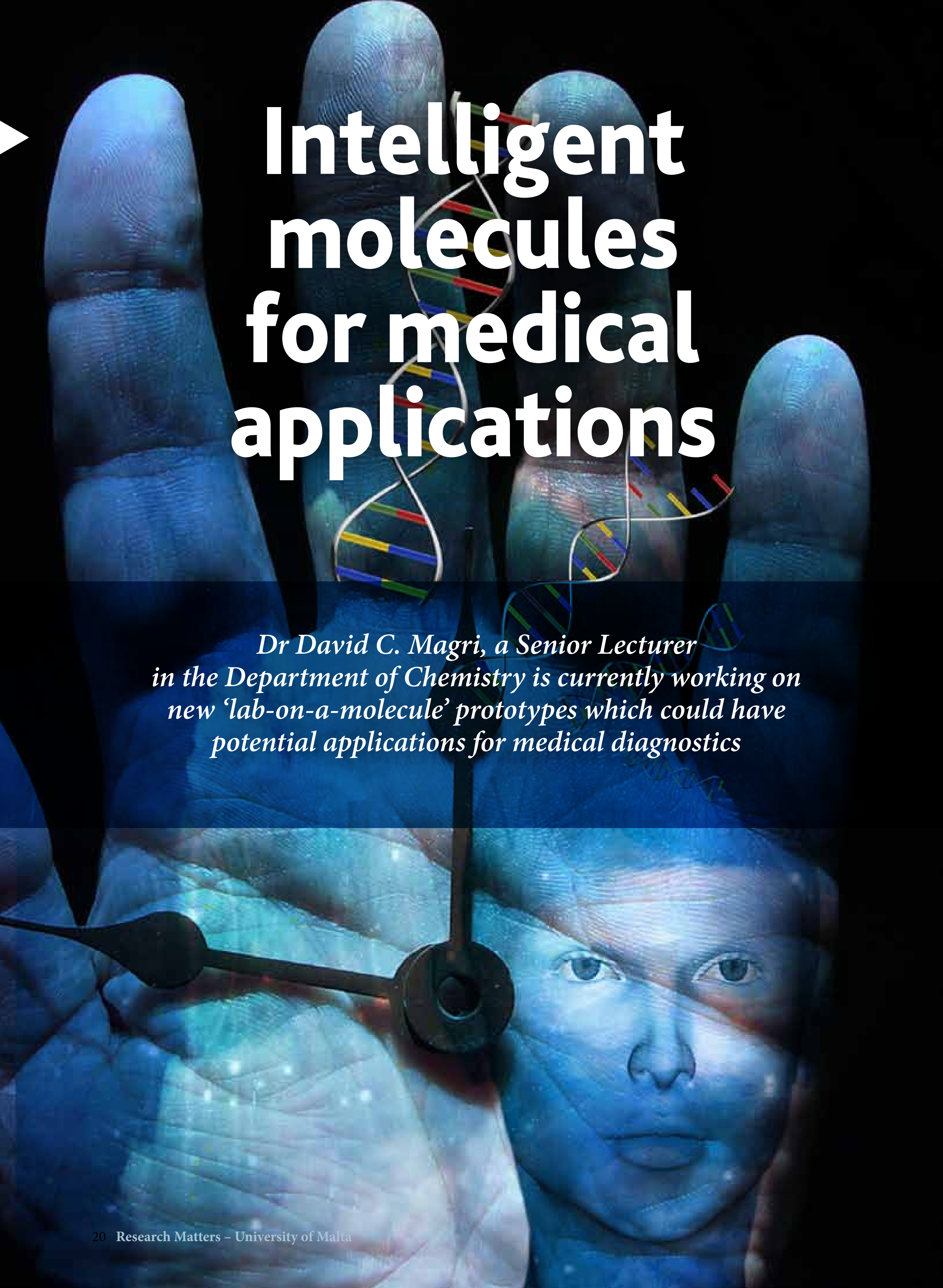


Intelligent molecules for medical applications

Dr David C. Magri, a Senior Lecturer in the Department of Chemistry is currently working on new 'lab-on-a-molecule' prototypes which could have potential applications for medical diagnostics

