Coh}\rangle$ $h$ |
| Iclust | mutual information | 17 | 51 | 16 | 41 | 14 | 33 |
| $K$–means | PC | 11 (13) | 30 (43) | 11 (11) | 31 (31) | 10 (12) | 19 (30) |
| $K$–means | $|PC|$ | 9 (15) | 27 (50) | 8 (14) | 24 (40) | 8 (16) | 26 (42) |
| $K$–medians | Euclidean | 7 (15) | 23 (52) | 9 (15) | 26 (39) | 5 (16) | 13 (51) |
| $K$–medians | PC | 11 (15) | 35 (51) | 13 (16) | 34 (48) | 10 (15) | 35 (46) |
| $K$–medians | $|PC|$ | 12 (15) | 38 (41) | 16 (16) | 43 (39) | 13 (11) | 37 (35) |
| $K$–medians | Euclidean | 16 (18) | 49 (52) | 15 (14) | 39 (44) | 13 (16) | 43 (51) |
| $\langle K$–means $\rangle$ | | 11.0 (15.2) | 33.7 (48.2) | 12.0 (14.3) | 32.8 (40.2) | 9.8 (14.3) | 28.8 (42.5) |
| Hier - Comp. linkage | PC | 9 (13) | 29 (41) | 10 (10) | 25 (30) | 7 (12) | 19 (34) |
| Hier - Comp. linkage | $|PC|$ | 9 (10) | 25 (26) | 12 (9) | 31 (27) | 7 (10) | 17 (26) |
| Hier - Comp. linkage | Euclidean | 1 (13) | 2 (43) | 3 (11) | 8 (32) | 1 (8) | 2 (27) |
| Hier - Avg. linkage | PC | 5 (7) | 17 (20) | 5 (5) | 18 (17) | 4 (4) | 11 (12) |
| Hier - Avg. linkage | $|PC|$ | 5 (4) | 17 (10) | 5 (2) | 18 (8) | 4 (2) | 10 (4) |
| Hier - Avg. linkage | Euclidean | 1 (9) | 2 (29) | 1 (4) | 1 (17) | 2 (6) | 6 (16) |
| Hier - Centr. linkage | PC | 4 (3) | 12 (10) | 4 (3) | 12 (10) | 4 (2) | 11 (8) |
| Hier - Centr. linkage | $|PC|$ | 4 (4) | 12 (12) | 3 (4) | 7 (11) | 4 (2) | 9 (4) |
| Hier - Sing. linkage | Euclidean | 0 (4) | 0 (13) | 0 (4) | 0 (12) | 1 (2) | 1 (8) |
| Hier - Sing. linkage | PC | 2 (2) | 8 (8) | 2 (2) | 7 (7) | 2 (2) | 8 (8) |
| Hier - Sing. linkage | $|PC|$ | 2 (0) | 6 (0) | 1 (0) | 5 (0) | 0 (0) | 0 (0) |
| Hier - Sing. linkage | Euclidean | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| $\langle$ Hier. $\rangle$ | | 3.5 (5.8) | 10.8 (17.7) | 3.8 (4.5) | 11.0 (14.2) | 3.0 (4.2) | 7.8 (12.2) |
TABLE VII Coherence results for the ESR data with respect to the three Gene Ontologies with $N_c = 15$ clusters. The column and row definitions are as in Table VI. Again, in parenthesis we present the results where the input are the log$_2$ of the expression ratio profiles.

| $N_c = 15$ | | | | | | |
|---|---|---|---|---|---|---|
| Algorithm $^a$ | Similarity $^b$ | $N_c^{\text{pos}}$ $^c$ | $(\text{Coh})$ $^d$ | $N_c^{\text{pos}}$ $^e$ | $(\text{Coh})$ $^f$ | $N_c^{\text{pos}}$ $^g$ | $(\text{Coh})$ $^h$ |
| Ichust | mutual information | 12 | 51 | 14 | 54 | 14 | 52 |
| $K$-means | PC | 7 (14) | 29 (55) | 8 (13) | 32 (49) | 7 (10) | 18 (38) |
| $K$-means | $|\text{PC}|$ | 10 (14) | 40 (47) | 9 (11) | 32 (37) | 8 (12) | 27 (38) |
| $K$-means | Euclidean | 10 (12) | 33 (50) | 8 (13) | 36 (46) | 3 (11) | 14 (44) |
| $K$-medians | PC | 11 (13) | 40 (46) | 11 (13) | 41 (49) | 10 (14) | 41 (47) |
| $K$-medians | $|\text{PC}|$ | 11 (14) | 42 (50) | 11 (13) | 31 (44) | 10 (11) | 35 (38) |
| $K$-medians | Euclidean | 11 (14) | 50 (58) | 12 (13) | 42 (43) | 11 (13) | 46 (61) |
| ⟨$K$-means⟩ | | 10.0 (13.5) | 39.0 (51.0) | 9.8 (12.7) | 35.7 (44.7) | 8.2 (11.8) | 30.2 (44.3) |
| Hier - Comp. linkage | PC | 8 (11) | 32 (43) | 9 (8) | 31 (31) | 6 (9) | 20 (44) |
| Hier - Comp. linkage | $|\text{PC}|$ | 4 (8) | 17 (29) | 7 (7) | 21 (29) | 5 (8) | 15 (32) |
| Hier - Comp. linkage | Euclidean | 0 (8) | 0 (33) | 1 (8) | 2 (29) | 1 (6) | 2 (27) |
| Hier - Avg. linkage | PC | 5 (5) | 21 (22) | 4 (5) | 18 (21) | 4 (3) | 13 (12) |
| Hier - Avg. linkage | $|\text{PC}|$ | 4 (4) | 15 (13) | 3 (3) | 11 (12) | 3 (2) | 5 (5) |
| Hier - Avg. linkage | Euclidean | 2 (7) | 8 (36) | 1 (4) | 1 (22) | 2 (4) | 8 (14) |
| Hier - Centr. linkage | PC | 4 (3) | 16 (13) | 4 (3) | 16 (15) | 4 (3) | 14 (12) |
| Hier - Centr. linkage | $|\text{PC}|$ | 4 (3) | 16 (11) | 3 (3) | 7 (11) | 4 (3) | 11 (6) |
| Hier - Centr. linkage | Euclidean | 0 (3) | 0 (15) | 0 (3) | 0 (11) | 0 (2) | 0 (11) |
| Hier - Sing. linkage | PC | 2 (2) | 11 (11) | 2 (2) | 9 (9) | 2 (2) | 11 (11) |
| Hier - Sing. linkage | $|\text{PC}|$ | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Hier - Sing. linkage | Euclidean | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (0) | 6 (0) |
| ⟨Hier.⟩ | | 2.8 (4.5) | 11.3 (18.8) | 2.8 (3.8) | 9.7 (15.8) | 2.7 (3.5) | 8.8 (14.5) |
TABLE VIII Coherence results for the ESR data with respect to the three Gene Ontologies with $N_c = 10$ clusters. The column and row definitions are as in Table VII. Again, in parenthesis we present the results where the input are the $\log_2$ of the expression ratio profiles.

