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General Certificate of Secondary Education  
Higher Tier  
June 2014

## Mathematics (Linear)

4365/1H

### Paper 1

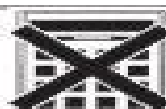
Monday 9 June 2014 9.00 am to 10.30 am

**H**

For this paper you must have:

- mathematical instruments.

You must **not** use a calculator



#### Time allowed

- 1 hour 30 minutes

#### Instructions

- Use black ink or black ball-point pen. Draw diagrams in pencil.
- Fill in the boxes at the top of this page.
- Answer **all** questions.
- You must answer the questions in the spaces provided. Do not write outside the box around each page or on blank pages.
- Do all rough work in this book.

#### Information

- The marks for questions are shown in brackets.
- The maximum mark for this paper is 70.
- The quality of your written communication is specifically assessed in Questions 2, 15 and 16. These questions are indicated with an asterisk (\*).
- You may ask for more answer paper, tracing paper and graph paper. These must be tagged securely to this answer book.

#### Advice

- In all calculations, show clearly how you work out your answer.

For Examiner's Use	
Examiner's Initials	
Pages	Mark
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**4365/1H**

4365 1h June 2014

**United States. Congress**



## 4365 1h June 2014:

Bacterial Exotoxins: How Bacteria Fight the Immune System Inka Sastalla, Denise M. Monack, Katharina F. Kubatzky, 2016-10-07 Bacterial pathogenicity factors are functionally diverse. They may facilitate the adhesion and colonization of bacteria, influence the host immune response, assist spreading of the bacterium by e.g. evading recognition by immune cells or allow bacteria to dwell within protected niches inside the eukaryotic cell. Exotoxins can be single polypeptides or heteromeric protein complexes that act on different parts of the cells. At the cell surface they may insert into the membrane to cause damage, bind to receptors to initiate their uptake or facilitate the interaction with other cell types. For example, bacterial superantigens specifically bind to major histocompatibility complex MHC II molecules on the surface of antigen presenting cells and the T cell receptor while cytolysins cause pore formation. For intracellular activity, exotoxins need to be translocated across the eukaryotic membrane. Gram negative bacteria can directly inject effector proteins in a receptor independent manner by use of specialized needle apparatus such as bacterial type II, III or type IV secretion systems. Other methods of translocation include the phagocytic uptake of bacteria followed by toxin secretion or receptor mediated endocytosis which allows the targeting of distinct cell types. Receptor based uptake is initiated by the binding of heteromeric toxin complexes to the cell surface and completed by the translocation of the effector proteins across the endosomal membrane. In the cytosol, toxins interact with specific eukaryotic target proteins to cause post translational modifications that often result in the manipulation of cellular signalling cascades and inflammatory responses. It has become evident that the actions of some bacterial toxins may exceed their originally assumed cytotoxic function. For example, pore forming toxins do not only cause cytolysis but may also induce autophagy, pyroptosis or activation of the MAPK pathways resulting in adjustment of the host immune response to infection and modification of inflammatory responses both locally and systemically. Other recently elucidated examples of the immunomodulatory function of cell death inducing exotoxins include TcdB of *Clostridium difficile* which activates the inflammasome through modification of cellular Rho GTPases or the Staphylococcus toxin which activates mast cells. The goal of this research topic was to gather current knowledge on the interaction of bacterial exotoxins and effector proteins with the host immune system. The following 16 research and review articles in this special issue describe mechanisms of immune modification and evasion and provide an overview over the complexity of bacterial toxin interaction with different cells of the immune system. The Congressional Globe United States. Congress, 1868 **Survey of Current Business**, 1969 Quasars at All Cosmic Epochs Paola Marziani, Mauro D'Onofrio, Ascensión del Olmo, Deborah Dultzin, 2018-10-05 The last 50 years have seen a tremendous progress in the research on quasars. From a time when quasars were unforeseen oddities, we have come to a view that considers quasars as active galactic nuclei with nuclear activity, a coming of age experienced by most or all galaxies in their evolution. We have passed from a few tens of known quasars of the early 1970s to the 500 000 listed in the catalogue of the Data Release 14 of

the Sloan Digital Sky Survey Not surprisingly accretion processes on the central black holes in the nuclei of galaxies the key concept in our understanding of quasars and active nuclei in general have gained an outstanding status in present day astrophysics Accretion produces a rich spectrum of phenomena in all bands of the electromagnetic spectrum The power output of highly accreting quasars has impressive effects on their host galaxies All the improvement in telescope light gathering and in computing power notwithstanding we still miss a clear connection between observational properties and theory for quasars as provided for example by the H R diagram for stars We do not yet have a complete self consistent view of nuclear activity with predictive power as we do for main sequence stellar sources At the same time quasars offer many windows open onto the unknown On small scales quasar properties depend on phenomena very close to the black hole event horizon On large scales quasars may effect evolution of host galaxies and their circum galactic environments Quasars potential to map the matter density of the Universe and help reconstruct the Universe s spacetime geometry is still largely unexploited The times are ripe for a critical assessment of our present knowledge of quasars as accreting black holes and of their evolution across the cosmic time The foremost aim of this research topic is to review and contextualize the main observational scenarios following an empirical approach to present and discuss the accretion scenario and then to analyze how a closer connection between theory and observation can be achieved identifying those aspects of our understanding that are still on a shaky terrain and are therefore uncertain knowledge This research topic covers topics ranging from the nearest environment of the black hole to the environment of the host galaxies of active nuclei and to the quasars as markers of the large scale structure and of the geometry of spacetime of the Universe The spatial domains encompass the accretion disk the emission and absorption regions circum nuclear starbursts the host galaxy and its interaction with other galaxies Systematic attention is devoted to some key problems that remain outstanding and are clearly not yet solved the existence of two quasar classes radio quiet and radio loud and in general the systematic contextualization of quasar properties the properties of the central black hole the dynamics of the accretion flow in the inner parsecs and the origin of the accretion matter the quasars small and large scale environment the feedback processes produced by the black hole into the host galaxy quasar evolutionary patterns from seed black holes to the present day Universe and the use of quasars as cosmological standard candles The timing is appropriate as we are now witnessing a growing body of results from major surveys in the optical UV X near and far IR and radio spectral domains Radio instrumentation has been upgraded to linear detector a change that resembles the introduction of CCDs for optical astronomy making it possible to study radio quiet quasars at radio frequencies Herschel and ALMA are especially suited to study the circum nuclear star formation processes The new generation of 3D magnetohydrodynamical models offers the prospective of a full physical modeling of the whole quasar emitting regions At the same time on the forefront of optical astronomy applications of adaptive optics to long slit spectroscopy is yielding unprecedented results on high redshift quasars Other measurement techniques like 2D and photometric reverberation

mapping are also yielding an unprecedented amount of data thanks to dedicated experiments and instruments Thanks to the instrumental advances ever growing computing power as well as the coming of age of statistical and analysis techniques the smallest spatial scales are being probed at unprecedented resolution for wide samples of quasars On large scales feedback processes are going out of the realm of single object studies and are entering into the domain of issues involving efficiency and prevalence over a broad range of cosmic epochs The Research Topic Quasars at all Cosmic Epochs collects a large fraction of the contributions presented at a meeting held in Padova sponsored jointly by the National Institute for Astrophysics the Padova Astronomical Observatory the Department of Physics and Astronomy of the University of Padova and the Instituto de Astrofísica de Andalucía IAA of the Consejo Superior de Investigaciones Científicas CSIC The meeting has been part of the events meant to celebrate the 250th anniversary of the foundation of the Padova Observatory

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