



An Application of a Multivariate Estimation of Distribution Algorithm to Cancer Chemotherapy

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Abstract

Chemotherapy treatment for cancer is a complex optimisation problem with a large number of interacting variables and constraints. A number of different probabilistic algorithms have been applied to it with varying success. Here we apply two further estimation of distribution algorithms to the problem; UMDA and hBOA. The latter is the first EDA using a multivariate probabilistic model to be applied to the chemotherapy problem. While instinct would lead us to predict that the more sophisticated algorithm would yield better performance on a complex problem like this, we show that it is outperformed by the algorithms using the simpler univariate model.

Chemotherapy and EAs

- Highly complex method of treatment
- Requires balancing the tumour reducing effect of several drugs against their toxic side effects.
- In this instance: 10 drugs, 16 dose levels, 10 treatment intervals
- With binary representation chromosomes are 400 bits

We have previously described [1] the application of numerous evolutionary algorithms to the chemotherapy problem using a mathematical model of tumour response to drug treatment.

Problem Complexity

Like many other real-world problems, the chemotherapy problem has a large number of interactions between variables.



- 79800 possible bivariate interactions
- We ran the Linkage Detection Algorithm [2] to find interactions (linkage) present between variables
- 50491 interactions found (mean over 30 runs, SD 109.5)
- Does not necessarily mean that a multivariate model is needed for optimisation of this problem, but provides motivation to consider applying a multivariate EDA

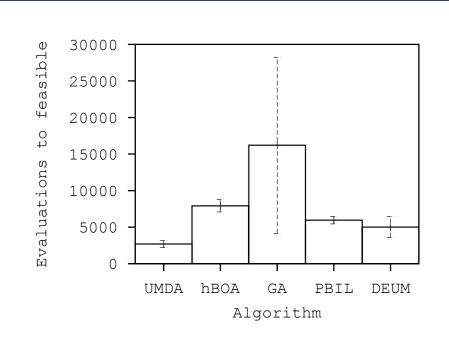
Experiments

The multivariate EDA we applied to the problem was the Hierarchical Bayesian Optimisation Algorithm (hBOA) [3], which uses a Bayesian network to factorise the joint probability distribution of good solutions. For comparison we also applied a univarate EDA – the Univariate Marginal Distribution Algorithm (UMDA) [4]. The results for these were then compared to those previously published for other algorithms. We ran two experiments with each:

- an efficiency experiment comparing the number of fitness evaluations required to find a feasible solution (where the patient survives)
- a *quality experiment* comparing the best fitness found after a fixed number of fitness evaluations

Efficiency Results

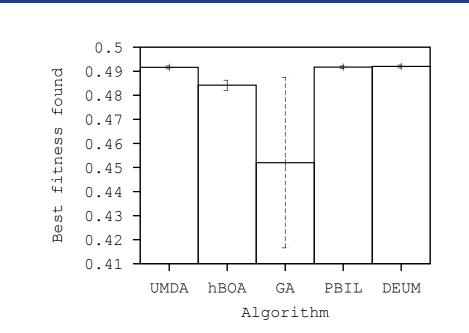
Algorithm	Mean fitness	Std Dev
	evaluations	
UMDA	2695.5	490.3
hBOA	7917.6	843.0
Genetic Algorithm	16208.1	12045.8
PBIL	5959.5	522.4
Univariate DEUM	5015.8	1426.9



	Diff in	Std Error	t-test	p-value
	means			
UMDA vs hBOA	5222.1	178.049	25.2857	< 0.0001
UMDA vs GA	13512.6	2201.073	6.1391	< 0.0001
UMDA vs PBIL	3264.0	130.805	24.9532	< 0.0001
UMDA vs	2320.4	275.466	8.4236	< 0.0001
Univariate DEUM				
hBOA vs GA	8290.5	2204.631	3.7605	0.0004
hBOA vs PBIL	1958.1	181.066	10.8143	< 0.0001
hBOA vs	2901.7	302.583	9.5898	< 0.0001
Univariate DEUM				

Quality Results

Algorithm	Mean best	Std Dev
	fitness found	
UMDA	0.4916	0.0006
hBOA	0.4842	0.0021
Genetic Algorithm	0.4520	0.0354
PBIL	0.4917	0.0005
Univariate DEUM	0.4920	0.0006



	Diff in	Std Error	t-test	p-value
	means			
UMDA vs hBOA	0.0074	0.000	18.5581	< 0.0001
UMDA vs GA	0.0396	0.006	6.1262	< 0.0001
UMDA vs PBIL	0.0001	0.000	0.7013	0.4859
UMDA vs	0.0004	0.000	2.5820	0.0124
Univariate DEUM				
hBOA vs GA	0.0322	0.006	4.9734	< 0.0001
hBOA vs PBIL	0.0075	0.000	19.0296	< 0.0001
hBOA vs	0.0078	0.000	19.5612	< 0.0001
Univariate DEUM				

Conclusions

In both experiments the GA is outperformed by all the EDAs, reinforcing the findings of previous GA - EDA comparisons. It is perhaps unexpected that the univariate algorithms outperform hBOA. We believe this is because many of the interactions within the problem are unnecessary for optimisation. Thus hBOA constructs a complex model of the problem which is very expensive to search and ultimately counterproductive – in essence being preoccupied by the additional complexity which simpler algorithms are able to ignore. Although a complex problem itself, this instance of the chemotherapy problem uses a relatively simple model of tumour growth. More complex models including factors such as more antagonistic drugs and cancers is likely to include higher order interactions. Multivariate EDAs such as hBOA could take advantage of this to give a more pronounced improvement in performance.

References

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[4] Mühlenbein, H. & Paaß, G. 1996. From Recombination of Genes to the Estimation of Distributions I. Binary Parameters. In PPSN IV: Proceedings of the 4th International Conference on Parallel Problem Solving from Nature, Springer-Verlag, 178-187.