| $N_c = 10$ | Algorithm | Similarity | $N_p$ | $\langle Coh \rangle$ | $N_p$ | $\langle Coh \rangle$ | $N_p$ | $\langle Coh \rangle$ |
|------------|-----------|------------|-------|-----------------|-------|-----------------|-------|-----------------|
|            | Iclust    | mutual information | 7     | 50              | 7     | 43              | 9     | 53              |
|            | $K$-means | PC          | 8 (9) | 45 (52)         | 8 (8) | 44 (47)         | 7 (9) | 37 (56)         |
|            | $K$-means | $|PC|$       | 7 (9) | 41 (48)         | 6 (8) | 42 (41)         | 8 (8) | 39 (48)         |
|            | $K$-means | Euclidean   | 5 (10)| 27 (62)         | 6 (10)| 30 (57)         | 3 (8) | 22 (55)         |
|            | $K$-medians | PC         | 9 (10)| 51 (57)         | 8 (9) | 45 (53)         | 9 (10)| 49 (54)         |
|            | $K$-medians | $|PC|$      | 7 (9) | 45 (52)         | 8 (9) | 50 (47)         | 9 (8) | 41 (56)         |
|            | $K$-medians | Euclidean  | 7 (9) | 48 (62)         | 8 (9) | 46 (60)         | 7 (9) | 49 (58)         |
|            | ( $K$-means ) |           | 7.2 (9.3)| 42.8 (55.5) | 7.3 (8.8)| 42.8 (50.8) | 7.2 (8.7)| 39.5 (54.5) |
|            | Hier - Comp. linkage | PC      | 6 (8) | 33 (44)         | 7 (5) | 43 (32)         | 5 (7) | 26 (43)         |
|            | Hier - Comp. linkage | $|PC|$  | 4 (6) | 24 (33)         | 6 (5) | 32 (37)         | 5 (6) | 22 (30)         |
|            | Hier - Comp. linkage | Euclidean | 2 (7) | 12 (41)         | 2 (7) | 8 (39)          | 2 (5) | 7 (32)          |
|            | Hier - Avg. linkage | PC      | 3 (4) | 19 (30)         | 3 (4) | 20 (30)         | 3 (3) | 18 (19)         |
|            | Hier - Avg. linkage | $|PC|$  | 2 (4) | 8 (20)          | 1 (3) | 7 (19)          | 1 (2) | 1 (7)           |
|            | Hier - Avg. linkage | Euclidean | 0 (4) | 0 (33)          | 0 (5) | 0 (28)          | 0 (4) | 0 (20)          |
|            | Hier - Centr. linkage | PC      | 3 (3) | 19 (19)         | 3 (3) | 21 (20)         | 3 (3) | 18 (18)         |
|            | Hier - Centr. linkage | $|PC|$  | 4 (3) | 19 (21)         | 3 (3) | 11 (17)         | 4 (3) | 16 (9)          |
|            | Hier - Centr. linkage | Euclidean | 0 (3) | 0 (21)          | 1 (3) | 2 (17)          | 0 (3) | 0 (9)           |
|            | Hier - Sing. linkage | PC      | 2 (2) | 16 (16)         | 2 (2) | 13 (14)         | 2 (2) | 17 (17)         |
|            | Hier - Sing. linkage | $|PC|$  | 0 (0) | 0 (0)           | 0 (0) | 0 (0)           | 0 (0) | 0 (0)           |
|            | Hier - Sing. linkage | Euclidean | 0 (0) | 0 (0)          | 0 (0) | 0 (0)          | 0 (0) | 0 (0)          |
|            | ( Hier. ) |           | 2.2 (3.7)| 12.5 (23.2) | 2.3 (3.3)| 13.1 (21.1) | 2.1 (3.2)| 10.4 (17.0) |
TABLE IX Coherence results for the ESR data with respect to the three Gene Ontologies with $N_c = 5$ clusters. The column and row definitions are as in Table VI. Again, in parenthesis we present the results where the input are the $\log_2$ of the expression ratio profiles.

| $N_c = 5$ | Algorithm $^a$ | Similarity $^b$ | $N^p_{BP} c$ | $\langle Coh \rangle^d$ | $N^p_{MF} c$ | $\langle Coh \rangle^f$ | $N^p_{CC} g$ | $\langle Coh \rangle^h$ |
|-----------|----------------|----------------|--------------|----------------|--------------|----------------|--------------|----------------|
|           | Iclust         | mutual information | 5          | 75             |              | 77            |              | 5                          | 86             |
|           | $K$–means      | PC              | 5 (5)       | 62 (65)        | 5 (5)        | 63 (65)       | 5 (5)        | 75 (73)                    |
|           | $K$–means      | $|PC|$          | 5 (5)       | 61 (70)        | 5 (5)        | 62 (67)       | 5 (5)        | 75 (70)                    |
|           | $K$–means      | Euclidean       | 3 (5)       | 43 (71)        | 3 (5)        | 35 (56)       | 3 (4)        | 39 (65)                    |
|           | $K$–medians    | PC              | 5 (5)       | 64 (62)        | 5 (5)        | 65 (63)       | 5 (5)        | 72 (72)                    |
|           | $K$–medians    | $|PC|$          | 5 (5)       | 57 (59)        | 5 (5)        | 52 (58)       | 5 (5)        | 75 (69)                    |
|           | $K$–medians    | Euclidean       | 4 (5)       | 52 (71)        | 4 (5)        | 59 (60)       | 4 (4)        | 68 (57)                    |
| $\langle K$–means $\rangle$ |                |                | 4.5 (5.0)   | 56.5 (66.3)    | 4.5 (5.0)    | 56.0 (61.5)   | 4.5 (4.7)   | 67.3 (67.7)                |
|           | Hier - Comp. linkage | PC     | 4 (4)       | 42 (44)        | 4 (4)        | 52 (46)       | 4 (4)        | 37 (57)                    |
|           | Hier - Comp. linkage | $|PC|$ | 4 (4)       | 47 (51)        | 5 (3)        | 34 (44)       | 3 (4)        | 30 (45)                    |
|           | Hier - Comp. linkage | Euclidean | 1 (3)       | 11 (37)        | 2 (4)        | 13 (49)       | 0 (4)        | 0 (36)                     |
|           | Hier - Avg. linkage | PC      | 3 (3)       | 38 (39)        | 3 (3)        | 40 (47)       | 3 (3)        | 36 (37)                    |
|           | Hier - Avg. linkage | $|PC|$ | 0 (1)       | 0 (6)         | 0 (1)        | 0 (13)        | 0 (2)        | 0 (8)                      |
|           | Hier - Avg. linkage | Euclidean | 0 (2)       | 0 (31)        | 0 (3)        | 0 (30)        | 0 (2)        | 0 (33)                    |
|           | Hier - Centr. linkage | PC | 3 (2)       | 39 (32)        | 3 (2)        | 41 (27)       | 3 (2)        | 36 (33)                    |
|           | Hier - Centr. linkage | $|PC|$ | 3 (1)       | 21 (8)        | 2 (0)        | 19 (0)        | 3 (1)        | 13 (6)                     |
|           | Hier - Centr. linkage | Euclidean | 0 (1)       | 0 (8)         | 0 (0)        | 0 (0)         | 0 (1)        | 0 (6)                      |
|           | Hier - Sing. linkage | PC | 2 (2)       | 32 (32)        | 2 (2)        | 27 (27)       | 2 (2)        | 33 (33)                    |
|           | Hier - Sing. linkage | $|PC|$ | 0 (0)       | 0 (0)         | 0 (0)        | 0 (0)         | 0 (0)        | 0 (0)                      |
| $\langle$ Hier. $\rangle$ |                |                | 1.7 (1.9)   | 19.2 (24.0)    | 1.8 (1.8)    | 18.8 (23.6)   | 1.5 (2.1)   | 15.4 (24.5)                |
TABLE X  Enriched GO annotations in the *Iclust* solution with *Nc* = 20 clusters. Clusters are ordered as in Figure 2, Figure 3, and Figure 4. Only annotations with a *P*-value below 0.05 (Bonferroni corrected) are presented. *a* Cluster index, number of repressed genes in the cluster, and number of induced genes in the cluster. *b* Cluster coherence (in percentage) in each of the three Gene Ontologies. *c* Enriched annotations for the GO<sub>BP</sub> ontology. In parentheses: \((x/K, p)\) stands for the number of genes in the cluster to which this annotation is assigned, the number of genes in the ESR module to which this annotation is assigned, and the Bonferroni corrected *P*-value, respectively. *d* Enriched annotations for the GO<sub>MF</sub> ontology. Parenthesis are as in the previous column. *e* Enriched annotations for the GO<sub>CC</sub> ontology. Parenthesis are as in the previous column.