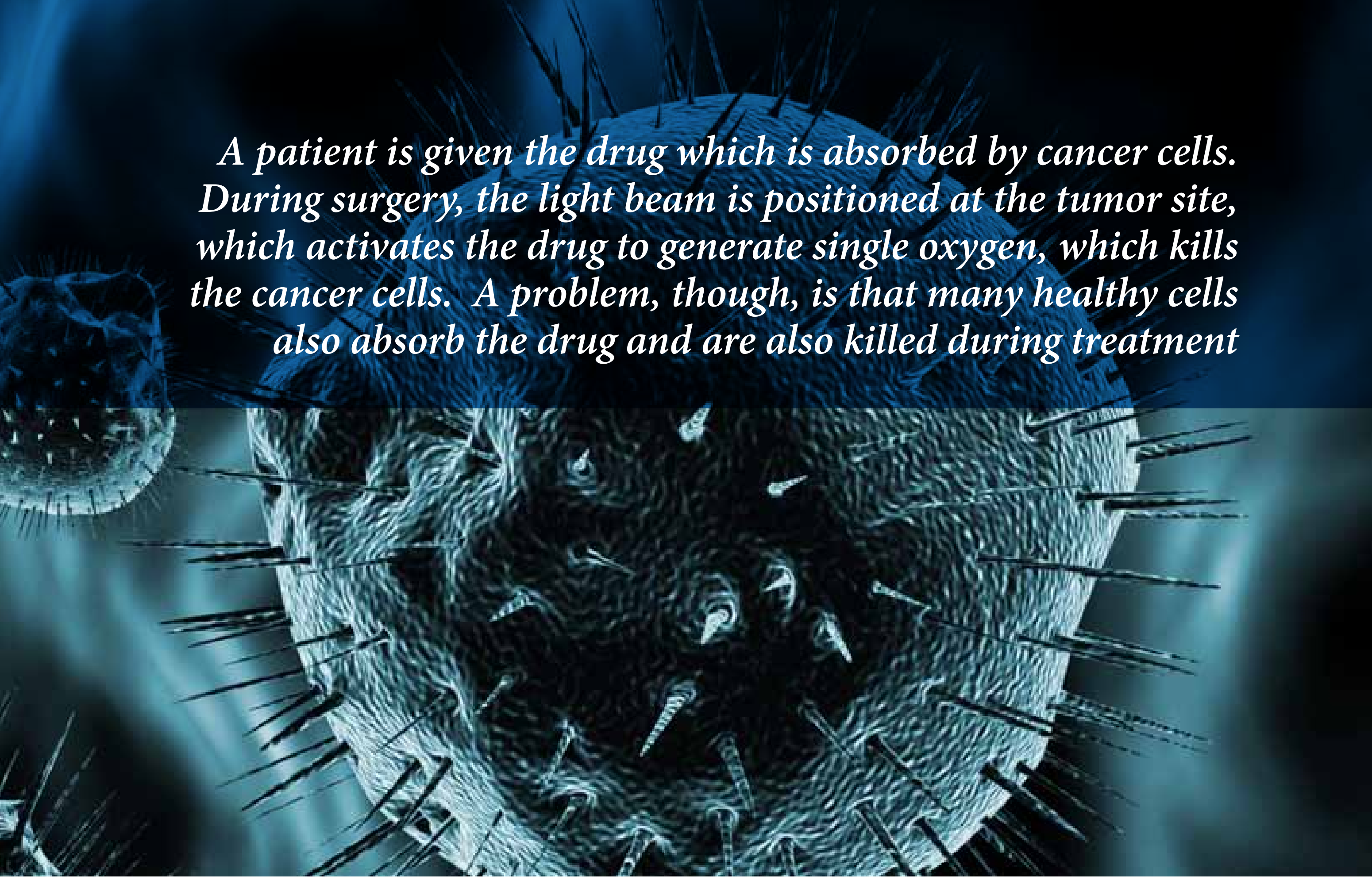
Engineering is normally a discipline associated with building large structures such as towers, bridges and cars. Chemistry is also a discipline associated with building structures, but really tiny ones, at dimensions even smaller than the realm of nanotechnology. Hence, the chemist who builds molecules can be considered a molecular engineer.

Organic chemistry is the central discipline of making molecules. Molecules are designed and synthesised to have useful functions. As molecular engineers, chemists not only perform chemical transformations-reacting chemicals together to make other chemicals-they spend considerable time planning, designing, studying and testing them too.

