COPD, Statistics, and Network Inference

Towards a New Privacy-Centric Search Engine for Mobile Apps: Search by Privacy

Periodiek

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Ideas behind a seemingly simplistic puzzle

FMF

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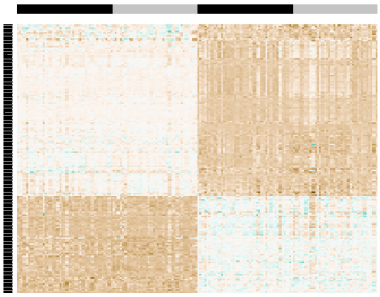
A group of bioinformaticians and statisticians participating in the Data Science and Systems Complexity Center (DSSC) try to unravel the underlying mechanism behind complex diseases by extending current statistical models with tools from statistics, mathematics, and bioinformatics.

A)



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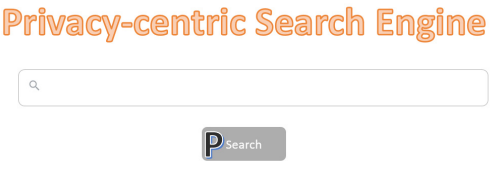
The Perio's own Robert Modderman has developed a mathematics-inspired puzzle game "Digits". What are the underlying ideas when developing such a game? Take a glance at the least visible and most abstract aspect of puzzle game development.

18 - Towards a New Privacy-Centric Search Engine for Mobile Apps: Search by Privacy

There is a mobile app for almost everything we do. Currently, there are millions of third party applications for mobile phones that users can install from online markets, including malicious applications that could pose serious security and privacy risks to users.



In this Periodiek

From the Editor in Chief

The last Perio of the calendar year 2019 (hopefully you will find it on your doormat before that statement becomes false). I previously already stepped down as editor in chief, but due to some internal reasons I have decided to make one more Perio before I really stop in my current position.

This Perio is a bit more mathematics oriented than usual, but also for the less mathematically inclined I think there are some very interesting articles, with subjects ranging from biology, app development, privacy and machine learning. Sadly, there is no interview this issue. But don't worry, it will be back next time.

Jonah Stalknecht

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From the Board

AUTHOR: **FLORIS DRENT**

Greetings! If you have not met me by now, you have not been visiting the FMF very often. My name is Floris and I am the Commissioner of Educational Affairs of the 61st board of the FMF. I decided to do a board year for a couple of reasons, one of them is wanting an adventurous change of pace before I finish my master's and become an adult person. It also sounded like a great opportunity to meet and help new people.

I joined the board long after the then-candidates were announced. I only have to finish two courses for my master's this year and I planned to work as a high school teacher this academic year while doing so. However, I also thought about how I can always be a teacher, but this is basically the only opportunity for me to do board year. So of course, as someone with an interest in education in general, I joined up for the position of Education, seeing education to be the cradle of civilisation! The Commissioner of Educational Affairs ~~lies on the couch and drinks beer~~ is responsible for the book sale, catch-up sessions and the exam database. Besides that, the position takes care of all the communication between the university, for example the lecturers or academic advisors, and the FMF. Besides that, the position offers a lot of freedom to organise anything that adds to the education of students of our association. A good example is the first cool thing I organised, namely a guest lecture from Statistics Netherlands for the mathematics course Statistics. That went absolutely amazing. Another cool thing I got to do and what I still try to do is to welcome all the new first years and to make them feel at home. I think that will remain my favourite activity.

Even though we are now in the first few months as a new board, it has already been a whole new learning experience where I have made many mistakes. Hopefully things go more smoothly next period with organising catch-up sessions, ordering books and various other activities. The position also educates the person doing it.

The one thing I hope to organise as Education this year is recap sessions where we go over some mathematics and physics problems that have been collecting dust in the corner of our memories. I would also like to organise another snowdoll crafting session, which we also did last year. Secretly I hope that people will organise another bubble football tournament, since I missed the previous one. And of course I am looking forward to the upcoming KBE and active members' dinner and activity, especially the dinner.

Besides that, I hope that we as a board do not push ourselves too much, brute force activities but that we can all enjoy our board year with our lives next to it. I am saying this because we are noticeably understaffed and we also have a lot of stuff to do next to our board year, but I am convinced that we can make the FMF sail through this sea. I am incredibly blessed to have such great people as my fellow board members and I will admit that they are one of the reasons why I joined up as a board member after their candidate announcement.

If you have any interesting ideas for educational activities, do not hesitate to come to me and perhaps we can work something out!

XOXO - Floris

FIGURE 1: Floris at the Craftcie snowdoll.

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The Physics and Mathematics in my Machine Learning Research

AUTHOR: **SREEJITA GHOSH**

While doing groceries in the supermarket or during my solo travels I have sometimes struck up conversations with co-passengers and fellow shoppers about what I do. Some of them from a physics and mathematics background were aware how machine learning is used in their respective fields to ease their work. However, when I said that machine learning itself uses physics, statistics, and calculus they seemed genuinely surprised. I thought this might be a nice platform to elaborate on this topic rather than while waiting for a train on a platform, or in the rain outside a supermarket.

In my research I am developing a probabilistic prototype based classifier to identify patients with certain rare steroidogenic disorders. This classifier is presented with some medical data from healthy subjects and patients, during the 'training' phase. It learns from that data the profile of each of the conditions, thus creating a 'prototype' profile for each of them. When data from a new subject is presented to this classifier it compares it to all the prototypes, and computes which of the prototypes this new subject's profile is most similar to. The closer the new measured profile is to a prototype, the more likely the profile is affected by the condition represented by the prototype. Sometimes a patient is affected by more than one condition (medically known as comorbidities). In such a scenario, if the classifier assigns the label of just one condition, then the other slightly less expressed condition might go unnoticed and untreated. This is where a probabilistic classifier is more advantageous than a deterministic one. The probabilistic classifier my team and I have developed informs about what the chances are of a new subject of having each of the conditions it had learned during training. When the probabilities of a new subject of being affected by certain conditions are significant then the doctors would know that the person has comorbidities and can devise a treatment plan accordingly.

In addition to these, our classifier can make these decisions even in difficult situations, for example when some entries in the medical dataset are missing. For a human being it seems intuitive, but in terms of prediction and data analysis this is a big problem. Our method is able to take its decision on only the subset of the available measurements of a subject, and not be negatively affected by the missing entries. The other attractive aspect of our classifier is that it is interpretable and can produce visualizations of the problem it is facing. This means one can see which measurements are more relevant and which are less relevant for a classification problem at hand, and it can show the decision boundaries for each of the conditions learned. But how do we make the classifier do these? The answer is physics, and to explain how exactly, I need to first take you on a detour.