| C<sup>a</sup> | Coh.<sup>b</sup> | BP Enriched annot.<sup>c</sup> | MF Enriched annot.<sup>d</sup> | CC Enriched annot.<sup>e</sup> |
|---|---|---|---|---|
| c12 | 18 | nucleoside monophosphate metabolism (5/6.0.0032) | diphosphotransferase activity (4/4.0.0047) | - |
| Rep : 57 | MF : 9 | ribonucleoside monophosphate metabolism (5/6.0.0032) | - | - |
| Ind : 3 | CC : 0 | purine ribonucleoside monophosphate (5/6.0.0032) | - | - |
| | | histidine biosynthesis (4/4.0.0076) | - | - |
| | | histidine family amino acid metabolism (4/4.0.0076) | - | - |
| | | purine nucleoside monophosphate biosynthesis (4/4.0.0076) | - | - |
| | | ribonucleoside monophosphate biosynthesis (4/4.0.0076) | - | - |
| | | biogenic amine biosynthesis (4/4.0.0076) | - | - |
| | | amine biosynthesis (7/16.0.0187) | - | - |
| | | amino acid derivative biosynthesis (4/5.0.0359) | - | - |
| c15 | 67 | tRNA aminoacylation for protein transl. (8/14.0.00) | tRNA ligase activity (9/17.0.00) | - |
| Rep : 12 | MF : 75 | - | RNA ligase activity (9/17.0.00) | - |
| Ind : 0 | CC : 0 | - | ligase activity, forming carbon-oxyg (9/17.0.00) | - |
| | | - | ligase activity, forming aminoacyl-t (9/17.0.00) | - |
| | | - | ligase activity, forming phosphoric (9/17.0.00) | - |
| | | - | ligase activity (9/23.0.00) | - |
| c14 | 57 | vacuolar acidification (3/3.0.0010) | hydrogen-transporting ATPase activity (3/3.0.0005) | - |
| Rep : 11 | MF : 43 | monovalent inorganic cation homeostasis (3/4.0.0038) | ion transporter activity (4/8.0.0006) | - |
| Ind : 1 | CC : 53 | hydrogen ion homeostasis (3/5.0.0033) | monovalent inorganic cation transporter (3/4.0.0020) | - |
| | | organelle organization and biogenesis (6/38.0.0080) | vascular membrane (3/8.0.00673) | - |
| | | vascular transport (3/5.0.0093) | chaper.-contain. T-compl. (3/3.0.0001) | - |
| | | cation homeostasis (3/7.0.0317) | hydrolase activity, acting on acid a (3/9.0.0382) | - |
| | | asparagine biosynthesis (2/2.0.0488) | hydrolase activity, acting on acid a (3/9.0.0382) | - |
| | | aspartate family amino acid biosynthesis (2/2.0.0488) | hydrolase activity, acting on acid a (3/9.0.0382) | - |
| c10 | 0 | - | - | - |
| Rep : 30 | MF : 0 | - | - | - |
| Ind : 1 | CC : 0 | - | - | - |
| c2 | 100 | protein biosynthesis (15/189.0.00) | structural constituent of ribosome (12/127.0.0001) | - |
| Rep : 17 | MF : 80 | macromolecule biosynthesis (15/189.0.00) | structural molecule activity (12/128.0.0001) | - |
| Ind : 0 | CC : 100 | biosynthesis (15/236.0.00) | - | - |
| | | translational elongation (5/10.0.00) | - | - |
| | | protein metabolism (15/252.0.00) | - | - |
| | | - | - | - |
| c3 | 17 | transcription from Pol II promoter (5/11.0.0077) | ribonuclease activity (4/10.0.039) | DNA-direct. RNA polymer. II-core (4/7.0.004) |
| Rep : 20 | MF : 15 | - | - | DNA-direct. RNA polymer. II-holo (4/9.0.012) |
| Ind : 6 | CC : 23 | - | - | cytoplasm. exosomes. (RNase compl.) (3/5.0.028) |
| c20 | 25 | cell communication (5/18.0.0147) | vacuole (7/26.0.0014) | - |
| Rep : 0 | MF : 0 | signal transduction (4/12.0.0359) | storage vacuole (5/20.0.0288) | - |
| Ind : 38 | CC : 22 | - | lytic vacuole (5/20.0.0288) | - |
| | | - | vacuole (sensu Fungi) (5/20.0.0288) | - |
| C^a | Coh.^c | BP Enriched annot.^c | MF Enriched annot.^d | CC Enriched annot.^e |
|-----|---------|-----------------------|-----------------------|-----------------------|
| c6  | BP : 0  | Rep : 3               | MF : 33               | CC : 7               |
|     |         | oxidoreductase activity (6/37,0.0255) | peroxisomal matrix (2/2,0.0353) |
| c8  | BP : 0  | Rep : 3               | MF : 0                | Ind : 22              |
|     |         | cAMP-depend. prot. kinase compl. (2/2,0.012) | cytoplasm (20/525,0.0139) |
| c11 | BP : 63 | Rep : 0               | MF : 58               | Ind : 34              |
|     | carbohydrate biosynthesis (5/8,0.00) | hexose biosynthesis (4/5,0.0002) | kinase activity (5/27,0.0027) |
|     |         | alcohol biosynthesis (4/5,0.0002) | protein serine/threonine kinase acti (3/6,0.0035) |
|     |         | monosaccharide biosynthesis (4/5,0.0002) | cAMP-depend. prot. kinase acti (2/2,0.012) |
|     |         | regulation of carbohydrate metabolism (3/3,0.0015) | cyclic-nucleotide dependent protein (2/2,0.0014) |
|     |         | regulation of glucoegenesis (3/3,0.0015) | cAMP-depend. prot. kinase acti (2/2,0.012) |
|     |         | negative regulation of carbohydrate metabolism (3/3,0.0015) | negative regulation of carbohydrate metabolism (3/3,0.0015) |
|     |         | energy pathways (6/25,0.0015) | negative regulation of metabolism (3/3,0.0015) |
|     |         | energy derivation by oxidation of or (6/25,0.0015) | energy pathways (6/25,0.0015) |
|     |         | phosphorophylylation (4/9,0.0037) | energy derivation by oxidation of or (6/25,0.0015) |
|     |         | main pathways of carbohydrate metabo (4/11,0.0093) | main pathways of carbohydrate metabo (4/11,0.0093) |
|     |         | pyruvate metabolism (3/3,0.0002) | pyruvate metabolism (3/3,0.0002) |
|     |         | pyruvate dehydrogenase bypass (3/3,0.0002) | pyruvate dehydrogenase bypass (3/3,0.0002) |
|     |         | pyruvate dehydrogenase bypass (3/3,0.0002) | pyruvate dehydrogenase bypass (3/3,0.0002) |
|     |         | fermentation (2/2,0.0189) | fermentation (2/2,0.0189) |
|     |         | ethanol fermentation (2/2,0.0189) | ethanol fermentation (2/2,0.0189) |
|     |         | glycylcotic fermentation (2/2,0.0189) | glycylcotic fermentation (2/2,0.0189) |
|     |         | alcohol metabolism (4,25,0.0303) | alcohol metabolism (4,25,0.0303) |
| c13 | BP : 40 | Rep : 16              | MF : 20               | Ind : 0               |
|     |         | pyruvate dehydrogenase bypass (3/3,0.0002) | pyruvate dehydrogenase bypass (3/3,0.0002) |
|     |         | pyruvate dehydrogenase bypass (3/3,0.0002) | pyruvate dehydrogenase bypass (3/3,0.0002) |
|     |         | pyruvate dehydrogenase bypass (3/3,0.0002) | pyruvate dehydrogenase bypass (3/3,0.0002) |
|     |         | fermentation (2/2,0.0189) | fermentation (2/2,0.0189) |
|     |         | ethanol fermentation (2/2,0.0189) | ethanol fermentation (2/2,0.0189) |
|     |         | glycylcotic fermentation (2/2,0.0189) | glycylcotic fermentation (2/2,0.0189) |
|     |         | alcohol metabolism (4,25,0.0303) | alcohol metabolism (4,25,0.0303) |
| c1  | BP : 73 | Rep : 13              | MF : 36               | Ind : 0               |
|     |         | translational elongation (4/10,0.0004) | translation factor activity, nucleic (4/29,0.0253) |
|     |         | nascent polypep.-associat. compl. (2/2,0.002) | translation factor activity, nucleic (4/29,0.0253) |
|     |         | transl. elong. fact. actvi (3/7,0.003) | translation factor activity, nucleic (4/29,0.0253) |
|     |         | nascent polypeptide association (2/2,0.0096) | translation factor activity, nucleic (4/29,0.0253) |
