

Independent component analysis of gene expression data

Wolfram Liebermeister, Theoretische Biophysik
Humboldt-Universität zu Berlin, Germany
wolfram.liebermeister@rz.hu-berlin.de

We applied independent component analysis (ICA) to gene expression data, inferring hidden variables which we term "expression modes". According to the ICA model, the modes exert linear influences on the genes with minimal statistical dependences between them. The dominant modes obtained from a set of yeast data could be related to separate biological functions. A projection to these modes helps to determine sets of coregulated genes, to visualize the data and to compress them in a biologically meaningful way.

The problem

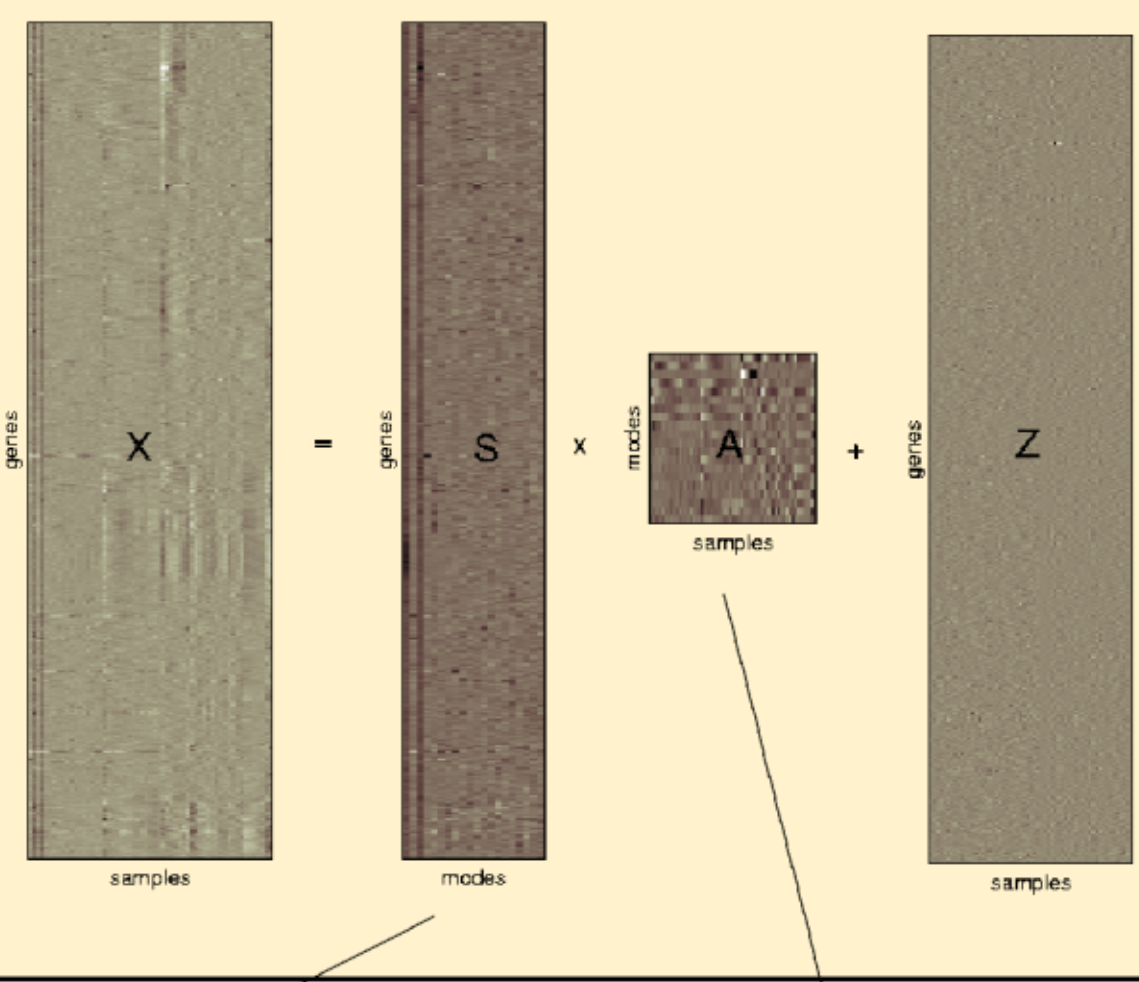
Cells react to external stimuli and to their internal needs by the induction or repression of genes. Genomic scale patterns of gene expression can be observed using high-throughput methods like the microarray technique. One may hope that correlations in these large data sets reveal causal relationships between the genes. This is the main idea behind various kinds of genetic network models, like linear, nonlinear, or discrete dynamical systems, or Bayesian networks. However, it seems that until now the microarray data are too noisy and that the number of experiments is not yet sufficient to reconstruct detailed large-scale genetic networks. Thus, methods are needed to reduce large amounts of data to their most relevant aspects, in particular the coregulation of genes and characteristic patterns of cell sample types. One has to keep in mind that with all multivariate methods the results may depend heavily on data metric, and thus on the normalization scheme used.