When data from different classes or groups are in a mixture together there is disorder, thus the entropy is high. However when the data from different groups are separated such that all data of the same group/class are together or close to each other and away from data of other classes, there is less disorder: this is what a classifier tries to do. Thus in very simple terms the aim of a classifier is to lower the entropy of the system. The cost functions of machine learning models (for example a classifier), which ensure that it is doing its job correctly, can be entropy functions. So when

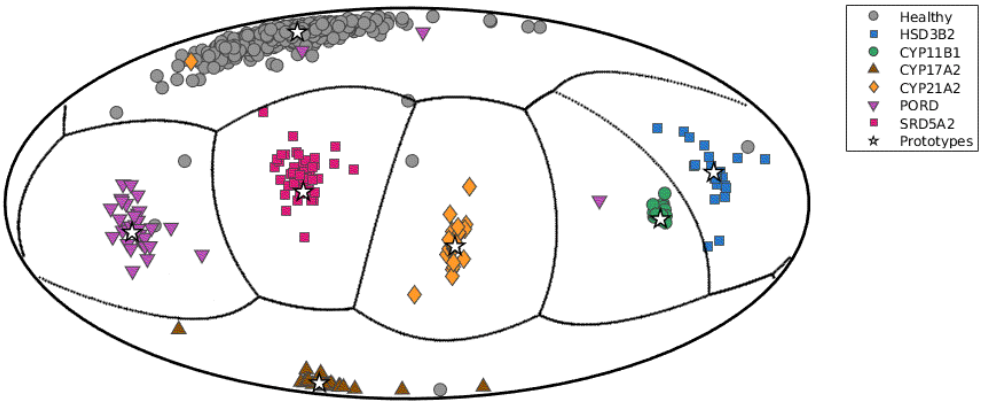

FIGURE 1: This visualization represents how our classifier performs classification. The subjects close to the class boundaries are those that exhibit traits of both the classes sharing the boundaries. Subjects placed away from all decision boundaries are those with more secure classification.

data of subjects suffering from different disorders and comorbidities are presented during training phase the model tries to group the subjects in a way such that the entropy is lowest.

The interpretability aspect of the classifier comes from the fact that all the available features of a novel subject are compared to those of the prototypes'. However, not all the features are of equal importance or as we refer to it: relevance. If all features are considered to be of equal relevance or of the incorrect importance then the classification would be wrong, and there would be a rise in disorder, thus an increase in entropy. The cost function thus steers the classifiers into assigning different (adaptive) weights or relevance to different features or groups of features in a relevance matrix. This matrix not only makes the classifier more accurate, it also makes the models interpretable and help in knowledge extraction.

The relevance matrix, in addition to containing information about which features are important or are less important, also contains information about which features (even if individually not that important) together form a relevant trait for the problem at hand. The off-diagonal elements inform us about the pairwise relations and combined relevance of features while the diagonal elements point towards the individual relevance of each feature. The relevance matrix is analogical to covariance matrix. Eigenvalue decomposition of covariance matrix provides us with the intrinsic dimensions of a data, showing which directions have maximum variance, similar to the diagonals of a relevance matrix, which inform about the discriminative directions which best separate data from different classes. The probabilities of class/condition membership are computed, based on how the entropy rises or is lowered when a certain subject is grouped with different prototypes. And the relevance matrix is computed on how the probability of a subject's class/condition membership using the adaptive weights on the features affects the cost function (entropy function).

Thus, machine learning is used not just to make sense of a large number of data generated from physics experiments, it itself uses principles of physics and mathematics to develop solutions.

Acknowledgements

The author would like to thank Dr. Bunte and Mohammad Mohammadi for proofreading and checking for technical correctness.

COPD, Statistics, and Network Inference

AUTHORS: VICTOR BERNAL[1], PETER HORVATOVICH[2], VICTOR GURYEV[3], MARCO GRZEGORCZYK[1]

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We are a group of bioinformaticians and statisticians participating in the Data Science and Systems Complexity Center (DSSC) at the University of Groningen. As part of our work, we support medical researchers to understand molecular networks, and to gain more insight from their genomic, proteomic or metabolomic data. The idea is to unravel the underlying mechanism behind complex diseases by extending current statistical models with tools from our disciplines (e.g. statistics, mathematics, and bioinformatics); so as to find tailor-made approaches. In this article, we outline one of our collaborative projects with the group of Respiratory Research at the University Medical Center Groningen.

Chronic obstructive pulmonary disease (COPD)

A cell is the most basic unit of life. Cells synthesize proteins in a controlled (regulated) way to perform specific biological tasks. The process of protein synthesis consists of two phases. During the transcription phase, DNA code is copied to a new molecule of messenger RNA (mRNA). Subsequently, during the translation phase the mRNA is "decoded" to build a protein. The amounts of messenger RNA (mRNA) molecules are usually referred to as gene expression.

Chronic obstructive pulmonary disease (COPD) is a persistent inflammation and obstruction of the airways and currently it is the third leading cause of death[1]. Risk factors for COPD include smoking, air pollution or indoor cooking, and the severity of COPD depends on the genetic predispositions. In bronchial cells of COPD patients, the expressions of certain genes and the cellular disorders increase with the disease stage. To diagnose COPD and to develop a medical treatment, clinicians and medical scientists require a good understanding of how the cellular regulatory networks are affected by the different COPD stages.

To diagnose COPD it is necessary to collect tissue samples from the bronchial epithelium, which is an invasive and inconvenient intervention for the patients. Thus, there is an urgent need for less invasive alternatives. In this context, medical researchers are investigating whether the genetic profiles from nasal epithelium (cells from the outer surface) can be used as a proxy for the bronchial epithelium.

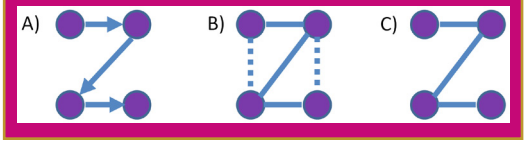
Genetic expression signatures in the airway have led to biomarkers (indicators for a particular biological state) for COPD and asthma. For instance, nasal and bronchial biopsies show similar responses to cigarette smoke stimulation ex vivo[2]. Bronchial expression between current and former smokers has been used to derive and validate a biomarker for lung cancer[3], and recently lung cancer-associated gene expression was detectable from nasal epithelium[4].

Our collaborators Kai Impkamp, Maarten van den

Berge, Alen Faiz and their colleagues from UMCG have performed (genome wide) gene expression profiling on 77 patients, taking nasal and bronchial epithelial brushes from them. Among the 77 patients there are 41 ex-smokers and 36 patients who never smoked. The goal of our collaboration is to search for similar "disruptions of genetic regulations" in nasal and bronchial epithelium. To gain more insight into this, we complemented earlier statistical exploratory techniques with Gaussian Graphical Model (GGM) analyses of the data[5].

GGMs are network models that can be used to represent the connectivity of genes (or transcripts, proteins or metabolites). Pairs of genes, whose expression values are related (have a significant partial correlation), are connected by undirected edges. The main advantage of partial correlation over the standard Pearson correlation can be best illustrated with a simple example. Consider the true regulatory network shown in Figure 1A. The Pearson correlation between the variables X and Y is denoted by r_{XY} and can be computed as

FIGURE 1: Illustration: Genetic network with 4 nodes. Each node represents a gene and the edges connect the nodes according to a statistical association measure, estimated from data. A) The true regulatory network. B) The network based on Pearson correlation. The dashed edges are spurious pseudo-dependencies. C) The network based on partial correlations (i.e. GGM) where pseudo-dependencies are avoided.

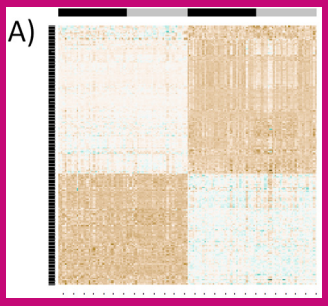


$$r_{XY} = \frac{\sum_{i=1}^{n}(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{n}(x_i - \bar{x})^2}\sqrt{\sum_{i=1}^{n}(y_i - \bar{y})^2}}$$

where x_i and y_i are the i-th observation from the variables X and Y, and $\bar{x}$ and $\bar{y}$ are the corresponding sample means. The Pearson correlation measures how (linearly) dependent the two variables X and Y are. We observe in Figure 1B that Pearson correlations lead to pseudo-dependencies (dashed lines) that are not in the true network. This is because the Pearson correlation does not distinguish between direct and indirect dependencies. In contrast, the partial correlation is the correlation that remains after removing all confounding effects (see Figure 1C). Mathematically, it is the correlation that is still there when the values of all the other variables are kept fixed (i.e. when conditioning on all the other variables); symbolically $r_{XY|\text{all others}}$. Partial correlations therefore measure only direct (linear) dependencies, making GGMs a popular and widely applied tool to study protein pathways[6] and gene regulatory networks[7], where the number of proteins/genes are usually large.