|     |         | methionine metabolism (2/2,0.0096) | methionine metabolism (2/2,0.0096) |
|     |         | translation regulator activity (4/31,0.0528) | translation regulator activity (4/31,0.0528) |
|     |         | translation regulator activity (4/31,0.0528) | translation regulator activity (4/31,0.0528) |
|     |         | nascent polypeptide association (2/2,0.0096) | nascent polypeptide association (2/2,0.0096) |
|     |         | methionine metabolism (2/2,0.0096) | methionine metabolism (2/2,0.0096) |
|     |         | translation regulator activity (4/31,0.0528) | translation regulator activity (4/31,0.0528) |
|     |         | translation regulator activity (4/31,0.0528) | translation regulator activity (4/31,0.0528) |
|     |         | nascent polypeptide association (2/2,0.0096) | nascent polypeptide association (2/2,0.0096) |
|     |         | methionine metabolism (2/2,0.0096) | methionine metabolism (2/2,0.0096) |
|     |         | translation regulator activity (4/31,0.0528) | translation regulator activity (4/31,0.0528) |
| c17 | BP : 80 | Rep : 7               | MF : 33               | Ind : 3               |
|     |         | S phase of mitotic cell cycle (4/10,0.00) | DNA-direct DNA polymer activ (2/4,0.015) |
|     |         | α DNA polymer. activ. (2/2,0.003) | DNA-direct DNA polymer activ (2/4,0.015) |
|     |         | DNA replication (4/10,0.00) | replication fork (2/4,0.0060) |
|     |         | DNA replication and chromosome cycle (4/14,0.00) | DNA replication and chromosome cycle (4/14,0.00) |
|     |         | mitotic cell cycle (4/14,0.00) | DNA replication (4/10,0.00) |
|     |         | cell cycle (4/22,0.0002) | DNA replication (4/10,0.00) |
|     |         | DNA metabolism (4/24,0.0003) | DNA replication (4/10,0.00) |
|     |         | DNA dependent DNA replication (3/6,0.0004) | DNA replication and chromosome cycle (4/14,0.00) |
|     |         | cell proliferation (4/27,0.0004) | cell proliferation (4/27,0.0004) |
|     |         | DNA replication, priming (2/2,0.0016) | DNA replication, priming (2/2,0.0016) |
|     |         | DNA replication initiation (2/3,0.0048) | DNA replication initiation (2/3,0.0048) |
|     |         | DNA strand elongation (2/4,0.0095) | DNA strand elongation (2/4,0.0095) |
|     |         | DNA repair (2/8.0.0438) | DNA repair (2/8.0.0438) |
| c5  | BP : 24 | Rep : 6               | MF : 45               | Ind : 26              |
|     |         | regulation of redox homeostasis (3/5,0.0358) | oxidoreductase activity (9/37,0.00) |
|     |         | coxidoreductase activity (9/37,0.00) | oxidoreductase activity (9/37,0.00) |
|     |         | regenredox homeostasis (3/5,0.0358) | regenredox homeostasis (3/5,0.0358) |
|     |         | oxygen and reactive oxygen species m (4/12,0.0455) | oxygen and reactive oxygen species m (4/12,0.0455) |
|     |         | mitochondr. intermembr. space (3/6,0.017) | mitochondr. intermembr. space (3/6,0.017) |
| C^a | Coh.^b | BP Enriched annot.^c | MF Enriched annot.^d | CC Enriched annot.^e |
|-----|--------|----------------------|----------------------|----------------------|
| c4  | 62     | carbohydrate metabolism (11/35.00) | catalytic activity (24/280.0008) | α, α-trehalose-phosphate synt (3/3.0.005) |
|     | 1      | response to stress (10/50.00050) | hydrolase activity, acting on carbon (3/4.0.0201) | - |
| 46  | 7      | -                     | -                      | -                     |
| c19 | 45     | response to stress (14/50.000)  | heat shock protein activity (6/8.0.00) | - |
|     | 0      | -                     | oxidoreductase activity (9/37.0.0031) | - |
| 49  | 0      | -                     | chaperone activity (6/19.0.0139) | - |
| c7  | 89     | nucleobase, nucleoside, nucleotide a (46/188.00) | - | nucleus (83/288.00) |
|     | 0      | transcription, DNA-dependent (35/117.00) | - | nucleolus (40/118.00) |
| 9   | 78     | transcription (35/119.00) | RNA metabolism (33/119.00) | DNA-direct. RNA polymer. III comp (7/13.0.03) |
|     |        | RNA processing (31/110.0.00) | RNA processing (25/90.0.0008) | - |
|     |        | ribosome biogenesis (30/110.0001) | ribosome biogenesis (32/136.0.013) | - |
|     |        | transcription from Pol I promoter (28/102.0.0002) | cellular process (48/263.0.0037) | - |
|     |        | rRNA processing (25/90.0.0008) | cell growth and/or maintenance (47/256.0.0044) | - |
|     |        | ribosome biogenesis and assembly (32/136.0.013) | cytoplasm organization and biogenesis (35/172.0.042) | - |
|     |        | - | - | - |
| c16 | 96     | ribosome biogenesis (48/110.00) | snRNA binding (14/25.0.00) | nucleolus (49/118.0.00) |
|     | 87     | RNA binding (21/70.0.00) | mRNA binding (21/70.0.00) | nucleolus (68/288.00) |
| 1   | 88     | RNA metabolism (44/110.0.00) | RNA binding (21/70.0.00) | - |
|     |        | RNA processing (44/110.0.00) | RNA processing (44/110.0.00) | - |
|     |        | cytoplasm organization and biogenesis (52/172.0.00) | cytoplasm organization and biogenesis (52/172.0.00) | - |
|     |        | transcription from Pol I promoter (40/102.0.00) | - | - |
|     |        | rRNA processing (37/90.0.00) | - | - |
|     |        | transcription, DNA-dependent (41/117.0.00) | - | - |
|     |        | transcription (41/119.00) | - | - |
|     |        | - | - | - |
| c9  | 62     | RNA metabolism (17/119.00025) | binding (19/129.0.0006) | nucleolus (18/118.0.0336) |
|     | 48     | RNA processing (16/110.0.0039) | - | - |
| 8   | 33     | nucleobase, nucleoside, nucleotide a (21/188.000883) | - | - |
|     |        | transcription, DNA-dependent (15/117.0.00369) | - | - |
|     |        | transcription (15/119.0.0451) | - | - |
| c18 | 100    | protein biosynthesis (112/189.0.00) | struct. constit. of riboso. (110/127.0.00) | cytos. riboso. (sensu Baka.) (110/132.0.00) |
|     | 122    | macromolecule biosynthesis (112/189.0.00) | struct. molecul. activ. (110/128.0.00) | - |
| 0   | 99     | biosynthesis (112/236.0.00) | ribosome (110/153.00) | - |
|     |        | protein metabolism (112/252.0.00) | cytosol (110/165.00) | - |
|     |        | metabolism (112/523.0.00) | ribonucleoprotein complex (110/186.0.00) | - |
|     |        | ribosomal small subunit assembly and (8/10.0.0013) | cytosol, large riboso. subunit (62/75.0.00) | - |
|     |        | regulation of translational fidelity (6/7.0.00082) | cytosol, small riboso. subunit (48/56.0.00) | - |
|     |        | regulation of translation (8/12.0.0107) | small ribosomal subunit (48/56.0.00) | - |
|     |        | ribosomal subunit assembly (15/36.0.0263) | eukaryotic 48S initiation complex (48/56.0.00) | - |
|     |        | - | eukaryotic 43S preinitiation complex (49/61.0.00) | - |
TABLE XI Coherence results for the SP500 data with respect to the GICS companies’ annotations with \( N_c = 20 \) clusters. 