Yeast data from Eisen et al. (1998)

The gene expression matrix X contains intensity ratios related to relative mRNA levels of 2467 yeast open reading frames (ORFs). The samples represent timecourses different situations: cell replication cycle (synchronization with the mating α factor or using small G1 cells obtained by elutriation), sporulation, heat shock, response to a reducing agent, cold shock and diauxic shift from fermentation to respiration. We preprocessed the data by shifting the gene and sample means to zero, replacing the missing values by zeros and projecting the data to their first 20 principal components. The higher principal components are contained in the additive noise term Z .

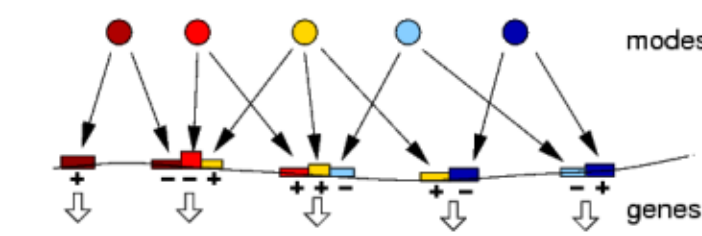
Independent component analysis (ICA)

Independent component analysis (see [6]) determines a linear decomposition $X = S A$ with minimal statistical dependences (as quantified by the mutual information) between the "independent components" (columns of S). As a consequence, the single components become as "informative" as possible, which means that their distributions have minimal entropies. In contrast to PCA, ICA introduces a non-orthogonal basis to take into account data structure beyond the linear correlations. The components have no natural order, and they are scaled to unit variance by convention. In the fastica algorithm used [7], the expensive calculation of entropies is avoided by using a "contrast" function that compares the components' distributions to the normal distribution.



Linear models of gene expression data

Clusterings (for instance hierarchical, k-means, self-organized maps) are a widely used method to determine sets of coregulated genes or sets of cell samples with similar gene expression. In a more detailed view, each gene's expression depends on a group of cellular regulators that may act together in some nonlinear way. Linear models implement the idea of a combinatorial control, describing the expression levels of genes as linear functions of common hidden variables.

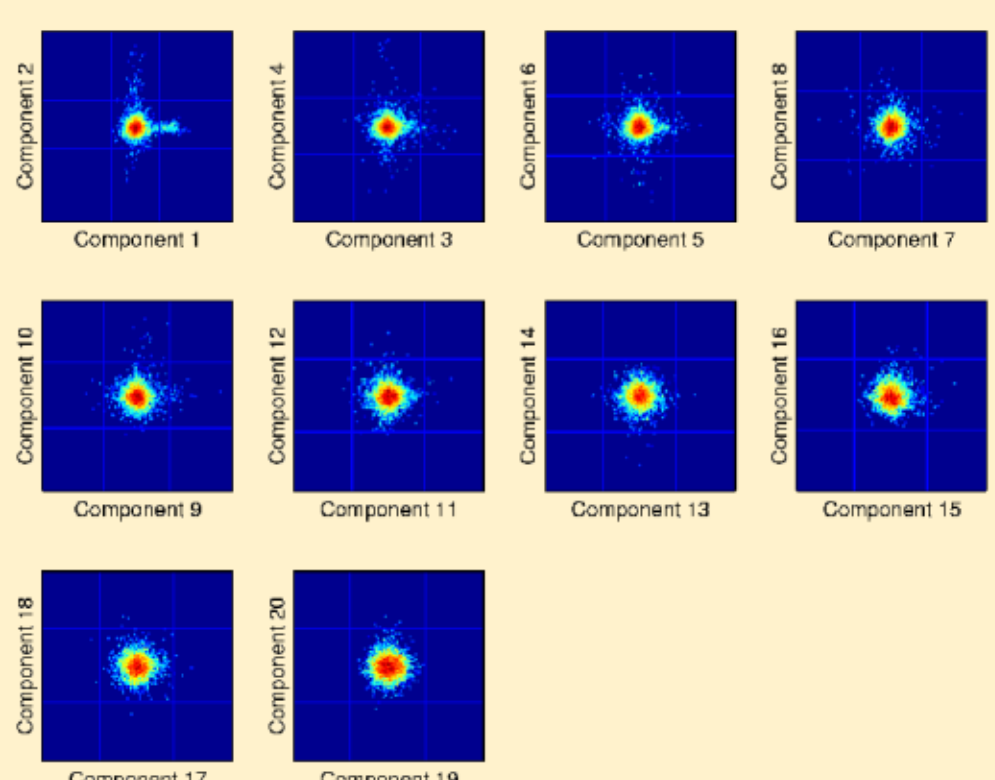


Technically, the gene expression matrix X is split into a product $X = S A$, representing each gene profile (row of X) as a linear combination of "mode profiles" (the rows of A), the coefficients ("components") being contained in the columns of S . Linear models like principal component analysis (PCA) [1], the plaid model [3], REDUCE [4], or ICA rely on different criteria to determine the modes. It would be desirable that some of the modes could be related to biological causes of variation, like regulators of gene expression, cellular functions, or responses to experimental treatments. The components would then describe the modes' influences on the genes. Once a small number of effective key variables has been identified, they may be described by simple dynamic models (see for example [5]).