For large networks, it is important to have an accurate error control when identifying the statistically significant non-zero partial correlations. For instance, 100 genes can have up to $0.5 \cdot 100 \cdot 99 = 4950$ pairwise connections that have to be tested for significance. A tiny inaccuracy in the statistical tests, e.g. 1%, would be repeated 4950 times, and translated into approximately 49 false positive edges. In our recent work[8], we have proposed a new statistical test that controls the error rates accurately. Within this collaborative project, we have applied our new statistical test to infer gene regulatory networks from bronchial and nasal samples and to study the (dis)similarities of the two networks.

FIGURE 2: Analysis of the gene expression data.



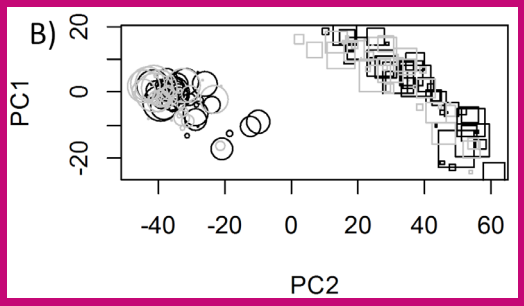


FIGURE 2A: Heatmap of standardized differential expression patterns. The upper black/grey strip shows the smoker/non-smoker groups. The nasal (left) and the bronchial (right) samples appear as two blocks. The low-middle-high expression levels are represented in a green-white-brown color scale.

FIGURE 2B: Results of Principal Component Analysis (PCA). Each symbol refers to a patient: smokers/non-smokers are in black/grey, and the symbol types indicate whether it the sample comes from nasal (circles) or bronchial (squares) tissues. The size of the symbols reflects the weights of the third principal component. It can be seen that the tissue type nasal/bronchial (circles/squares) leads to a clear separation, while the smoking status (black/grey) does not.

Figure 2A shows the expressions of the genes, and the different blocks correspond to the two tissues (nasal and bronchial). It can be clearly seen that there is a tissue-related difference in the expression values. Our network analyses have shown that the differences are mainly caused by the morphology of the tissues (nasal vs. bronchial) and less affected by the smoking status. For instance, genes with no overlap in the network were associated to cilium (a type of slender protuberances), typically found in the bronchi but not in the nose. Moreover, it appears that the smoking factor does not differentiate the tissue responses (Figure 2B).

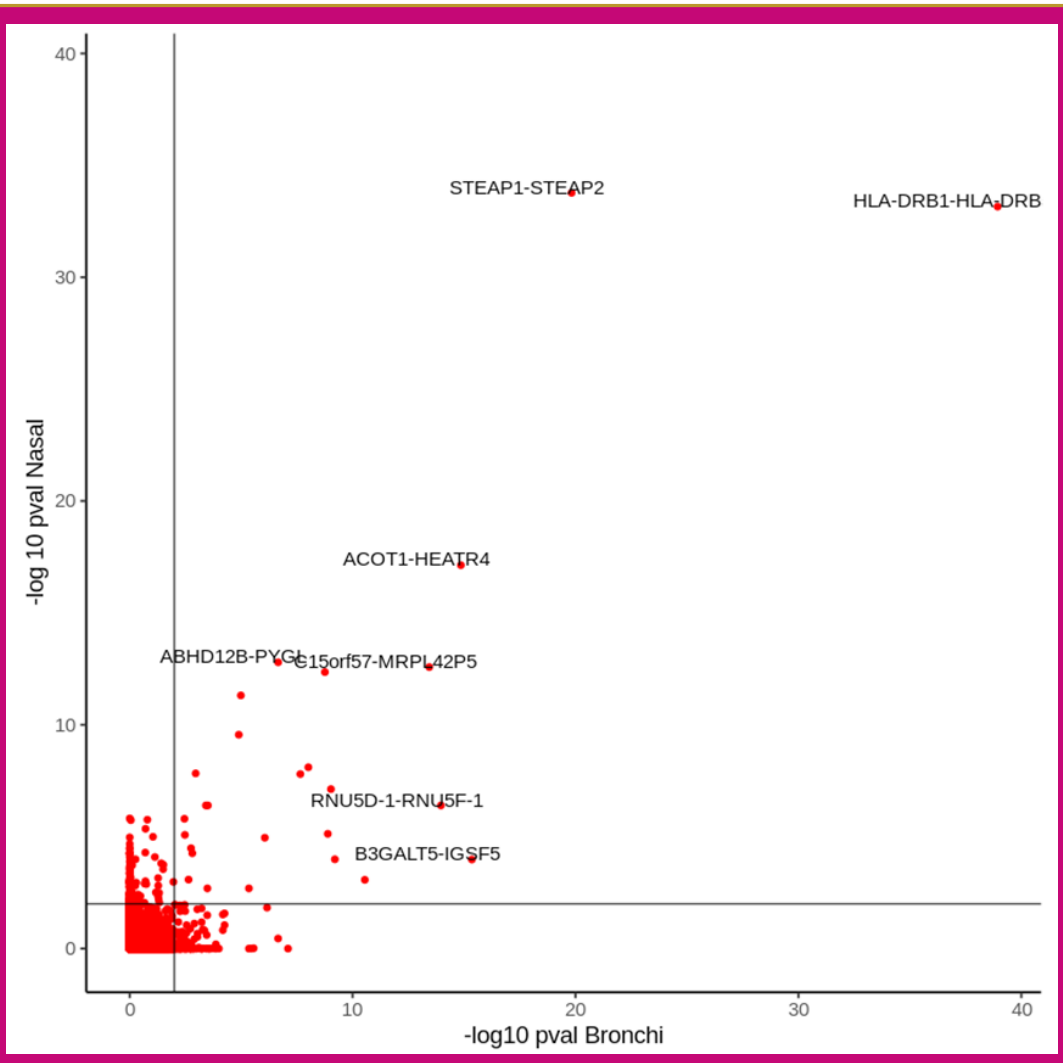


FIGURE 3: Comparison of the nasal and the bronchial epithelial gene expression networks. Scatter plot of –log10 (p-values) in the two tissue types. The upper right and lower left quadrants (separated by gray lines) are the regions where edges appear that are in both networks either significant (upper right) or non-significant (lower left). A large amount of points in these quadrants indicates similarity between the two networks.

Figure 3 shows the strength/significance of the inferred edges. The panel is divided into four quadrants, where points in the upper right quadrant are significant in both networks, and points in the lower left quadrant are non-significant in both networks. The overlapping edges between the bronchial network and nasal network (i.e. displayed in the upper right quadrant) are mostly related to inflammatory and immunological responses. Interestingly several pair of genes belong to the same gene family, like HLA-DQB1, HLA-DRB1, HLA-DRB5 and HLA-DQA1, which are all interconnected. Some other gene pairs are SAA1-SAA2, STEAP1-STEAP2, RNU5F-1 -RNU5D-1, MT2A-MT1L, CD207- CDH17.