\(^a\)Clustering algorithm. In the \( \langle K\text{-means} \rangle \) row we present the average results of all the six \( K\text{-means} \) variants. For each of these variants we performed 100 runs from which the best solution is chosen. In the \( \langle \text{Hier.} \rangle \) row we present the average results of all the 12 Hierarchical clustering variants. 

\(^b\)Correlation measure used by the algorithm. \( PC \) stands for the (centered) Pearson Correlation. \( |PC| \) is the absolute value of this correlation. \( \text{Euclidean} \) stands for the Euclidean distance. 

\(^c\)Number of clusters with a positive coherence. 

\(^d\)Average coherence of all 20 clusters.

| \( N_c = 20 \) | Algorithm \(^a\) | Similarity \(^b\) | \( N_{pos} \) \(^c\) | \( \langle \text{Coh} \rangle \) \(^d\) |
|---|---|---|---|---|
| Ichust | mutual information | 20 | 86 |
| \( K\text{-means} \) | \( PC \) | 19 | 74 |
| \( K\text{-means} \) | \( |PC| \) | 17 | 69 |
| \( K\text{-means} \) | \( \text{Euclidean} \) | 15 | 58 |
| \( K\text{-medians} \) | \( PC \) | 20 | 85 |
| \( K\text{-medians} \) | \( |PC| \) | 20 | 88 |
| \( K\text{-medians} \) | \( \text{Euclidean} \) | 20 | 81 |
| \( \langle K\text{-means} \rangle \) | | 18.5 | 75.8 |
| \( \text{Hier - Comp. linkage} \) | \( PC \) | 16 | 70 |
| \( \text{Hier - Comp. linkage} \) | \( |PC| \) | 16 | 70 |
| \( \text{Hier - Comp. linkage} \) | \( \text{Euclidean} \) | 4 | 12 |
| \( \text{Hier - Avg. linkage} \) | \( PC \) | 7 | 32 |
| \( \text{Hier - Avg. linkage} \) | \( |PC| \) | 7 | 32 |
| \( \text{Hier - Avg. linkage} \) | \( \text{Euclidean} \) | 0 | 0 |
| \( \text{Hier - Centr. linkage} \) | \( PC \) | 2 | 10 |
| \( \text{Hier - Centr. linkage} \) | \( |PC| \) | 2 | 10 |
| \( \text{Hier - Centr. linkage} \) | \( \text{Euclidean} \) | 0 | 0 |
| \( \text{Hier - Sing. linkage} \) | \( PC \) | 2 | 10 |
| \( \text{Hier - Sing. linkage} \) | \( |PC| \) | 2 | 10 |
| \( \text{Hier - Sing. linkage} \) | \( \text{Euclidean} \) | 0 | 0 |
| \( \langle \text{Hierarchical} \rangle \) | | 4.8 | 21.3 |
TABLE XII Coherence results for the SP500 data with respect to the GICS companies' annotations with $N_c = 15$ clusters. The column and row definitions are as in Table XI.

| $N_c = 15$ | Algorithm $^a$ | Similarity $^b$ | $N^pos$ $^c$ | $\langle Coh \rangle$ $^d$ |
|------------|----------------|-----------------|-------------|-------------------|
| Ichost     | mutual information | 15 | 93 |
| $K$–means      | PC          | 12 | 69 |
| $K$–means      | $|PC|$      | 13 | 68 |
| $K$–means      | Euclidean   | 11 | 54 |
| $K$–medians   | PC          | 15 | 90 |
| $K$–medians   | $|PC|$      | 15 | 88 |
| $K$–medians   | Euclidean   | 15 | 85 |
| $\langle K$–means $\rangle$ | | 13.5 | 75.7 |
| Hier - Comp. linkage | PC | 11 | 63 |
| Hier - Comp. linkage | $|PC|$ | 11 | 63 |
| Hier - Comp. linkage | Euclidean | 2 | 5 |
| Hier - Avg. linkage | PC | 6 | 32 |
| Hier - Avg. linkage | $|PC|$ | 6 | 32 |
| Hier - Avg. linkage | Euclidean | 0 | 0 |
| Hier - Centr. linkage | PC | 1 | 7 |
| Hier - Centr. linkage | $|PC|$ | 1 | 7 |
| Hier - Centr. linkage | Euclidean | 0 | 0 |
| Hier - Sing. linkage | PC | 1 | 7 |
| Hier - Sing. linkage | $|PC|$ | 1 | 7 |
| Hier - Sing. linkage | Euclidean | 0 | 0 |
| $\langle$ Hierarchical $\rangle$ | | 3.3 | 18.6 |
TABLE XIII Coherence results for the SP500 data with respect to the GICS companies’ annotations with \( N_c = 10 \) clusters. The column and row definitions are as in Table XI.