Principal component analysis (PCA)

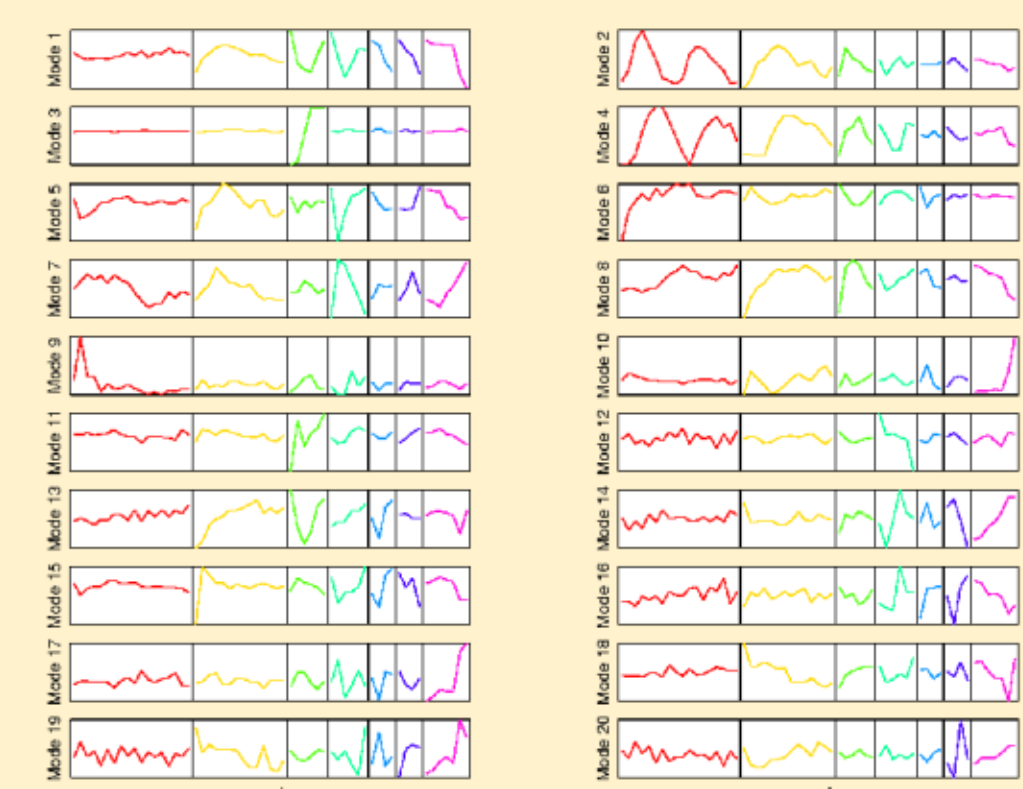
Principal component analysis rotates the data to a new orthonormal basis which is formed by the eigenvectors of the data covariance matrix. In this new basis, linear correlations are removed, and a minimal number of the new variables ("principal components") explains a maximal amount of data variance. PCA is widely used to reduce the data dimensionality, while maintaining a maximal amount of variance and filtering out variation that is likely to represent noise. Usually, there is no obvious biological interpretation for the single components.