In conclusion, our statistical results suggest that the bronchial manifestation of the COPD (e.g. inflammation) could be diagnosed from the nose (see [9] for more details). Although controlling the amount of false positives in large-scale networks is a challenging task and leads to inference uncertainty, the similarity of the two networks (nasal vs. bronchial) has a plausible biological signature. We hope that the ease of taking nasal samples will lead to more nasal data in the future, so that more statistical analyses can be performed and more data-based evidence can be provided. This ultimately might then help diagnosing COPD with less invasive methods. For more details about our study, we refer to our paper[9].

Acknowledgements

We acknowledge the Data Science and Systems Complexity Center (DSSC) at the University of Groningen for the support obtained for this project.

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Judie Ibrahim

Student Aviation Studies,
Hogeschool van Amsterdam, 23 jaar

''Toen ik op zoek was naar een stage heb ik veel bedrijven aangeschreven, van drie bedrijven kreeg ik een aanbieding. Ik koos voor Thales omdat het een internationaal georiënteerd bedrijf is met meer dan 85% export. Tijdens mijn opdracht bij Thales hield ik mij bezig met het analyseren van het kostprijscalculatie proces en onderzocht ik waar dat mogelijk te verbeteren. Aangezien ik bij Aviation Studies mij vooral bezig houd met techniek zocht ik juist een stage waar ik mij bezig kon houden met bedrijfskundige processen. Het onderwerp van de opdracht bij Thales was mij onbekend, maar juist daarom wilde ik ermee aan de slag en zag ik het als een uitdaging.

Ik ben van mening dat je met een oprechte interesse theorie wel eigen kunt maken. Toen ik bij Thales aan de slag ging was ik verrast over de open cultuur. Je kunt iedereen aanspreken en er wordt tijd voor je vrijgemaakt om je verder te helpen. Als je zelf initiatief neemt dan liggen er veel kansen. Na mijn advies te hebben geïmplementeerd ben ik van plan om in september te beginnen met een de Master Business Administration aan de UvA in Amsterdam.

Ik denk dat dat de combinatie van een technische Bachelor met een Bedrijfskundige master je helpt om met twee verschillende brillen naar oplossingen te zoeken. Ik onderhoud contact met mijn stagebegeleider en hoop dat ik na mijn master bij Thales aan de slag kan.''

> "Als student is je grootste angst dat je afstudeeronderzoek in een lade verdwijnt. Bij Thales word je echt serieus genomen en is er vertrouwen in je. Zo wordt mijn advies omtrent een nieuwe methode van kostencalculatie zelfs in 2016 geïmplementeerd."

Op zoek naar een stage, af
Start jouw carrière bij Thales. K

"Tijdens mijn studie was ik mij al aan het oriënteren op de arbeidsmarkt. Ik was op zoek naar een technisch bedrijf met een interessant product waar ik mijn natuurkunde achtergrond zou kunnen inzetten. Op de BètaBedrijvenBeurs in Nijmegen kwam ik in gesprek met een recruiter van Thales. Zij nodigde me uit op het hoofdkantoor om samen de mogelijkheden bij Thales te bespreken. Eén van de vacatures sprong er voor mij meteen uit, namelijk die voor de functie van Trial Conductor. Hiernaar heb ik gesolliciteerd en na een paar gesprekken werd ik aangenomen. Inmiddels werk ik al een paar maanden met veel plezier bij Thales.

Als Trial Conductor bouw ik voort op de tijdens mijn studie opgedane kennis. Regelmatig zal ik met een team naar het buitenland gaan om onze radarsystemen op marineschepen te testen. Daar laten we op zee aan de klant zien dat het systeem inderdaad zo goed is als beloofd in het contract. Dit doen we door middel van allerlei scenario's. Zo laten we bijvoorbeeld een F-16 invliegen om te zien wanneer de radar deze voor het eerst detecteert.

Tijdens mijn sollicitatie kreeg ik ook een aanbod van een ander technisch bedrijf, maar de goede sfeer bij Thales was voor mij doorslaggevend. De mensen hier zijn erg behulpzaam en nemen de tijd om je iets uit te leggen. Thales voldoet zeker aan het beeld dat ik ervan had: een high tech bedrijf met een fijne werksfeer."

"Als Trial Conductor bouw ik voort op de tijdens mijn studie opgedane kennis. Regelmatig zal ik met een team naar het buitenland gaan om onze radarsystemen op marineschepen te testen."

Annelot Schuring

Afgestudeerd in Natuurkunde,
Radboud Universiteit Nijmegen, 24 jaar

studeerplek of eerste baan?
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Digits

Ideas behind a seemingly simplistic puzzle game

AUTHOR: **ROBERT MODDERMAN**

Many aspects will come into play when developing a puzzle game: graphics, gameplay, possibly a self-tracking score system, and so many more. Too many to mention in an article this short. Besides (of course) referring to the latest mobile Android app I developed under the name *Cogitare Puzzle Games*, I will let you take a glance at the least visible and most abstract aspect of puzzle game development: the underlying ideas.

Before continuing to the most rigourous part, why not check out the free, ad-free game just now? You can use the QR-codes below.[1]

A game. Nice! How does it work?

The main idea is to eliminate all the numbers given on the screen. This can be achieved by simply dragging them all over the place. When two numbers touch, they annihilate if they are equal or fuse into a third number if they are unequal. If the moving number is bigger then the numbers will fuse into their sum, and if the moving number is smaller then they will fuse into their difference. So, in order to eliminate these numbers, the set of rules tells us that we must end up with two numbers of exactly the same value. How else could we eliminate *all* numbers?

Let's say that, in the level shown at the right, you start to move numbers around. Perhaps you move the '8' against the '10' and - POOF! - the '8' and the '10' fuse into a '2' and you are left with the numbers (2, 5, 6, 7). Let's see, what can we do with these. Somewhat disappointingly, nothing. Any further action will lead to two remaining numbers being unequal. But wait: what if instead of moving the '8' to the '10' we would have moved the '10' against the '8'? Then, we have the numbers (18, 7, 6, 5). Moving then the '7' to the '6', we obtain (18, 13, 5), moving the '13' to the '18' yields (5, 5) and these numbers can be annihilated!

A first analysis

Maybe you noticed that the numbers (10, 8, 7, 6, 5) satisfy the relation 10 + 8 = 7 + 6 + 5. This equation is precisely corresponding to the way we solved the puzzle in the end: we added the '10' to the '8' to obtain (18, 7, 6, 5), we added the '7' to the '6' to obtain (18, 13, 5) and subtracted the '13' from the '18' to obtain (5, 5). Apparently, 10 + 8 is a μ_2-linear combination of the numbers 7, 6, 5 (with μ_n the set of complex n-roots of unity; in this case, we have $\mu_2 = \{\pm 1\}$) but 10 - 8 is *not* a μ_2-linear combination of 7, 6, 5. Indeed: all μ_2-linear combinations of 7, 6, 5 yielding positive value are

$$7+6+5=18,$$
$$7+6-5=8,$$
$$7-6+5=6,$$
$$-7+6+5=4,$$

1 Or simply visit

play.google.com/store/apps/developer?id=Cogitare

and 18 *does* but 2 *does not* appear on this list. Does this mean that any such level consisting of positive integers $(x_1, \ldots, x_n)$ with $n \geqslant 2$ is solvable if and only if there exist $\sigma_1, \ldots, \sigma_n \in \mu_2$ such that