| \( N_c = 10 \) Algorithm \(^a\) | Similarity \(^b\) | \( N^c_{pos} \) \(^c\) | \( \langle Coh \rangle \) \(^d\) |
|----------------|-------------|-------------|-----------|
| Ichart         | mutual information | 10          | 91        |
| \( K \)–means  | PC          | 10          | 84        |
| \( K \)–means  | \( |PC| \)    | 10          | 85        |
| \( K \)–means  | Euclidean   | 8           | 63        |
| \( K \)–medians | PC          | 10          | 90        |
| \( K \)–medians | \( |PC| \)    | 10          | 90        |
| \( K \)–medians | Euclidean   | 10          | 77        |
| ( \( K \)–means \) |             | 9.7         | 81.5      |
| Hier - Comp. linkage   | PC          | 8           | 64        |
| Hier - Comp. linkage   | \( |PC| \)    | 8           | 64        |
| Hier - Comp. linkage   | Euclidean   | 4           | 22        |
| Hier - Avg. linkage    | PC          | 2           | 20        |
| Hier - Avg. linkage    | \( |PC| \)    | 2           | 20        |
| Hier - Avg. linkage    | Euclidean   | 0           | 0         |
| Hier - Centr. linkage  | PC          | 1           | 10        |
| Hier - Centr. linkage  | \( |PC| \)    | 1           | 10        |
| Hier - Centr. linkage  | Euclidean   | 0           | 0         |
| Hier - Sing. linkage   | PC          | 0           | 0         |
| Hier - Sing. linkage   | \( |PC| \)    | 0           | 0         |
| Hier - Sing. linkage   | Euclidean   | 0           | 0         |
| ( Hierarchical \)      |             | 2.2         | 17.5      |
TABLE XIV Coherence results for the SP500 data with respect to the GICS companies’ annotations with $N_c = 5$ clusters. The column and row definitions are as in Table XI.

| $N_c = 5$ | Algorithm $^a$ | Similarity $^b$ | $N_{pos}^c$ | $\langle Coh \rangle^d$ |
|-----------|-----------------|-----------------|-------------|-----------------|
| Iclust    | mutual information | 5              | 88          |
| $K$–means | PC              | 5              | 90          |
| $K$–means | $|PC|$           | 5              | 87          |
| $K$–means | Euclidean       | 4              | 54          |
| $K$–medians | PC           | 5              | 90          |
| $K$–medians | $|PC|$        | 5              | 92          |
| $K$–medians | Euclidean     | 5              | 84          |
| ( $K$–means ) |               | 4.8            | 82.8        |
| Hier - Comp. linkage | PC | 4           | 66          |
| Hier - Comp. linkage | $|PC|$ | 5           | 84          |
| Hier - Comp. linkage | Euclidean | 3            | 36          |
| Hier - Avg. linkage | PC               | 1            | 20          |
| Hier - Avg. linkage | $|PC|$          | 1            | 20          |
| Hier - Avg. linkage | Euclidean      | 0            | 0           |
| Hier - Centr. linkage | PC | 0           | 0           |
| Hier - Centr. linkage | $|PC|$ | 0           | 0           |
| Hier - Centr. linkage | Euclidean | 0            | 0           |
| Hier - Sing. linkage | PC | 0           | 0           |
| Hier - Sing. linkage | $|PC|$ | 0           | 0           |
| Hier - Sing. linkage | Euclidean | 0            | 0           |
| ( Hierarchical ) |               | 1.2           | 18.8        |
### TABLE XV Enriched GICS annotations in the Iclust solution with $N_c = 20$ clusters for the SP500 data. Clusters are ordered as in Figure 11, Figure 12, and Figure 13. Only annotations with a $P$-value below 0.05 (Bonferroni corrected) are presented.

- **C** Cluster index.
- **C size** Cluster size.
- **Coh.** Cluster coherence (in percentage).
- **Enriched annot.** Enriched annotations. In parentheses: $(x/K, p)$ stands for the number of companies in the cluster to which this annotation is assigned, the number of companies in the entire data to which this annotation is assigned, and the Bonferroni corrected $P$-value, respectively.

