Development of the Next Generation of On-line Radiochromatography Detectors

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Abstract

Since the 1980s, on-line radiochromatography (RC) measurements have formed an integral part of metabolite profiling studies and are nowadays coupled with advanced HPLC, UHPLC and MS analysis techniques. Currently, the commercially available on-line detectors are being pushed to their operational limits as demands for better sensitivity and higher resolution are ever-increasing, along with the added pressure from desirable shorter run-times. Part of this demand is being fuelled by the necessity to work with much lower levels of β-radioactivity and so a significant improvement in the signal to noise ratio will be of paramount importance in the near future. In this work, we describe and present some experimental results of an on-going research collaboration that aims to identify key areas for on-line radio-detector instrument development and improvement through appealing to both the fundamental physics of the measurement process and the latest technological advances. The collaboration is between the University of Sheffield’s Department of Physics and Astronomy and LabLogic Systems Ltd. and is funded by the UK Government’s Knowledge Transfer Partnership (KTP) initiative. The culmination of the work will see future generations of LabLogic’s β-RAM® on-line radiochromatography detector leading the way in terms of resolution and reproducibility, as well as providing a detailed insight into the fundamental scientific processes that are in play.

Solutions

Understanding the Detection Process

Efficient energy transfer

Primary Scintillation Interaction

Secondary Scintillation Interaction

Efficient energy transfer

Absorption and emission

Matching with detector

Pulse area analysis may be used to good effect in order to determine which events are due to the decay of the β-isotope and which arise from random coincidence events.

Pulse area → Charge → β Energy

H Pulses

C Pulses

This type of real-time analysis enables different isotopes to be identified in complex samples and may bring benefits to other applications such as environmental monitoring.

Eliminating Detector Cross-talk

The main source of random coincidences is from ‘cross-talk’ between the PMT detectors. Cross-talk arises from the emission of thermal electrons from the photocathode of the PMTs and as a result of the geometry of the measurement. Current practice attempts to eliminate these via pulse height comparison, reduced operating HV and discriminator window settings.

On-Line LSC and its Limitations

LabLogic β-RAM® Model 5

TDCR = T/D: Triple Events/ Double Events

System Threshold

Discriminators

Coincidence window (~10s ns)

Dark counts = 2N1N2τ

The primary objective of this work is to improve the limit of detection by an order of magnitude to enable 10 dpm to be resolved in a single chromatography peak. New methods and technologies are being sought to maximise the detected signal and minimise the sources of noise.

The main limitations affecting on-line LSC/RC measurements are:

- Unwanted sources of background
- Aging detector and signal processing technology
- Compatibility with advancing HPLC/UHPLC systems
- Sub-optimal chromatographic separation
- Due to the dynamic nature of the measurement process

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References


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