$$\sum_{i=1}^{n} \sigma_i x_i = 0\,?$$

A linear algebra perspective

Well, yes. But first, some notation. We let a given state $\mathbf{x} = \begin{bmatrix} x_1 & \cdots & x_n \end{bmatrix}^\intercal$ be represented by a vector $\mathbf{x} \in \mathbb{Z}^n$. The state $\mathbf{x}$ is said to be *initial* if all its entries are nonzero. Now, let $i \to j$ denote the event that x_i is replaced by $x_j \pm x_i$ (addition if $x_i > x_j$, and subtraction otherwise) and x_j is replaced by zero. This action will change the state $\mathbf{x}$ into the state

$$\begin{cases} \Sigma^{i \leqslant j}\mathbf{x}, & x_i \leqslant x_j, \\ \Sigma^{i > j}\mathbf{x}, & x_i > x_j, \end{cases}$$

where we define the matrices

$$\begin{cases} \Sigma^{i \leqslant j} = I - I_{j,j} + I_{i,j} - 2I_{i,i}, \\ \Sigma^{i > j} = I - I_{j,j} + I_{i,j}. \end{cases}$$

where $I_{\alpha,\beta}$ is the matrix that has a one on the α-th entry of the β-th column and zeros elsewhere, and I is the $n \times n$ identity matrix. Before proving things, let us apply this notation to the intial state $\mathbf{x} = \begin{bmatrix} 10 & 8 & 7 & 6 & 5 \end{bmatrix}^\intercal$. In the new notation, note that the sequence $1 \to 2, 3 \to 4, 3 \to 1, 5 \to 3$ solves the puzzle (i.e., yields the zero vector as final state). Indeed:

$$\begin{aligned} \begin{bmatrix} 10 & 8 & 7 & 6 & 5 \end{bmatrix}^\intercal &\xrightarrow{1 \to 2} \begin{bmatrix} 18 & 0 & 7 & 6 & 5 \end{bmatrix}^\intercal \\ &\xrightarrow{3 \to 4} \begin{bmatrix} 18 & 0 & 13 & 0 & 5 \end{bmatrix}^\intercal \\ &\xrightarrow{3 \to 1} \begin{bmatrix} 0 & 0 & 5 & 0 & 5 \end{bmatrix}^\intercal \\ &\xrightarrow{5 \to 3} \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \end{bmatrix}^\intercal. \end{aligned}$$

The matrix representing the third move is given by

$$\begin{aligned} \Sigma^{3 \leqslant 1} &= I - I_{1,1} - 2I_{3,3} + I_{3,1} \\ &= I + \begin{bmatrix} -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & -2 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix} \\ &= \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & -1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix} \end{aligned}$$

and one indeed checks that

$$\underbrace{\begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & -1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix}}_{\Sigma^{3 \leqslant 1}} \begin{bmatrix} 18 \\ 0 \\ 13 \\ 0 \\ 5 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 5 \\ 0 \\ 5 \end{bmatrix}.$$

The mechanism of this example can, in a straightforward way, be extended to any n-dimensional state. This means that, given any state $\mathbf{x} \in \mathbb{Z}^n$, the vector $\Sigma^{i \leqslant j}\mathbf{x}$ respectively $\Sigma^{i > j}\mathbf{x}$ indeed *is* the result of the event $i \to j$ if $x_i \leqslant x_j$ or $x_i > x_j$, respectively. For our example, this means that

$$\begin{aligned} \mathbf{x} &\xrightarrow{1 \to 2} \Sigma^{1>2}\mathbf{x} \\ &\xrightarrow{3 \to 4} \Sigma^{3>4}\Sigma^{1>2}\mathbf{x} \\ &\xrightarrow{3 \to 1} \Sigma^{3 \leqslant 1}\Sigma^{3>4}\Sigma^{1>2}\mathbf{x} \\ &\xrightarrow{5 \to 3} \Sigma^{5 \leqslant 3}\Sigma^{3 \leqslant 1}\Sigma^{3>4}\Sigma^{1>2}\mathbf{x} \end{aligned}$$

which must yield the zero vector at the end. We now compute

$$\Sigma^{5 \leqslant 3}\Sigma^{3 \leqslant 1}\Sigma^{3>4}\Sigma^{1>2} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 1 & 1 & -1 & -1 & -1 \end{bmatrix}$$

and we immediately can read off our $\sigma_1, \ldots, \sigma_5$ from the bottom row! Now, the following question arises: can we prove this phenomenon in general? Let's find out!

We now consider the general n-dimensional case again. Let's show some basic results. First, it is not hard to show that for arbitrary $i, j, k, l \in \{1, \ldots, n\}$ we have $I_{i,j}I_{k,l} = \delta_{jk}I_{il}$. Furthermore, given two matrices $A, B \in \mathbb{Z}^{n \times n}$ having the property that every column contains $n - 1$ zeros and one entry in μ_2, the product AB also has this 'μ_2-column property'. Indeed, by definition of A, B, we can write

$$A = \sum_{i=1}^{n} a_i I_{y_i,i},$$

$$B = \sum_{j=1}^{n} b_j I_{z_j,j},$$

where the a_i and b_j are in μ_2, and the y_i and z_j are in $\{1, \ldots, n\}$.

We now compute that

$$\begin{aligned} AB &= \sum_{i=1}^{n} a_i I_{y_i,i} \sum_{j=1}^{n} b_j I_{z_j,j} \\ &= \sum_{i=1}^{n}\sum_{j=1}^{n} a_i b_j I_{y_i,i} I_{z_j,j} \\ &= \sum_{j=1}^{n}\sum_{i=1}^{n} a_i b_j I_{y_i,i} I_{z_j,j} \\ &= \sum_{j=1}^{n}\sum_{i=1}^{n} a_i b_j \delta_{iz_j} I_{y_i,j} \\ &= \sum_{j=1}^{n} \underbrace{a_{z_j} b_j}_{\in \mu_2} I_{y_{z_j},j} \end{aligned}$$

and it follows that AB satisfies the μ_2-column property as well.

We now consider any sequence $i_1 \to j_1, \ldots, i_t \to j_t$ of events that solves the initial state $\mathbf{x}$. This means that $i_s \neq j_s$ for all $s \in \{1, \ldots, t\}$; $i_s \neq j_1, \ldots, j_{s-1}$ for all $s \geqslant 2$; all j_s are distinct; and there exist matrices $\Sigma^{i_s \to j_s} \in \{\Sigma^{i_s \leqslant j_s}, \Sigma^{i_s > j_s}\}$ such that

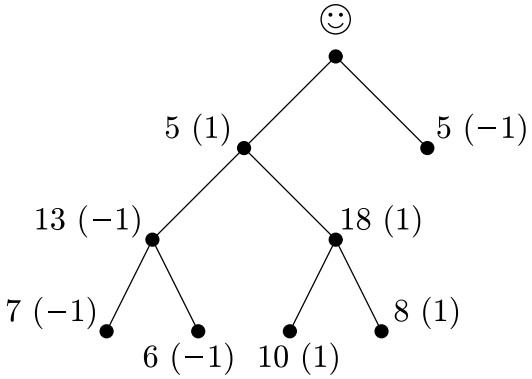
$$\underbrace{\Sigma^{i_t \to j_t} \Sigma^{i_{t-1} \to j_{t-1}} \cdots \Sigma^{i_1 \to j_1}}_{=:\Sigma} \mathbf{x} = 0.$$

By how $\Sigma^{i \leqslant j}$ and $\Sigma^{i > j}$ were defined, we see that each $\Sigma^{i_s \to j_s}$ has the μ_2-column property, and it inductively follows that Σ has this property as well! For all $i \in \{1, \ldots, n\}$, we let $\sigma_i \in \mu_2$ be the unique nonzero entry $\in \mu_2$ of the i-th column of Σ. Since $\Sigma \mathbf{x} = 0$, it follows that $\sum_{i=1}^{n} \sigma_i x_i = 0$.