| Cluster | C size | Coh. | Enriched annotations |
|---------|--------|------|----------------------|
| 11 | 18 | 100 | 4530 Semiconductors & Semiconductor Equipment (16/19, 0.000000) 453010 Semiconductors & Semiconductor Equipment (16/19, 0.000000) 45301020 Semiconductors (12/15, 0.000000) 45 Information Technology (18/81, 0.000000) 45301010 Semiconductor Equipment (4/4.0, 0.000013) |
| 9 | 20 | 95 | 45 Information Technology (19/81, 0.000000) 4520 Technology Hardware & Equipment (10/35, 0.000000) 4510 Software (6/15, 0.000155) 452010 Communications Equipment (5/14, 0.0001970) 45201020 Communications Equipment (5/14, 0.0001970) 45103010 Application Software (4/8.0, 0.023868) 45203020 Electronic Manufacturing Services (3/4.0, 0.04177) |
| 12 | 21 | 95 | 45 Information Technology (17/81, 0.000000) 4520 Technology Hardware & Equipment (13/35, 0.000000) 452020 Computer Hardware (5/7, 0.000035) 452010 Communications Equipment (6/14, 0.000132) 45201020 Communications Equipment (6/14, 0.000132) 452020 Computer & Peripherals (5/10, 0.000383) 501020 Wireless Telecommunication Services (2/2.0, 0.0400138) 50102010 Wireless Telecommunication Services (2/2.0, 0.0400138) |
| 10 | 20 | 65 | 2510 Automobiles & Components (6/9.0, 0.000005) 251010 Auto Components (4/9.0, 0.000063) 201010 Aerospace & Defense (4/9.0, 0.000068) 20101010 Auto Parts & Equipment (3/4.0, 0.00730) 201010 Capital Goods (7/37, 0.009990) 25102010 Automobile Manufacturers (2/2.0, 0.046560) |
| 16 | 10 | 30 | 25301020 Hotels Resort & Cruise Lines (3/4.0, 0.000546) 2530 Hotels Restaurant & Leisure (3/11, 0.020860) 253010 Hotels Restaurant & Leisure (3/11, 0.020860) |
| 18 | 176 | 19 | 351010 Health Care Equipment & Supplies (13/13, 0.000033) 35101010 Health Care Equipment (11/11, 0.000186) 2020 Commercial Services & Supplies (14/12, 0.009850) 202010 Commercial Services & Supplies (14/12, 0.009850) 2030 Transportation (9/9.0, 0.00371) |
| 3 | 17 | 83 | 351020 Health Care Providers & Services (9/16, 0.000000) 3510 Health Care Equipment & Supplies (9/20, 0.000000) 35 Health Care (10/47, 0.000000) 35102030 Managed Health Care (4/5.0, 0.000015) 35102015 Health Care Services (2/4.0, 0.045569) 35102020 Health Care Facilities (2/4.0, 0.045569) |
| Co. | C size | Coh. | Enriched annot. |
|-----|--------|------|-----------------|
| c14 | 18     | 94   | 3520 Pharmaceuticals (10/13, 0.000000) |
|     |        |      | 352010 Pharmaceuticals (10/13, 0.000000) |
|     |        |      | 3520 Pharmaceuticals & Biotechnology (10/18, 0.000000) |
|     |        |      | 35 Health Care (12/47, 0.000000) |
|     |        |      | 561010 Diversified Telecommunication Services (5/9, 0.000000) |
|     |        |      | 56101020 Integrated Telecommunication Services (5/9, 0.000000) |
|     |        |      | 56 Telecommunication Services (5/11, 0.000000) |
|     |        |      | 5610 Telecommunication Services (5/11, 0.000000) |
| c5  | 18     | 94   | 30 Consumer Staples (17/35, 0.000000) |
|     |        |      | 3020 Food Beverage & Tobacco (12/19, 0.000000) |
|     |        |      | 302020 Food Products (9/10, 0.000000) |
|     |        |      | 30202030 Packaged Food & Meat (6/9, 0.000000) |
|     |        |      | 3030 Household & Personal Products (4/6, 0.000000) |
|     |        |      | 303010 Household Products (3/4, 0.000000) |
|     |        |      | 30301010 Household Products (3/4, 0.000000) |
|     |        |      | 302010 Beverages (3/6, 0.000000) |
| c15 | 9      | 83   | 4040 Real Estate (5/6, 0.000000) |
|     |        |      | 404010 Real Estate (5/6, 0.000000) |
|     |        |      | 40401020 Real Estate Investment Trusts (5/6, 0.000000) |
|     |        |      | 40 Financials (5/80, 0.000000) |
| c2  | 15     | 93   | 2540 Media (10/14, 0.000000) |
|     |        |      | 254010 Media (10/14, 0.000000) |
|     |        |      | 25401040 Publishing (7/7, 0.000000) |
|     |        |      | 25 Consumer Discretionary (14/83, 0.000000) |
|     |        |      | 25401020 Broadcasting & Cable TV (2/3, 0.000000) |
|     |        |      | 252010 Household Durables (3/11, 0.000000) |
| c17 | 23     | 100  | 2550 Retailing (19/30, 0.000000) |
|     |        |      | 25 Consumer Discretionary (21/83, 0.000000) |
|     |        |      | 255030 Multi-line Retail (9/11, 0.000000) |
|     |        |      | 255040 Specialty Retail (10/17, 0.000000) |
|     |        |      | 25503010 Department Stores (5/7, 0.000000) |
|     |        |      | 25503020 General Merchandise Stores (4/4, 0.000000) |
|     |        |      | 25504010 Apparel Retail (3/3, 0.000000) |
|     |        |      | 25504040 Specialty Stores (4/8, 0.000000) |
|     |        |      | 30101040 Hypermart & Super Centers (2/2, 0.000000) |
| c4  | 19     | 100  | 55 Utilities (19/36, 0.000000) |
|     |        |      | 5510 Utilities (19/36, 0.000000) |
|     |        |      | 551010 Electric Utilities (14/22, 0.000000) |
|     |        |      | 55101010 Electric Utilities (14/22, 0.000000) |
|     |        |      | 551020 Gas Utilities (3/6, 0.000000) |
|     |        |      | 55102010 Gas Utilities (3/6, 0.000000) |
| c13 | 23     | 100  | 4030 Insurance (19/21, 0.000000) |
|     |        |      | 403010 Insurance (19/21, 0.000000) |
|     |        |      | 40 Financials (23/80, 0.000000) |
|     |        |      | 40301040 Property & Casualty Insurance (9/9, 0.000000) |
|     |        |      | 40301020 Life & Health Insurance (6/7, 0.000000) |
|     |        |      | 40301030 Multi-line Insurance (3/3, 0.000000) |
|     |        |      | 401020 Thrift & Mortgage Finance (3/6, 0.000000) |
|     |        |      | 40102010 Thrift & Mortgage Finance (3/6, 0.000000) |
| c7  | 15     | 100  | 4020 Diversified Financials (15/24, 0.000000) |
|     |        |      | 402030 Capital Markets (13/16, 0.000000) |
|     |        |      | 40 Financials (15/80, 0.000000) |
|     |        |      | 40203020 Investment Banking & Brokerage (6/7, 0.000000) |
|     |        |      | 40203010 Asset Management & Custody Banks (6/8, 0.000000) |
| c1  | 21     | 100  | 401010 Commercial Banks (21/23, 0.000000) |
|     |        |      | 4010 Banks (21/23, 0.000000) |
|     |        |      | 40101015 Regional Banks (16/17, 0.000000) |
|     |        |      | 40 Financials (21/80, 0.000000) |
|     |        |      | 40101010 Diversified Banks (5/6, 0.000000) |
| C^a | C size^b | Coh.^c | Enriched annot.\textsuperscript{d} |
|-----|---------|--------|-----------------------------------|
| c8  | 23      | 83     | 201060 Machinery (12/14,0.000000)  
2010 Capital Goods (16/37,0.000000)  
20 Industrials (16/58,0.000000)  
20106020 Industrial Machinery (7/9,0.000000)  
20106010 Construction & Farm Machinery & Heavy Trucks (5/5,0.000004)  
151050 Paper & Forest Products (3/5,0.023469) |
| c19 | 14      | 93     | 151010 Chemicals (11/14,0.000000)  
15 Materials (13/33,0.000000)  
1510 Materials (13/33,0.000000)  
15101020 Diversified Chemicals (5/6,0.000001)  
15101050 Specialty Chemicals (4/5,0.000002)  
15101040 Industrial Gases (2/2,0.009226)  
15103020 Paper Packaging (2/3,0.027226) |
| c6  | 13      | 100    | 10 Energy (13/23,0.000000)  
1010 Energy (13/23,0.000000)  
101010 Energy Equipment & Services (7/7,0.000000)  
10102020 Oil & Gas Exploration & Production (6/7,0.000000)  
10101020 Oil & Gas Equipment & Services (4/4,0.000002)  
101020 Oil & Gas (6/16,0.000005)  
10101010 Oil & Gas Drilling (3/3,0.000010) |
| c20 | 8       | 100    | 101020 Oil & Gas (8/16,0.000000)  
10 Energy (8/23,0.000000)  
1010 Energy (8/23,0.000000)  
10102010 Integrated Oil & Gas (5/6,0.000000)  
10102030 Oil & Gas Refining & Marketing & Transportation (2/3,0.004224) |
TABLE XVI Coherence results for the EachMovie data with respect to the movie genre annotations with $N_c = 20$ clusters. 

aClustering algorithm. In the ( $K$–means ) row we present the average results of all the six $K$–means variants. For each of these variants we performed 100 runs from which the best solution is chosen. In the ( Hier. ) row we present the average results of all the 12 Hierarchical clustering variants. 

bCorrelation measure used by the algorithm. $PC$ stands for the (centered) Pearson Correlation. $|PC|$ is the absolute value of this correlation. $Euclidean$ stands for the Euclidean distance. 

cNumber of clusters with a positive coherence. 

dAverage coherence of all 20 clusters.

| $N_c = 20$ | Algorithm | Similarity | $N_{pos}$ | $\langle Coh \rangle$ |
|------------|-----------|------------|-----------|----------------|
| Ichust     | mutual information | 15 | 54 |
| $K$–means  | $PC$      | 1 | 3 |
| $K$–means  | $|PC|$    | 2 | 4 |
| $K$–means  | $Euclidean$ | 5 | 12 |
| $K$–medians | $PC$      | 2 | 5 |
| $K$–medians | $|PC|$    | 4 | 8 |
| $K$–medians | $Euclidean$ | 2 | 6 |
| ( $K$–means ) |          | 2.7 | 6.3 |
| Hier - Comp. linkage | $PC$ | 17 | 55 |
| Hier - Comp. linkage | $|PC|$ | 16 | 51 |
| Hier - Comp. linkage | $Euclidean$ | 10 | 34 |
| Hier - Avg. linkage | $PC$ | 12 | 43 |
| Hier - Avg. linkage | $|PC|$ | 12 | 43 |
| Hier - Avg. linkage | $Euclidean$ | 5 | 19 |
| Hier - Centr. linkage | $PC$ | 4 | 16 |
| Hier - Centr. linkage | $|PC|$ | 4 | 16 |
| Hier - Centr. linkage | $Euclidean$ | 2 | 8 |
| Hier - Sing. linkage | $PC$ | 0 | 0 |
| Hier - Sing. linkage | $|PC|$ | 0 | 0 |
| Hier - Sing. linkage | $Euclidean$ | 1 | 5 |
| ( Hierarchical ) | | 6.9 | 24.2 |
TABLE XVII Coherence results for the EachMovie data with respect to the movie genre annotations with $N_c = 15$ clusters. The column and row definitions are as in Table XVI.