An exciting area of frontier research combines ideas from mathematics and computer science with chemistry to engineer intelligent molecules capable of performing calculations and information processing for medical applications. This involves making molecules with built-in logic operations according to Boolean algebraic functions (e.g. YES, NOT, OR, AND etc.). Just as individuals use these commands searching the internet for information, molecules can be designed to retrieve chemical information from a solution in a test tube.

A logic gate is an elementary unit normally associated with digital electronic circuits. Computers based on electric circuits count using binary, the universally adopted number system of 0s and 1s. A YES logic gate has two input states, 0 or 1, and two output states, 0 or 1, just like a working light bulb. When the switch is 'off' (input 0), the light bulb is 'off' (output 0). But when the switch is turned 'on' (input 1), the light bulb turns 'on' (input 1). NOT logic is the opposite of YES logic: an input of 0 returns an output of 1, while an input of 1 returns an output of 0.

AND and OR are examples of two-input logic gates, which have four possible output states. The four possible inputs states for both gates are 0,0; 0,1; 1,0; 1,1. OR logic is not selective as just one input is required to get an output-only the inputs 0,0 result in a 0 output. The other situation 0,1 and 1,0 and 1,1 all result in a 1 output. Choosing between which of two shirts to wear in the morning is a practical example of OR logic. As long as you go to work wearing at least one shirt (although you could wear two shirts, one on top of the other) OR logic is satisfied. AND logic is selective with an output of 1 only when two inputs conditions are satisfied with an input of 1. Love is a classic example of AND logic – it takes two to tango.

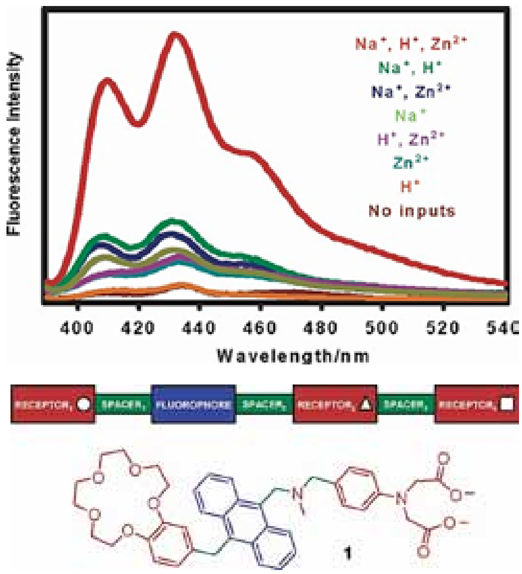


A patient is given the drug which is absorbed by cancer cells. During surgery, the light beam is positioned at the tumor site, which activates the drug to generate single oxygen, which kills the cancer cells. A problem, though, is that many healthy cells also absorb the drug and are also killed during treatment

Molecules able to perform these logic functions, and many others, have been reported in the scientific literature. Even more fascinating, though, is that even more complex molecules integrating many of these elementary logic functions have been demonstrated that can add and subtract numbers, play tit-tat-toe against a human opponent and operate as a security keypad lock like that on an ATM machine.

One example of an intelligent molecule is shown in Figure 1. This is an example of a 'lab-on-a-molecule', a tiny molecular device that is capable of detecting sets of at least three chemical species simultaneously. Upon irradiation with light, the intelligent molecule communicates the presence of sodium (Na^+), protons (H^+) and zinc (Zn^{2+}) ions in water by signaling a fluorescence signal. In the absence of one, or two or all three chemical species, the fluorescence light signal is low. However, when all three chemical species are present in solution the molecule gives off a bright light.

Figure 1
Fluorescence spectra in water or the eight experimental conditions. Only when all three analytes (sodium, zinc and protons) are present at high levels is a high fluorescence light signal observed (spectrum in red).