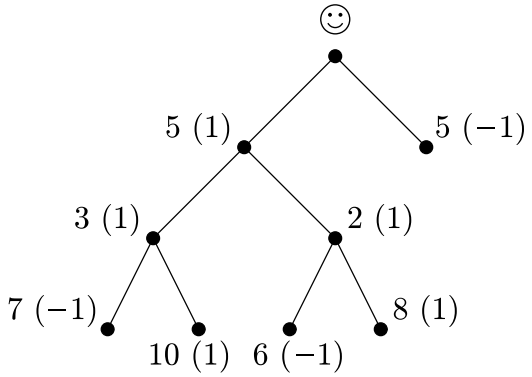
Conversely, if $\sigma_1, \ldots, \sigma_n \in \mu_2$ satisfy $\sum_{i=1}^{n} \sigma_i x_i = 0$, then it is not hard to show that the initial state $\mathbf{x}$ can *always* (whenever all its components are positive integers, of course) be solved. Try to convince yourself why that's always possible!

A graph-theoretical approach

What? Graphs? How can we use these? Well, a very special class of graphs is the set of all *trees*. The way we solved 'Single Level 4' can be represented by the following tree:



in which the *leaves* constitute the initial state, and their *ancestors* are the results of moves. In a sense, erasing two leaves from this tree yields another initial state with a dimension equal to that of the previous initial state minus 2. This point of view shows that there are many different orders in which levels of this type can be solved. For example, the level is solved whenever subtraction and annihilation take place whenever the two corresponding σ_i's differ and addition takes places whenever the two corresponding σ_i's are equal (where, in both cases, any parent 'inherits' the σ_i from the child with the biggest value). To illustrate this result, the tree



represents another solution. Things, however, become more interesting if one would design less canonical levels, extending the simplicity of being just a linear level consisting of adding and subtracting numbers only.

Restricting the game with itself

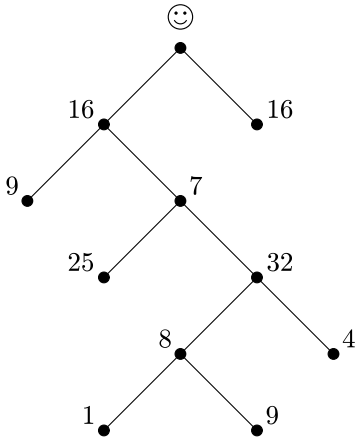
As you can see, in the following level (the 'Double' regime), the numbers are *entangled!* Try to find out in the app itself how it works! This time, the order of solving *does* matter and cannot be based purely on μ_2-coefficients. How I designed an algorithm to generate random entangled levels? By exploiting a very general scientific given I will explain in the end

- so stay tuned!

More operations

'Digits' (the name of the game, I didn't mention this in the introduction, but it is the title of the very article you are reading right now) also contains levels performing - besides addition and subtraction - multiplication and division.

If two unequal (equal numbers still annihilate) numbers x_i, x_j touch, then they will fuse into their sum or difference if the moving number x_i is odd (still based on which number is bigger), but they will fuse into their product $x_i x_j$ or quotient x_j/x_i (in the case $x_i > x_j$ respectively $x_i < x_j$) if x_i is even. For example, 'Bonus Level 3' can be solved as

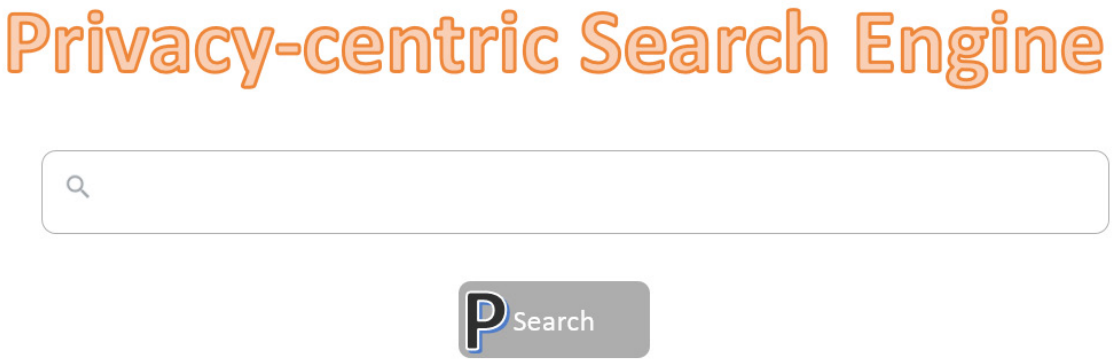


In this new level type the order of moving is of very big importance, meaning that levels of this type are by far the most difficult of the entire game. Ah, yes: how I designed algorithms to generate random levels of this type? The same as for the entangled level type (or 'Double' mode): by using the scientific given that computers are much better at arithmetic than humans and that therefore generating (random) levels can easily be brute-forced to obtain very challenging levels. In the end, this game is nothing else than the product of the fact that computers are much faster at arithmetic than humans, a (somewhat lazy) mathematics student, and, when playing around with some positive integers, his sudden realization that a very specific but quite interesting structure of integers was never exploited before to base a game on.

FIGURE 1: Some more screenshots from the app.

Towards a New Privacy-Centric Search Engine for Mobile Apps: Search by Privacy

AUTHOR: **FADI MOHSEN**



Without doubt, mobile phones have revolutionized our lives tremendously. Nowadays, we rely on these devices in numerous aspects; entertainment, education, business, sports and much more. There is a mobile app for almost everything we do such as chatting with friends, learning a new language, sending emails, and editing a picture or video. Mobile phones used to have a very simple design that allowed them to just text and call. As time goes by more and more features were added to them by the device and operating system vendors. Examples on the mobile phone vendors would be Sony, LG, and Apple. Examples on mobile OS venders would be Google, Windows, and Apple. These features were not good enough though to meet the various expectations and needs of mobile users. Thus, vendors have decided to open their platforms to be extended by third-parties, hence the name third-party apps. Currently, there are millions of third-party applications for mobile phones that users can install from online markets such as the Google Play store and Amazon App store for Android, and

Yet, these markets can also be used to distribute malicious applications that could pose serious security and privacy risks to users. Researchers and online market owners have been working extremely hard to detect bad applications and remove them before they can find their ways into users' devices. Nonetheless, there is another class of applications that are not malicious by design; however, they tend to collect as many information as possible from users' phones including their sensitive data. These applications are called intrusive.

Intrusive Applications

Intrusive apps are often offered for free; thus, users feel tempted to agree to their terms and conditions including the permission requests. Apps need users' approval to have access to the phone's resources and users' data. Studies have shown that users do not actually pay attention to these requests and tend to allow them without even reading them. Free applications include clickable links and ads to various products and services. The more users click on these ads the more money they make. In fact, these applications tend to collect as much information as possible about the users to be used in directed advertising. To put all of this in perspective, we did a little search on Google Play store looking for an app that displays the information of a mobile device, we entered the following: "Device Info". A total of 250 apps were returned as a result of submitting that query. The results are ranked in descending order according to the star ratings given by users. We picked the top rated application, the permission requests of that app is shown in Figure 1. Clearly, this application is asking for more than it needs to fulfill its promise, which is to simply display the device information. Yet, after choosing another application with the same rating and after retrieving its permission requests, see Figure 2, we came to a conclusion that application 1 was very conservative with its permission demands.