Independent components



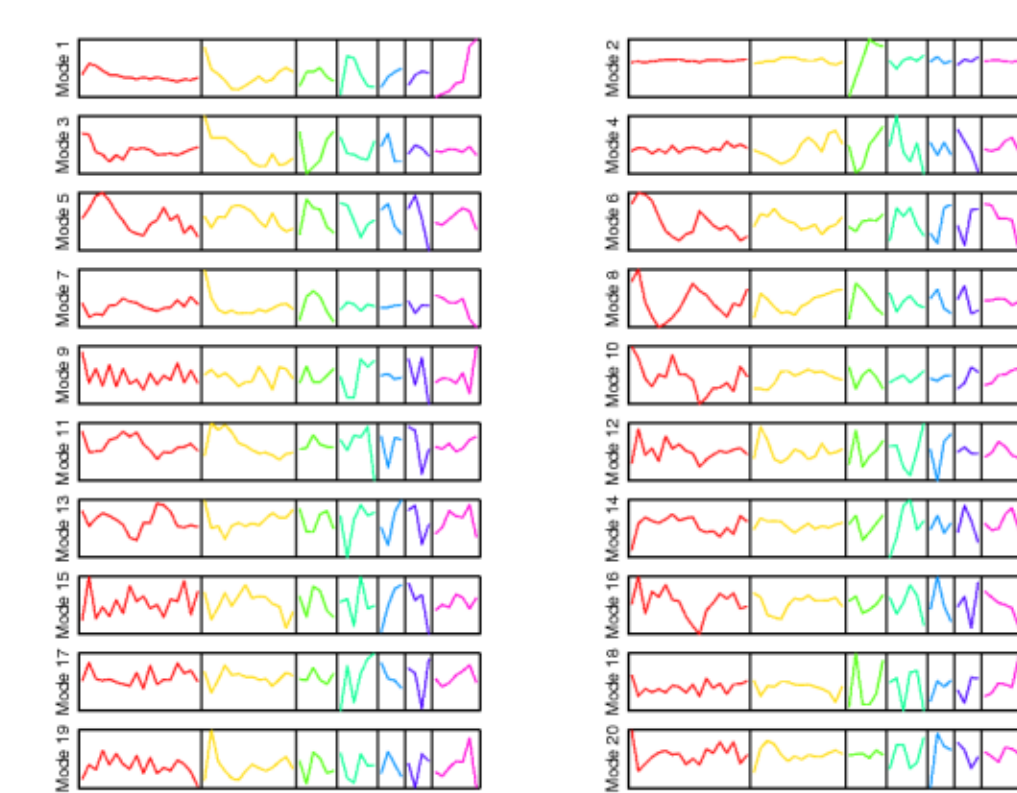
We interpret the independent components (columns of S) as influence weights of hidden variables termed "expression modes". Due to their high contrast, the dominant components show distributions with large tails, indicating specific groups of "target" genes. For each component, we determined these targets by excluding the most outlying genes until all remaining genes were inside $\sigma_{ij} = 4$ standard deviations from their median.

Expression mode profiles



Mode profiles (rows of A , samples shown on the abscissa) from yeast data obtained by ICA. The different gene profiles (rows of X) are represented as linear combinations of these basis patterns (up to a noise term). The colors indicate different experiments.

PCA expression modes



Mode profiles (basis vectors) from yeast data obtained by PCA.