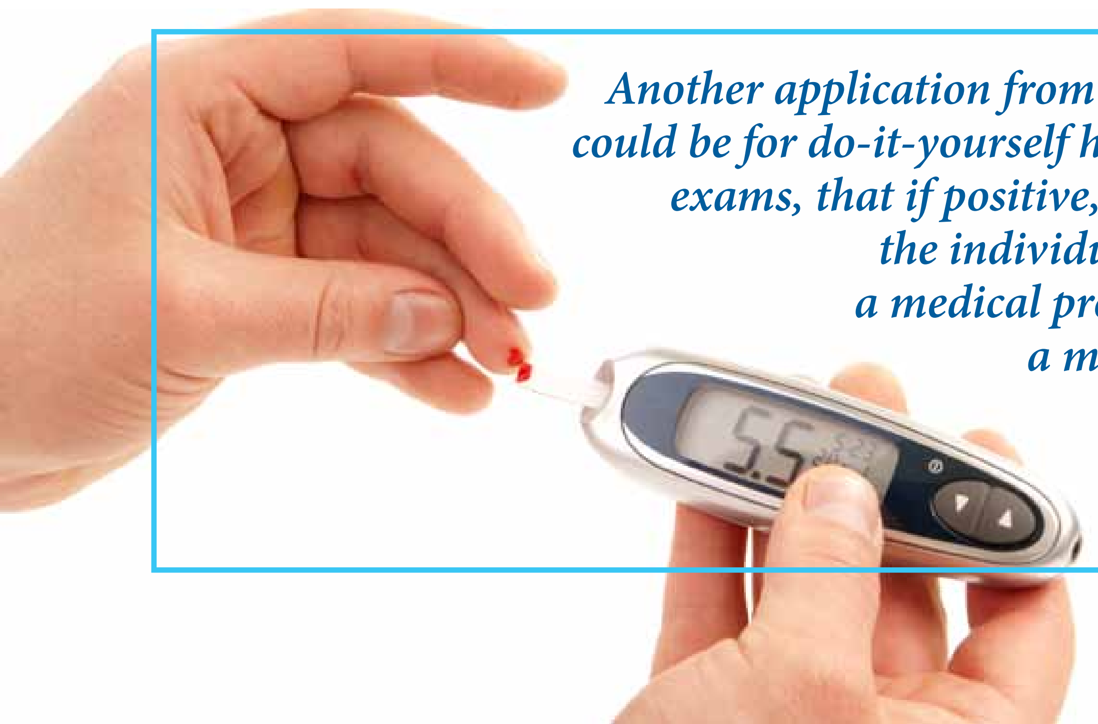
Medical applications

The development of a molecule specifically for renal dysfunction (kidney failure) is a realistic goal for medical diagnostics use as the condition is indicated by high levels of potassium, sodium and urea in the blood. Another application from this research could be for do-it-yourself home medical examinations, somewhat like a pregnancy test, that if positive would allow the individual to consult a medical professional for a more thorough examination.

Another illustration of the potential application of this type of research is in the use of photodynamic therapy (PDT). PDT is a promising treatment for cancer. The treatment requires a light source, a photo-sensitive drug and oxygen. A patient is given the drug which is absorbed by cancer cells. During surgery, the light beam is positioned at the tumor site, which activates the drug to generate single oxygen, which kills the cancer cells. A problem, though, is that many healthy cells also absorb the drug and are also killed during treatment. A research group at Bilkent University in Turkey has figured out a way around this problem using an intelligent molecule. The insides of some cancer cells are known to have higher levels of H^+ and Na^+ ion levels than those of normal cells. The Bilkent group demonstrated a photo-sensitive drug prototype that only worked after detecting high levels of both H^+ and Na^+ ions, according to an AND logic algorithm, so only cancer cells would be killed and not healthy cells. This concept is clearly an improvement over contemporary cancer treatments and could substantial improve the recovery time of patients after PDT treatment.

Carl James Mallia, a graduate student under the supervision of Dr David C. Magri at the University of Malta, is currently working on new 'lab-on-a-molecule' prototypes. Using many standard analytical techniques from nuclear magnetic resonance (NMR) and infra-red (IR) spectroscopy and mass spectrometry (MS), synthesized molecules are accurately characterized to confirm their identity and purity. Then the logic capabilities of the molecules are tested using ultraviolet-visible absorbance and fluorescence spectroscopy.

Molecules with built-in logic functions could have great potential applications for information processing and intelligent medical diagnostics. The use of one test, rather than many separate tests, to detect the presence of many analytes for a disease condition could, therefore, potentially improve the efficiency of v screening and treatment for various medical conditions. In the future, 'lab-on-a-molecule' technology could assist doctors, by not only measuring the analyte amounts, but also by making an intelligent decision on behalf (or in consultation) with the doctor. With the continual rising cost of health care for governments, the creation of intelligent molecules for the simultaneous detection of many analytes corresponding to specific diseases may assist doctors diagnose patients, reduce the cost of clinical testing, reduce waiting time for results and even speed up recovery time for patients. ●



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