Countering Intrusiveness

Users are usually tempted to install the intrusive apps, agree to their permission requests and tolerate annoying advertisements because they are in need of the services these applications provide. In addition, choosing the least intrusive application among 250 apps, like in the previous example, is definitely a non-trivial task. The question would then be how to help users avoid them or choose the least intrusive ones. In recent years, researchers have proposed a number

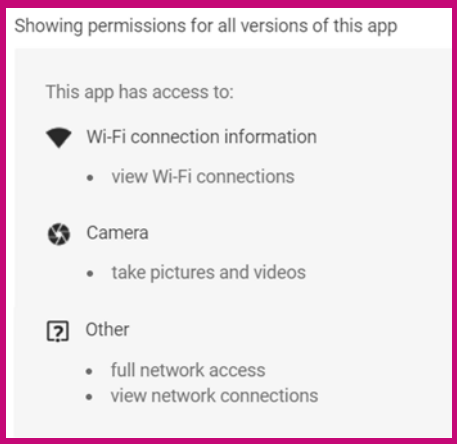


FIGURE 1: The permission requests of the most highly rated application.

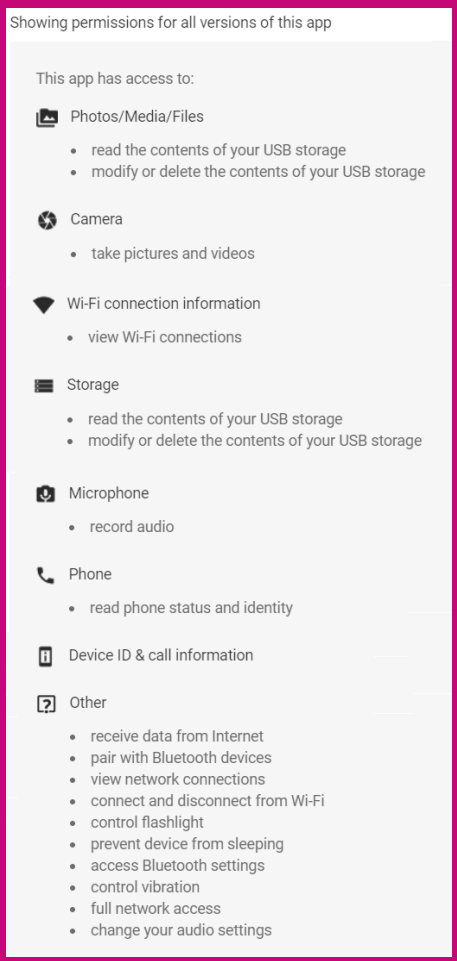


FIGURE 2: The permission request of another application with the same rank.

of solutions to counter intrusive apps. At their cores, these solutions have adopted different formulas for calculating a privacy score for each app. A privacy score of an app is calculated based primarily on its permission requests and other factors. Researchers have also diverged on employing the final solution. Some researchers went with a stand-alone application whereas others saw that it is best if it is integrated into the search engines.

Privacy Score

The privacy score of an app is an indicative of its intrusiveness and it is used by the search engines or stand-alone solutions to propose alternative applications. There are various ways to calculate a privacy score for Android mobile applications. One way would be to rely solely on the permission requests. For example, the privacy information used in the work of Hannah et. al [1] is composed of permission ratings that are gathered from human and using automated sources, the privacy information is then presented to the user to aid them make informative decisions. Similarly, Taylor and Martinovic [2] counted only on the permissions in their effort to counter what they called, starving permission-hungry apps. Sarma et. al [3] on the other hand relied on other information besides the permission requests, for instance, they used the category of the app and the permissions that are requested by other apps in the same category.

Privacy-centric Search Engine

In this work [4], we proposed and implemented a prototype of a security-centric search engine for Android mobile applications. The privacy score of an application is calculated based on its permission requests, registered broadcast receivers and users' preferences. A broadcast receiver is a component that allows Android applications to listen to events originating from the system or other applications. For example, an application can register to be notified whenever there is a new SMS, voicemail, or phone call. Previous works treated all permissions equally, even though some permissions might not be important to a particular user or to all users. Thus, in this work users' preferences are considered in calculating more accurate and customized privacy scores. The final prototype was built on top of the Elasticsearch engine [5]. It is worth mentioning here is that all of these attempts to score applications and rank them based on their security features are pure research and to the best of our knowledge, none of the online markets have adopted any of them.

A look at Existing Search Engines

Although Google Play store is the utmost known in the Android community; yet, there are other stores to download apps such as Amazon, F-Droid, GetJar, Aptoide, Uptodown, and APKUpdater. However, the majority of online app stores rank applications based on customer reviews. The reviews for the most part are targeted at the functionality of the app and less on the privacy and/or security properties. None of these stores use the security and privacy as a ranking factor. Although the security and privacy information are displayed to the end user on the app stores and upon installation or afterwards. It is quite challenging for users to conduct a comparison between applications and choose the least intrusive one. Thus, online stores are required to change the way they rank and recommend applications such that it takes the privacy of the user and security of their devices in consideration. This can be done by either changing it completely or at least providing it as an option. The results of previous and existing researches on this subject can be leveraged for this purpose.

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Recipe: Spinach Pancakes

4 people

AUTHOR: **J LAMMERS**

Ingredients:

- 6 pancakes
- 600 grams of spinach
- 1 onion
- Garlic
- Salt & pepper
- Brie
- Grated cheese
- Cayenne pepper powder

Preparing the filling

Wash the spinach and the the union and garlic.
Cook the spinach and, in the meantime, fry the unions and garlic until golden.
Drain the spinach and mix it with the unions, garlic, and seasoning (salt and pepper).
Cut the brie im long strips.

Filling the pancakes

Add a line of the spinach mixture in the middle of the pancake and add a strip of brie on top.
Roll the pancakes and put them on a baking tray.
The pancakes can now be stored in the fridge for later.

Preparing your final meal

When you are ready to eat, add some grated cheese and cayenne pepper on top of the pancakes and put them in the oven for ±15 minutes at 180° C.

Preparing your final meal

For non-vegetarian people, you can use bacon pancakes instead of regular pancakes.
If you want some more vegetables, you can also add some bell peppers to the mixture.

Do you have a good recipe you wish to share?
Contact us! perio@fmf.nl

Previous Brainwork

What time is it?

AUTHOR: **ROBERT MODDERMAN**

In the previous edition, we asked ourselves the question whether we would make it to the end of the exam (actually, *we* asked *you* whether *you* would make it to the end of the exam). The answer is: yes, you will make it to the end of the exam! Unfortunately, you *don't* have any time left to celebrate this given: as it turns out, the instant you take a look at the clocks coincides with the exact moment the exam is over! Let's find out why that's the case.

For simplicity, let us speak of durations (in minutes) instead of times. We cannot assign exact values to those, because (we postulate or believe that) the universe is a continuous time system. This means that the duration corresponding to the first clock is not simply 130, but we can assign an interval to it in which the actual duration must be. Then, the durations corresponding to the clocks are represented by the intervals [130, 131), [120, 121), [50, 51), [60, 61), [70, 71), [80, 81). These intervals are still small enough to conclude that the maximum difference between the clock durations is the difference yielded by the first and third clock, and this difference is in (79, 81). Since all clocks indicate the same time at t = 90, it then must be that the duration corresponding to the actual time is bigger than 79 + 90 = 169.