Target genes

Mode 1
ribosome, RPL10, RPL11A, RPL11B, RPL12A, RPL12B, RPL13A, RPL13B, RPL14A, RPL14B, RPL15A, RPL15B, RPL16A, RPL16B, RPL17A, RPL17B, RPL18A, RPL18B, RPL19A, RPL19B, RPL20A, RPL20B, RPL21A, RPL21B, RPL22A, RPL22B, RPL23A, RPL23B, RPL24A, RPL24B, RPL25A, RPL25B, RPL26A, RPL26B, RPL27A, RPL27B, RPL28A, RPL28B, RPL29A, RPL29B, RPL30A, RPL30B, RPL31A, RPL31B, RPL32A, RPL32B, RPL33A, RPL33B, RPL34A, RPL34B, RPL35A, RPL35B, RPL36A, RPL36B, RPL37A, RPL37B, RPL38A, RPL38B, RPL39A, RPL39B, RPL40A, RPL40B, RPL41A, RPL41B, RPL42A, RPL42B, RPL43A, RPL43B, RPL44A, RPL44B, RPL45A, RPL45B, RPL46A, RPL46B, RPL47A, RPL47B, RPL48A, RPL48B, RPL49A, RPL49B, RPL50A, RPL50B, RPL51A, RPL51B, RPL52A, RPL52B, RPL53A, RPL53B, RPL54A, RPL54B, RPL55A, RPL55B, RPL56A, RPL56B, RPL57A, RPL57B, RPL58A, RPL58B, RPL59A, RPL59B, RPL60A, RPL60B, RPL61A, RPL61B, RPL62A, RPL62B, RPL63A, RPL63B, RPL64A, RPL64B, RPL65A, RPL65B, RPL66A, RPL66B, RPL67A, RPL67B, RPL68A, RPL68B, RPL69A, RPL69B, RPL70A, RPL70B, RPL71A, RPL71B, RPL72A, RPL72B, RPL73A, RPL73B, RPL74A, RPL74B, RPL75A, RPL75B, RPL76A, RPL76B, RPL77A, RPL77B, RPL78A, RPL78B, RPL79A, RPL79B, RPL80A, RPL80B, RPL81A, RPL81B, RPL82A, RPL82B, RPL83A, RPL83B, RPL84A, RPL84B, RPL85A, RPL85B, RPL86A, RPL86B, RPL87A, RPL87B, RPL88A, RPL88B, RPL89A, RPL89B, RPL90A, RPL90B, RPL91A, RPL91B, RPL92A, RPL92B, RPL93A, RPL93B, RPL94A, RPL94B, RPL95A, RPL95B, RPL96A, RPL96B, RPL97A, RPL97B, RPL98A, RPL98B, RPL99A, RPL99B, RPS1, RPS2, RPS3, RPS4, RPS5, RPS6, RPS7, RPS8, RPS9, RPS10, RPS11, RPS12, RPS13, RPS14, RPS15, RPS16, RPS17, RPS18, RPS19, RPS20, RPS21, RPS22, RPS23, RPS24, RPS25, RPS26, RPS27, RPS28, RPS29, RPS30, RPS31, RPS32, RPS33, RPS34, RPS35, RPS36, RPS37, RPS38, RPS39, RPS40, RPS41, RPS42, RPS43, RPS44, RPS45, RPS46, RPS47, RPS48, RPS49, RPS50, RPS51, RPS52, RPS53, RPS54, RPS55, RPS56, RPS57, RPS58, RPS59, RPS60, RPS61, RPS62, RPS63, RPS64, RPS65, RPS66, RPS67, RPS68, RPS69, RPS70, RPS71, RPS72, RPS73, RPS74, RPS75, RPS76, RPS77, RPS78, RPS79, RPS80, RPS81, RPS82, RPS83, RPS84, RPS85, RPS86, RPS87, RPS88, RPS89, RPS90, RPS91, RPS92, RPS93, RPS94, RPS95, RPS96, RPS97, RPS98, RPS99, RPS100, RPS101, RPS102, RPS103, RPS104, RPS105, RPS106, RPS107, RPS108, RPS109, RPS110, RPS111, RPS112, RPS113, RPS114, RPS115, RPS116, RPS117, RPS118, RPS119, RPS120, RPS121, RPS122, RPS123, RPS124, RPS125, RPS126, RPS127, RPS128, RPS129, RPS130, RPS131, RPS132, RPS133, RPS134, RPS135, RPS136, RPS137, RPS138, RPS139, RPS140, RPS141, RPS142, RPS143, RPS144, RPS145, RPS146, RPS147, RPS148, RPS149, RPS150, RPS151, RPS152, RPS153, RPS154, RPS155, RPS156, RPS157, RPS158, RPS159, RPS160, RPS161, RPS162, RPS163, RPS164, RPS165, RPS166, RPS167, RPS168, RPS169, RPS170, RPS171, RPS172, RPS173, RPS174, RPS175, RPS176, RPS177, RPS178, RPS179, RPS180, RPS181, RPS182, RPS183, RPS184, RPS185, RPS186, RPS187, RPS188, RPS189, RPS190, RPS191, RPS192, RPS193, RPS194, RPS195, RPS196, RPS197, RPS198, RPS199, RPS200, RPS201, RPS202, RPS203, RPS204, RPS205, RPS206, RPS207, RPS208, RPS209, RPS210, RPS211, RPS212, RPS213, RPS214, RPS215, RPS216, RPS217, RPS218, RPS219, RPS220, RPS221, RPS222, RPS223, RPS224, RPS225, RPS226, RPS227, RPS228, RPS229, RPS230, RPS231, RPS232, RPS233, RPS234, RPS235, RPS236, RPS237, RPS238, RPS239, RPS240, RPS241, RPS242, RPS243, RPS244, RPS245, RPS246, RPS247, RPS248, RPS249, RPS250, RPS251, RPS252, RPS253, RPS254, RPS255, RPS256, RPS257, RPS258, RPS259, RPS260, RPS261, RPS262, RPS263, RPS264, RPS265, RPS266, RPS267, RPS268, RPS269, RPS270, RPS271, RPS272, RPS273, RPS274, RPS275, RPS276, RPS277, RPS278, RPS279, RPS280, RPS281, RPS282, RPS283, RPS284, RPS285, RPS286, RPS287, RPS288, RPS289, RPS290, RPS291, RPS292, RPS293, RPS294, RPS295, RPS296, RPS297, RPS298, RPS299, RPS300, RPS301, RPS302, RPS303, RPS304, RPS305, RPS306, RPS307, RPS308, RPS309, RPS310, RPS311, RPS312, RPS313, RPS314, RPS315, RPS316, RPS317, RPS318, RPS319, RPS320, RPS321, RPS322, RPS323, RPS324, RPS325, RPS326, RPS327, RPS328, RPS329, RPS330, RPS331, RPS332, RPS333, RPS334, RPS335, RPS336, RPS337, RPS338, RPS339, RPS340, RPS341, RPS342, RPS343, RPS344, RPS345, RPS346, RPS347, RPS348, RPS349, RPS350, RPS351, RPS352, RPS353, RPS354, RPS355, RPS356, RPS357, RPS358, RPS359, RPS360, RPS361, RPS362, RPS363, RPS364, RPS365, RPS366, RPS367, RPS368, RPS369, RPS370, RPS371, RPS372, RPS373, RPS374, RPS375, RPS376, RPS377, RPS378, RPS379, RPS380, RPS381, RPS382, RPS383, RPS384, RPS385, RPS386, RPS387, RPS388, RPS389, RPS390, RPS391, RPS392, RPS393, RPS394, RPS395, RPS396, RPS397, RPS398, RPS399, RPS400, RPS401, RPS402, RPS403, RPS404, RPS405, RPS406, RPS407, RPS408, RPS409, RPS410, RPS411, RPS412, RPS413, RPS414, RPS415, RPS416, RPS417, RPS418, RPS419, RPS420, RPS421, RPS422, RPS423, RPS424, RPS425, RPS426, RPS427, RPS428, RPS429, RPS430, RPS431, RPS432, RPS433, RPS434, RPS435, RPS436, RPS437, RPS438, RPS439, RPS440, RPS441, RPS442, RPS443, RPS444, RPS445, RPS446, RPS447, RPS448, RPS449, RPS450, RPS451, RPS452, RPS453, RPS454, RPS455, RPS456, RPS457, RPS458, RPS459, RPS460, RPS461, RPS462, RPS463, RPS464, RPS465, RPS466, RPS467, RPS468, RPS469, RPS470, RPS471, RPS472, RPS473, RPS474, RPS475, RPS476, RPS477, RPS478, RPS479, RPS480, RPS481, RPS482, RPS483, RPS484, RPS485, RPS486, RPS487, RPS488, RPS489, RPS490, RPS491, RPS492, RPS493, RPS494, RPS495, RPS496, RPS497, RPS498, RPS499, RPS500, RPS501, RPS502, RPS503, RPS504, RPS505, RPS506, RPS507, RPS508, RPS509, RPS510, RPS511, RPS512, RPS513, RPS514, RPS515, RPS516, RPS517, RPS518, RPS519, RPS520, RPS521, RPS522, RPS523, RPS524, RPS525, RPS526, RPS527, RPS528, RPS529, RPS530, RPS531, RPS532, RPS533, RPS534, RPS535, RPS536, RPS537, RPS538, RPS539, RPS540, RPS541, RPS542, RPS543, RPS544, RPS545, RPS546, RPS547, RPS548, RPS549, RPS550, RPS551, RPS552, RPS553, RPS554, RPS555, RPS556, RPS557, RPS558, RPS559, RPS560, RPS561, RPS562, RPS563, RPS564, RPS565, RPS566, RPS567, RPS568, RPS569, RPS570, RPS571, RPS572, RPS573, RPS574, RPS575, RPS576, RPS577, RPS578, RPS579, RPS580, RPS581, RPS582, RPS583, RPS584, RPS585, RPS586, RPS587, RPS588, RPS589, RPS590, RPS591, RPS592, RPS593, RPS594, RPS595, RPS596, RPS597, RPS598, RPS599, RPS600, RPS601, RPS602, RPS603, RPS604, RPS605, RPS606, RPS607, RPS608, RPS609, RPS610, RPS611, RPS612, RPS613, RPS614, RPS615, RPS616, RPS617, RPS618, RPS619, RPS620, RPS621, RPS622, RPS623, RPS624, RPS625, RPS626, RPS627, RPS628, RPS629, RPS630, RPS631, RPS632, RPS633, RPS634, RPS635, RPS636, RPS637, RPS638, RPS639, RPS640, RPS641, RPS642, RPS643, RPS644, RPS645, RPS646, RPS647, RPS648, RPS649, RPS650, RPS651, RPS652, RPS653, RPS654, RPS655, RPS656, RPS657, RPS658, RPS659, RPS660, RPS661, RPS662, RPS663, RPS664, RPS665, RPS666, RPS667, RPS668, RPS669, RPS670, RPS671, RPS672, RPS673, RPS674, RPS675, RPS676, RPS677, RPS678, RPS679, RPS680, RPS681, RPS682, RPS683, RPS684, RPS685, RPS686, RPS687, RPS688, RPS689, RPS690, RPS691, RPS692, RPS693, RPS694, RPS695, RPS696, RPS697, RPS698, RPS699, RPS700, RPS701, RPS702, RPS703, RPS704, RPS705, RPS706, RPS707, RPS708, RPS709, RPS710, RPS711, RPS712, RPS713, RPS714, RPS715, RPS716, RPS717, RPS718, RPS719, RPS720, RPS721, RPS722, RPS723, RPS724, RPS725, RPS726, RPS727, RPS728, RPS729, RPS730, RPS731, RPS732, RPS733, RPS734, RPS735, RPS736, RPS737, RPS738, RPS739, RPS740, RPS741, RPS742, RPS743, RPS744, RPS745, RPS746, RPS747, RPS748, RPS749, RPS750, RPS751, RPS752, RPS753, RPS754, RPS755, RPS756, RPS757, RPS758, RPS759, RPS760, RPS761, RPS762, RPS763, RPS764, RPS765, RPS766, RPS767, RPS768, RPS769, RPS770, RPS771, RPS772, RPS773, RPS774, RPS775, RPS776, RPS777, RPS778, RPS779, RPS780, RPS781, RPS782, RPS783, RPS784, RPS785, RPS786, RPS787, RPS788, RPS789, RPS790, RPS791, RPS792, RPS793, RPS794, RPS795, RPS796, RPS797, RPS798, RPS799, RPS800, RPS801, RPS802, RPS803, RPS804, RPS805, RPS806, RPS807, RPS808, RPS809, RPS810, RPS811, RPS812, RPS813, RPS814, RPS815, RPS816, RPS817, RPS818, RPS819, RPS820, RPS821, RPS822, RPS823, RPS824, RPS825, RPS826, RPS827, RPS828, RPS829, RPS830, RPS831, RPS832, RPS833, RPS834, RPS835, RPS836, RPS837, RPS838, RPS839, RPS840, RPS841, RPS842, RPS843, RPS844, RPS845, RPS846, RPS847, RPS848, RPS849, RPS850, RPS851, RPS852, RPS853, RPS854, RPS855, RPS856, RPS857, RPS858, RPS859, RPS860, RPS861, RPS862, RPS863, RPS864, RPS865, RPS866, RPS867, RPS868, RPS869, RPS870, RPS871, RPS872, RPS873, RPS874, RPS875, RPS876, RPS877, RPS878, RPS879, RPS880, RPS881, RPS882, RPS883, RPS884, RPS885, RPS886, RPS887, RPS888, RPS889, RPS890, RPS891, RPS892, RPS893, RPS894, RPS895, RPS896, RPS897, RPS898, RPS899, RPS900, RPS901, RPS902, RPS903, RPS904, RPS905, RPS906, RPS907, RPS908, RPS909, RPS910, RPS911, RPS912, RPS913, RPS914, RPS915, RPS916, RPS917, RPS918, RPS919, RPS920, RPS921, RPS922, RPS923, RPS924, RPS925, RPS926, RPS927, RPS928, RPS929, RPS930, RPS931, RPS932, RPS933, RPS934, RPS935, RPS936, RPS937, RPS938, RPS939, RPS940, RPS941, RPS942, RPS943, RPS944, RPS945, RPS946, RPS947, RPS948, RPS949, RPS950, RPS951, RPS952, RPS953, RPS954, RPS955, RPS956, RPS957, RPS958, RPS959, RPS960, RPS961, RPS962, RPS963, RPS964, RPS965, RPS966, RPS967, RPS968, RPS969, RPS970, RPS971, RPS972, RPS973, RPS974, RPS975, RPS976, RPS977, RPS978, RPS979, RPS980, RPS981, RPS982, RPS983, RPS984, RPS985, RPS986, RPS987, RPS988, RPS989, RPS990, RPS991, RPS992, RPS993, RPS994, RPS995, RPS996, RPS997, RPS998, RPS999, RPS1000, RPS1001, RPS1002, RPS1003, RPS1004, RPS1005, RPS1006, RPS1007, RPS1008, RPS1009, RPS1010, RPS1011, RPS1012, RPS1013, RPS1014, RPS1015, RPS1016, RPS1017, RPS1018, RPS1019, RPS1020, RPS1021, RPS1022, RPS1023, RPS1024, RPS1025, RPS1026, RPS1027, RPS1028, RPS1029, RPS1030, RPS1031, RPS1032, RPS1033, RPS1034, RPS1035, RPS1036, RPS1037, RPS1038, RPS1039, RPS1040, RPS1041, RPS1042, RPS1043, RPS1044, RPS1045, RPS1046, RPS1047, RPS1