| $N_c = 15$ | Algorithm $^a$ | Similarity $^b$ | $N_{pos}^c$ | $\langle Coh \rangle^d$ |
|------------|----------------|----------------|-------------|------------------|
| Ichst      | mutual information | 11 | 54 |
| $K$–means  | $PC$            | 1 | 2 |
| $K$–means  | $|PC|$          | 1 | 1 |
| $K$–means  | Euclidean       | 2 | 6 |
| $K$–medians| $PC$            | 2 | 5 |
| $K$–medians| $|PC|$          | 1 | 3 |
| $K$–medians| Euclidean       | 4 | 14 |
| $\langle K$–means $\rangle$ | $PC$ | 21.8 | 5.2 |
| Hier - Comp. linkage | $PC$ | 13 | 54 |
| Hier - Comp. linkage | $|PC|$ | 11 | 47 |
| Hier - Comp. linkage | Euclidean | 6 | 29 |
| Hier - Avg. linkage | $PC$ | 10 | 47 |
| Hier - Avg. linkage | $|PC|$ | 10 | 46 |
| Hier - Avg. linkage | Euclidean | 3 | 16 |
| Hier - Centr. linkage | $PC$ | 2 | 8 |
| Hier - Centr. linkage | $|PC|$ | 2 | 8 |
| Hier - Centr. linkage | Euclidean | 1 | 3 |
| Hier - Sing. linkage | $PC$ | 0 | 0 |
| Hier - Sing. linkage | $|PC|$ | 0 | 0 |
| Hier - Sing. linkage | Euclidean | 1 | 7 |
| $\langle$ Hierarchical $\rangle$ | | 4.9 | 22.1 |
TABLE XVIII Coherence results for the EachMovie data with respect to the movie genre annotations with $N_c = 10$ clusters. The column and row definitions are as in Table XVI.

| $N_c = 10$ | Algorithm $^a$ | Similarity $^b$ | $N_{pos} ^c$ | $\langle Coh \rangle ^d$ |
|------------|----------------|-----------------|-------------|----------------|
| Ichust     | mutual information | 9   | 57         |
| $K$–means  | PC              | 1   | 3     |
| $K$–means  | $|PC|$           | 1   | 6     |
| $K$–means  | Euclidean       | 4   | 20    |
| $K$–medians| PC              | 2   | 6     |
| $K$–medians| $|PC|$           | 2   | 6     |
| $K$–medians| Euclidean       | 6   | 27    |
| ( $K$–means ) |                 | 2.7 | 11.3  |
| Hier - Comp. linkage | PC | 8   | 43    |
| Hier - Comp. linkage | $|PC|$ | 8   | 44    |
| Hier - Comp. linkage | Euclidean | 5   | 36    |
| Hier - Avg. linkage | PC | 7   | 43    |
| Hier - Avg. linkage | $|PC|$ | 8   | 47    |
| Hier - Avg. linkage | Euclidean | 2   | 16    |
| Hier - Centr. linkage | PC | 2   | 12    |
| Hier - Centr. linkage | $|PC|$ | 2   | 12    |
| Hier - Centr. linkage | Euclidean | 1   | 4     |
| Hier - Sing. linkage | PC | 0   | 0     |
| Hier - Sing. linkage | $|PC|$ | 0   | 0     |
| Hier - Sing. linkage | Euclidean | 1   | 10    |
| ( Hierarchical ) |                  | 3.7 | 22.3  |
TABLE XIX Coherence results for the EachMovie data with respect to the movie genre annotations with $N_c = 5$ clusters. The column and row definitions are as in Table XVI.

| $N_c = 5$ | Algorithm $^a$ | Similarity $^b$ | $N_{pos}^c$ | $\langle Coh \rangle^d$ |
|-----------|----------------|-----------------|-------------|-------------------|
|           | Iclust         | mutual information | 5           | 48                |
|           | $K$–means      | PC              | 2           | 21                |
|           | $K$–means      | $|PC|$           | 2           | 19                |
|           | $K$–means      | Euclidean       | 3           | 30                |
|           | $K$–medians    | PC              | 4           | 32                |
|           | $K$–medians    | $|PC|$           | 2           | 19                |
|           | $K$–medians    | Euclidean       | 4           | 37                |
|           | ( $K$–means ) |                  | 2.8         | 26.3              |
|           | Hier - Comp. linkage | PC              | 5           | 51                |
|           | Hier - Comp. linkage | $|PC|$           | 5           | 41                |
|           | Hier - Comp. linkage | Euclidean       | 4           | 48                |
|           | Hier - Avg. linkage | PC              | 4           | 46                |
|           | Hier - Avg. linkage | $|PC|$           | 4           | 47                |
|           | Hier - Avg. linkage | Euclidean       | 2           | 21                |
|           | Hier - Centr. linkage | PC              | 2           | 23                |
|           | Hier - Centr. linkage | $|PC|$           | 2           | 23                |
|           | Hier - Centr. linkage | Euclidean       | 1           | 9                 |
|           | Hier - Sing. linkage | PC              | 0           | 0                 |
|           | Hier - Sing. linkage | $|PC|$           | 0           | 0                 |
|           | Hier - Sing. linkage | Euclidean       | 0           | 0                 |
|           | ( Hierarchical ) |                  | 2.4         | 25.8              |
TABLE XX Enriched genre annotations in the *Jclust* solution with $N_c = 20$ clusters for the EachMovie data. Clusters are ordered as in Figure 12, Figure 13, and Figure 14. Only annotations with a $P$-value below 0.05 (Bonferroni corrected) are presented. *a*Cluster index. *b*Cluster size. *c*Cluster coherence (in percentage). *d*Enriched annotations. In parentheses: $(x/K, p)$ stands for the number of movies in the cluster to which this annotation is assigned, the number of movies in the entire data to which this annotation is assigned, and the Bonferroni corrected $P$-value, respectively.

| $c$ | $\text{size}$ | Coh. | Enriched annot.  |
|-----|---------------|------|------------------|
| 14  | 10            | 0    | -                |
| 1   | 16            | 0    | -                |
| 19  | 10            | 50   | Art-Foreign (5/45, 0.005254) |
| 8   | 10            | 70   | Art-Foreign (7/45, 0.000019) |
| 18  | 22            | 0    | -                |
| 9   | 31            | 55   | Action (17/110, 0.000281) |
| 20  | 155           | 55   | Drama (68/160, 0.000170), Romance (30/61, 0.011591) |
| 1   | 19            | 95   | Classic (10/44, 0.000004), Drama (15/160, 0.000214) |
| 7   | 24            | 71   | Classic (10/44, 0.000007), Action (13/110, 0.003526) |
| 15  | 18            | 94   | Action (16/110, 0.000060), Thriller (10/90, 0.001778) |
| 5   | 32            | 39   | Thriller (12/90, 0.001778) |
| 13  | 15            | 0    | -                |
| 3   | 20            | 0    | -                |
| 10  | 15            | 0    | -                |
| 4   | 27            | 74   | Romance (12/61, 0.000100), Comedy (17/149, 0.0001613) |
| 6   | 11            | 100  | Comedy (11/149, 0.000001) |
| 16  | 16            | 87   | Comedy (13/149, 0.000012) |
| 17  | 21            | 76   | Action (16/110, 0.000060) |
| 11  | 14            | 71   | Family (10/67, 0.000003) |
| 12  | 14            | 100  | Family (13/67, 0.000000), Animation (8/25, 0.000000), Classic (5/44, 0.000034) |