Now, an important observation is that any pair of non-neighbouring clocks with the property that at all times exactly one of them runs has the property that if you sum their durations you will get the duration corresponding to the actual time. The only such pairs being able to surpass 169 but not exceed 180 are {1, 3} and {2, 4}. Both yield that the duration corresponding to the actual time is at least 180, so we must have equality and we conclude that the actual time is precisely 21:30 and that *the exam is over*.

We're not done yet. We still need to show that there exists a configuration in which this is all possible. Here is one. Let clock 1 run from 18:30 to 19:15 and from 20:05 to 21:30; let clock 2 run from 18:30 to 19:15 and from 20:15 to 21:30; let clock 3 run whenever clock 1 is *not* running; let clock 4 run whenever clock 2 is *not* running; let clock 5 run from 19:15 to 20:25; and let clock 6 run from 19:15 to 20:35. Indeed, at 20:00 (corresponding to t = 90), the clocks all indicate the same time (19:15 to be precise) and both {1, 3} and {2, 4} are special pairs. One easily checks that at the end the clocks indicate the times as initially given.

The puzzle was correctly solved by Rick Ploeg, Lianne de Jonge, and Gijsbert ten Hoven. For each one of you there's a cool prize available at the FMF room. Congratulations!

Brainwork: Seven Neighbors

AUTHOR: **ROBERT VAN DER MEER**

In a street near the center of Groningen, there live seven international guys next to each other. The Perio redaction interviewed each of them to get to know them. Are you able to find which of the seven men does not study?

We prepared some questions and went to the street. There, between orange coloured trees, the block — consisting of seven houses — was located. We went from door to door and asked the men the following:

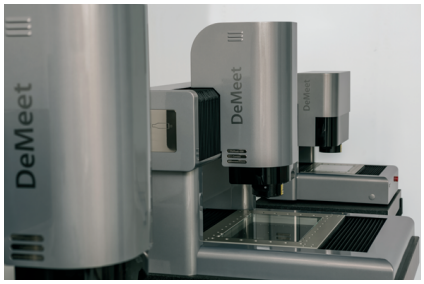
1. *Which country are you from?*
2. *What is the colour of your house?*
3. *What is the brand of your phone?*
4. *What is your favorite beer brand?*
5. *What is the name of your girlfriend?*
6. *What do you study at the moment?*

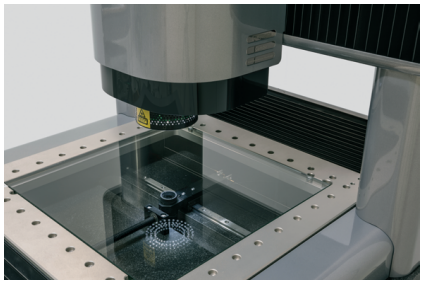
Due to the GDPR law, not everybody agreed on having all answered published in this magazine. Some men did not want us to let you know what beer brand they prefered, what phone they owned or what they studied. One man did not even want to share where he was from. And then of course, some guys did not have a girlfriend.

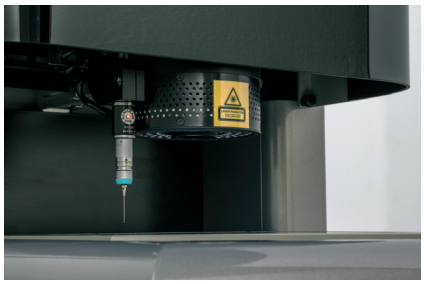
The aim of this puzzle

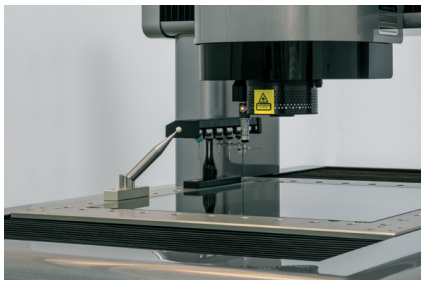
There is this one man in the block who said that he did *not* study this year, in contrast to the six other ones, who said they did. Your task is to deduce which man it is that does not study; where he is from, which beer brand he prefers, if he has a girlfriend and if so, what her name is, the brand of the phone he owns (if he does so) and the colour of his house. To get started, consider building a 7*6 table, with for every man a column and for every property a row. Base your deductions on the following facts:

1. The **Norwegian** guy lives in the third house from the left.
2. The **Swedish** guy lives directly to the right of the **Mathematics** student.
3. The **orange** house is directly to the left of the **blue** house, the **purple** house is directly to the right of the **blue** house.
4. The **Finnish** guy lives directly next to the **German** guy.
5. The **Amstel** drinker lives to the left of the **Chemistry** student and there are two houses between them.
6. There are two houses between the **green** house and the **Xiaomi** phone owner.
7. The only neighbor of **Heineken** studies **Physics**.
8. The **Nokia** owner is in love with **Janice**.
9. Directly to the right of the **Chinese** guy, there lives a **Swedish** guy.
10. The **Finnish** guy lives directly to the left of a **Cat** phone owner.
11. The boyfriend of **Silvia** lives directly to the left of the **blue** house.
12. The guy owning a **Samsung** phone drinks **Palm** beer.
13. The **Astronomy** student is in love with **Sandra**.
14. There are two houses between the guy drinking **Bavaria** and the **Astronomy** student.
15. The **German** guy lives directly next to the **white** house.
16. The **Chinese** guy lives directly next to the **purple** house.
17. The guy that drinks **Bavaria** lives directly to the right of the **Alcatel** phone owner.
18. There are three houses between the **Grolsch** drinker and the **Heineken** drinker.
19. The **British** guy is in love with **Julia**.
20. A direct neighbor of **Silvia**'s boyfriend drinks **Hertog Jan** beer.
21. There is one house between the **white** and **green** house.
22. There is one house between the **Alcatel** phone owner and the **red** house.
23. The only neighbor to the **red** house is in love with **Deborah**.
24. The direct neighbor of the **yellow** house drinks **Bavaria**.
25. The guy that does not study this year, has currently no girlfriend.









Schut Geometrische Meettechniek is een internationale organisatie met vijf vestigingen in Europa en de hoofdvestiging in Groningen. Het bedrijf is ISO 9001 gecertificeerd en gespecialiseerd in de ontwikkeling, productie, verkoop en service van precisie meetinstrumenten en -systemen.

Aangezien we onze activiteiten uitbreiden, zijn we continu op zoek naar enthousiaste medewerkers om ons team te versterken. Als jij wilt werken in een bedrijf dat mensen met ideeën en initiatief waardeert, dan is Schut Geometrische Meettechniek de plaats. De bedrijfsstructuur is overzichtelijk en de sfeer is informeel met een “no nonsense” karakter.

Op onze afdelingen voor de technische verkoop, software support en ontwikkeling van onze 3D meetmachines werken mensen met een academische achtergrond. Hierbij gaat het om functies zoals ***Sales Engineer***, ***Software Support Engineer***, ***Software Developer (C++)***, ***Electronics Developer*** en ***Mechanical Engineer***.

Je bent bij ons van harte welkom voor een oriënterend gesprek of een open sollicitatiegesprek of overleg over de mogelijkheden van een **stage-** of **afstudeerproject**. Wij raken graag in contact met gemotiveerde en talentvolle studenten.

Voor meer informatie kijk op **www.Schut.com** en **Vacatures.Schut.com**, of stuur een e-mail naar **Sollicitatie@Schut.com**.

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