048, RPS1049, RPS1050, RPS1051, RPS1052, RPS1053, RPS1054, RPS1055, RPS1056, RPS1057, RPS1058, RPS1059, RPS1060, RPS1061, RPS1062, RPS1063, RPS1064, RPS1065, RPS1066, RPS1067, RPS1068, RPS1069, RPS1070, RPS1071, RPS1072, RPS1073, RPS1074, RPS1075, RPS1076, RPS1077, RPS1078, RPS1079, RPS1080, RPS1081, RPS1082, RPS1083, RPS1084, RPS1085, RPS1086, RPS1087, RPS1088, RPS1089, RPS1090, RPS1091, RPS1092, RPS1093, RPS1094, RPS1095, RPS1096, RPS1097, RPS1098, RPS1099, RPS1100, RPS1101, RPS1102, RPS1103, RPS1104, RPS1105, RPS1106, RPS1107, RPS1108, RPS1109, RPS1110, RPS1111, RPS1112, RPS1113, RPS1114, RPS1115, RPS1116, RPS1117, RPS1118, RPS1119, RPS1120, RPS1121, RPS1122, RPS1123, RPS1124, RPS1125, RPS1126, RPS1127, RPS1128, RPS1129, RPS1130, RPS1131, RPS1132, RPS1133, RPS1134, RPS1135, RPS1136, RPS1137, RPS1138, RPS1139, RPS1140, RPS1141, RPS1142, RPS1143, RPS1144, RPS1145, RPS1146, RPS1147, RPS1148, RPS1149, RPS1150, RPS1151, RPS1152, RPS1153, RPS1154, RPS1155, RPS1156, RPS1157, RPS1158, RPS1159, RPS1160, RPS1161, RPS1162, RPS1163, RPS1164, RPS1165, RPS1166, RPS1167, RPS1168, RPS1169, RPS1170, RPS1171, RPS1172, RPS1173, RPS1174, RPS1175, RPS1176, RPS1177, RPS1178, RPS1179, RPS1180, RPS1181, RPS1182, RPS1183, RPS1184, RPS1185, RPS1186, RPS1187, RPS1188, RPS1189, RPS1190, RPS1191, RPS1192, RPS1193, RPS1194, RPS1195, RPS1196, RPS1197, RPS1198, RPS1199, RPS1200, RPS1201, RPS1202, RPS1203, RPS1204, RPS1205, RPS1206, RPS1207, RPS1208, RPS1209, RPS1210, RPS1211, RPS1212, RPS1213, RPS1214, RPS1215, RPS1216, RPS1217, RPS1218, RPS1219, RPS1220, RPS1221, RPS1222, RPS1223, RPS1224, RPS1225, RPS1226, RPS1227, RPS1228, RPS1229, RPS1230, RPS1231, RPS1232, RPS1233, RPS1234, RPS1235, RPS1236, RPS1237, RPS1238, RPS1239, RPS1240, RPS1241, RPS1242, RPS1243, RPS1244, RPS1245, RPS1246, RPS1247, RPS1248, RPS1249, RPS1250, RPS1251, RPS1252, RPS1253, RPS1254, RPS1255, RPS1256, RPS1257, RPS1258, RPS1259, RPS1260, RPS1261, RPS1262, RPS1263, RPS1264, RPS1265, RPS1266, RPS1267, RPS1268, RPS1269, RPS1270, RPS1271, RPS1272, RPS1273, RPS1274, RPS1275, RPS1276, RPS1277, RPS1278, RPS1279, RPS1280, RPS1281, RPS1282, RPS1283, RPS1284, RPS1285, RPS1286, RPS1287, RPS1288, RPS1289, RPS1290, RPS1291, RPS1292, RPS1293, RPS1294, RPS1295, RPS1296, RPS1297, RPS1298, RPS1299, RPS1300, RPS1301, RPS1302, RPS1303, RPS1304, RPS1305, RPS1306, RPS1307, RPS1308, RPS1309, RPS1310, RPS1311, RPS1312, RPS1313, RPS1314, RPS1315, RPS1316, RPS1317, RPS1318, RPS1319, RPS1320, RPS1321, RPS1322, RPS1323, RPS1324, RPS1325, RPS1326, RPS1327, RPS1328, RPS1329, RPS1330, RPS1331, RPS1332, RPS1333, RPS1334, RPS1335, RPS1336, RPS1337, RPS1338, RPS1339, RPS1340, RPS1341, RPS1342, RPS1343, RPS1344, RPS1345, RPS1346, RPS1347, RPS1348, RPS1349, RPS1350, RPS1351, RPS1352, RPS1353, RPS1354, RPS1355, RPS1356, RPS1357, RPS1358, RPS1359, RPS1360, RPS1361, RPS1362, RPS1363, RPS1364, RPS1365, RPS1366, RPS1367, RPS1368, RPS1369, RPS1370, RPS1371, RPS1372, RPS1373, RPS1374, RPS1375, RPS1376, RPS1377, RPS1378, RPS1379, RPS1380, RPS1381, RPS1382, RPS1383, RPS1384, RPS1385, RPS1386, RPS1387, RPS1388, RPS1389, RPS1390, RPS1391, RPS1392, RPS1393, RPS1394, RPS1395, RPS1396, RPS1397, RPS1398, RPS1399, RPS1400, RPS1401, RPS1402, RPS1403, RPS1404, RPS1405, RPS1406, RPS1407, RPS1408, RPS1409, RPS141